7TH HONG KONG INTERNATIONAL CANCER CONGRESS

5TH RESEARCH POSTGRADUATE SYMPOSIUM

FACULTY OF MEDICINE, THE UNIVERSITY OF HONG KONG

7 - 9
December 2000
Hong Kong

Faculty of Medicine

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7TH HONG KONG INTERNATIONAL CANCER CONGRESS

under auspices of

The Hong Kong Anti-Cancer Society

The Hong Kong Cancer Fund

Society for the Promotion of Hospice Care

International Union Against Cancer

The Chinese Anti-Cancer Association

Hospital Authority

and organized by

The University of Hong Kong

Queen Mary Hospital

WELCOME MESSAGE BY CHAIRMEN

SCIENTIFIC AND ORGANIZING COMMITTEES

Dear Colleagues,

We are delighted to welcome you to the 7th Hong Kong International Cancer Congress and the 5th Research Postgraduate Symposium.

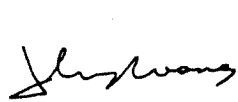
The Research Postgraduate Symposium (RPS) is organized annually by the Faculty of Medicine of The University of Hong Kong since 1996. Its aims are to facilitate academic interaction and intellectual advancement among research postgraduate (RPG) students and teaching staff. Sharing the same vision, the HKICC and RPS have organized the joint sessions on Thursday, 7 December 2000. In addition to cancer-related research, RPG students involve in other biomedical disciplines will also have the opportunity to present their work.

A scientific program of very high standard has been developed and international experts in different frontiers are invited. We have also devoted further efforts at the psychosocial aspects of care of the cancer patients. With the assistance of the voluntary and support groups, a strong 2-day program in these areas has been mounted.

For our many overseas participants, Hong Kong has the unique attraction of an Asian city combined with Western influences to allow everyone to visit with ease. English is widely spoken and used in most signages. You will find no difficulty in getting around for sightseeing, shopping, dining or any other activities.

We once again welcome all of you and trust that you will find your participation stimulating, educational and enjoyable.

Hextan Ngan
Chairman
Scientific Committee
7th HKICC



John Wong
Chairman
Organizing Committee
7th HKICC

Y.S. Chan
Associate Dean (Research)
Faculty of Medicine
The University of Hong Kong

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Surgery

CONGRESS INFORMATION

CONGRESS VENUE

All Scientific Sessions will take place at the Hong Kong Academy of Medicine Building (HKAMB), 99 Wong Chuck Hang Road, Aberdeen, Hong Kong.

CONGRESS SECRETARIAT

On-site Secretariat

Ground Floor
HKAMB

Tel : 2871 8883
Fax : 2871 8884

Congress Secretariat's Head Office

7th HKICC
Department of Surgery
University of Hong Kong Medical Centre
Queen Mary Hospital
Hong Kong

Tel : 2818 0232 / 2855 4235
Fax : 2818 1186

CERTIFICATE OF ATTENDANCE

A Certificate of Attendance is issued at the time of registration to delegates who are pre-registered.

For on-site registrants, a Certificate of Attendance will be available at the end of the Congress. No certificate will be issued after the Congress.

BADGES

Coloured badges will be used during the Congress. For identification purpose and admission to the session halls, participants are requested to wear their badges, which will be available upon registration.

CONGRESS INFORMATION

LUNCH AND COFFEE BREAK

Complimentary lunch and coffee/tea are served at Ground Floor and First Floor (Foyer), HKAMB on a first-come first-served basis.

OFFICIAL LANGUAGE

The official language of the Congress is English. No simultaneous translation will be provided.

MESSAGES AND MAIL

A board is available for posting messages and mail. The Organizing Committee regrets that deliveries cannot be made.

CME ACCREDITATION

The meeting is accredited by the following Colleges of Hong Kong Academy of Medicine:

- Anaesthesiologists (20 points)
- Community Medicine (10 points)
- Dental Surgeons (9 points)
- Emergency Medicine (6 points)
- Family Physicians (10 points)
- Obstetricians & Gynaecologists (7.5 points)
- Opthalmologists (12 points)
- Orthopaedic Surgeons (5 points)
- Otorhinolaryngologists (12.5 points)
- Paediatricians (12 points)
- Pathologists (17.5 points)
- Physicians (12 points)
- Psychiatrists (18 points)
- Radiologists (12 points)
- Surgeons (18 points)

REGISTRATION

REGISTRATION

Registration counters are located at Ground Floor, HKAMB. For on-site registration, payment may be made in cash or traveller's cheques (HK$ or US$) or Credit Cards.

REGISTRATION SCHEDULE

Registration will begin on Thursday, 7 December 2000 at Ground Floor, HKAMB. The schedule is as follows:

7 December 2000, Thursday	8:30 am - 5:30 pm
8 December 2000, Friday	8:00 am - 5:30 pm
9 December 2000, Saturday	8:00 am - 5:30 pm

REGISTRATION FEE

Full Registration

Overseas Medical Doctor	US$ 550
Overseas Nurse / Allied Health	US$ 300
Overseas Trainee	US$ 300
Overseas Accompanying Person	US$ 200
Local (HK) Medical Doctor	HK$ 2,000
Local (HK) Nurse / Allied Health	HK$ 600
Local (HK) Postgraduate Student	HK$ 600
Local (HK) Accompanying Person	HK$ 500

REGISTRATION

REGISTRATION FEE

Day Registration

Local (HK) Medical Doctor	HK$ 750 per day
Local (HK) Nurse / Allied Health	HK$ 250 per day

ENTITLEMENT

Full registration delegates are entitled to :

- participate in all Scientific Sessions
- visit the Exhibition
- lunch
- coffee and tea during morning and afternoon breaks
- receive a set of official publications
- attend the Opening Ceremony

Day registration delegates are entitled to :

- participate in Scientific Sessions on the day
- visit the Exhibition
- lunch
- coffee and tea during morning and afternoon breaks
- receive Scientific Program

Registered accompanying persons are entitled to :

- attend the Opening Ceremony
- two complimentary local tours

SCIENTIFIC PROGRAM INFORMATION

STATE-OF-THE-ART LECTURES

Ten international experts will give State-of-the-Art Lectures on various topics in environment, cancer treatment, communication skills and palliative care.

SYMPOSIA / DEBATE / INTERACTIVE SESSION

Parallel Symposia are arranged on topics for different specialties. Similar to last year, Debate and Interactive Sessions utilizing the Public Response System will take place to encourage communication between the stage and floor. For the 3 case summaries of the "Interactive Session", please refer to page 52.

FREE PAPER SESSIONS

These Free Paper Sessions are allocated 10 minutes (8 minutes presentation and 2 minutes discussion) for each speaker. Since the program is tight, presenters of papers are earnestly requested to adhere to the allocated time. The names of presenting authors and two co-authors can be found in the Authors' Index at the end of this Program Book.

ABSTRACTS

Abstracts for State-of-the-Art Lectures, Symposia, Workshops and Free Paper Sessions are numbered and arranged consecutively by sessions. All abstracts are printed at the end of this Program Book, where the name of the presenting author and two co-authors are given.

SCIENTIFIC PROGRAM INFORMATION

POSTERS

All presenters are requested to put up their posters at the First Floor (Foyer), HKAMB, before 9:00 am on Friday, 8 December 2000.

All Posters are available for viewing on 8 - 9 December 2000.

MEETING ROOM FACILITIES & SLIDE PREVIEW

Meeting rooms are equipped with facilities of single or double projection for 35 mm slides and a laser pointer.

The slides for each presentation should be received 24 hours before the presentation at the Slide Preview Room.

The opening hours of the Slide Preview Room are as follows:

7 December 2000, Thursday	8:30 am - 5:30 pm	Ground Floor
8 December 2000, Friday	8:00 am - 5:30 pm	Ground Floor
9 December 2000, Saturday	8:00 am - 5:30 pm	Ground Floor

EXHIBITION

The exhibition is at the Ground Floor, HKAMB and is open during the Congress hours. For further information, please see page 69.

Please visit the Exhibits. Coffee and tea will be provided during coffee/tea breaks.

PROGRAM AT A GLANCE

7 DECEMBER 2000, THURSDAY

Time \ Room	FR / JKMR / 702-3 / 803-4 / 903-4
8:30 am	Registration
9:00 am	FP FR 1 — 5th RPS Molecular Medicine FP 702-3 2 — 5th RPS Neuroscience / Musculoskeletal System FP 803-4 3 — 5th RPS Cardiovascular System, Endocrinology & Reproduction FP 903-4 4 — 5th RPS Renal System, Respiratory System, Gastrointestinal System & Blood-Related Studies
12:30 pm	Lunch
1:30 pm	FP FR 5 — YIA - Psychosocial Oncology FP JKMR 6 — YIA - Medical I FP 702-3 7 — Breast & Obstetrics & Gynaecology FP 803-4 8 — NPC & Cancer Genetics
3:00 pm	Coffee Break
3:30 pm	FP FR 9 — FP - Psychosocial Oncology FP JKMR 10 — YIA - Medical II FP 702-3 11 — Liver & Lung FP 803-4 12 — Gastric & Head & Neck
5:00 pm	

SAL - State-of-the-Art Lecture
SYM - Symposium
FP - Free Paper
Debate - Debate
IS - Interactive Session
WK - Workshop

Type of Session: SYM
Topic: Microarrays
LPYLT 32: Room / Session Number

FR - Function Room (2nd Floor)
JKMR - James Kung Meeting Room (2nd Floor)
Room 702&703 (7th Floor)
Room 803&804 (8th Floor)
Room 903&904 (9th Floor)

PROGRAM AT A GLANCE

8 DECEMBER 2000, FRIDAY

Time \ Room	RRSH / LPYLT / JKMR / PYKA		
8:30 am	**Opening Ceremony**		RRSH
9:00 am	HKICC Lecture **Environment & Cancer** W. Au, *U.S.A.*		RRSH 13
10:00 am	**Coffee Break**		
10:30 am	SAL **Environmental Contamination & Cancer** B.D. Goldstein *U.S.A.*		RRSH 14
11:10 am	SAL **Tobacco, Air & Cancer** A.J. Hedley, *H.K.*		RRSH 15
11:50 am	SAL **Advocacy & Policy** C. Loh, *H.K.*		RRSH 16
12:30 pm	**Lunch**		
1:30 pm	SYM LPYLT 17 **Colorectal Cancer & Environment**	SYM JKMR 18 **From Laboratory to Clinical Practice**	SYM PYKA 19 **Psychosocial Clinical Guidelines**
3:00 pm	**Coffee Break**		
3:30 pm	SYM LPYLT 20 **Hormonal Related Cancer**	SYM JKMR 21 **Brain & Skull Base Tumour**	SYM PYKA 22 **Psychosocial Clinical Guidelines**
5:00 pm			

JKMR - James Kung Meeting Room (2nd Floor)
LPYLT - Lim Por Yen Lecture Theatre (Ground Floor)
PYKA - Pao Yue Kong Auditorium (Ground Floor)
RRSH - Run Run Shaw Hall (1st Floor)

PROGRAM AT A GLANCE

9 DECEMBER 2000, SATURDAY

Time \ Room	LPYLT / JKMR / PYKA / 702 / 703 / 803 / 804
8:30 am	SYM LPYLT 23 **Blood Cancer** · SYM JKMR 24 **Cancer Genetics** · SYM PYKA 25 **Community Care**
10:00 am	**Coffee Break**
10:30 am	SAL LPYLT 26 **Microarrays** O. Kallioniemi, *U.S.A.* · SAL PYKA 29 **Consumers as Advocates in Cancer Care** S. Redman, *Australia*
11:10 am	SAL LPYLT 27 **New Development in Cancer Therapy** R.J. Mayer, *U.S.A.* · SAL PYKA 30 **Stress & Cancer** P.W.H. Lee, *H.K.*
11:50 am	SAL LPYLT 28 **Gastric Cancer** M.S. Karpeh, *U.S.A.* · SAL PYKA 31 **Quality of Life** R. Fielding, *H.K.*
12:30 pm	**Lunch**
1:30 pm	SYM LPYLT 32 **Microarrays** · SYM JKMR 33 **Environment / Communication** · Debate PYKA 34 **Colorectal Cancer** · WK 702/703/803/804 35/36/37/38 **Psychosocial Oncology**
3:00 pm	**Coffee Break**
3:30 pm	SYM LPYLT 39 **Paediatric Cancers** · SYM JKMR 40 **Musculoskeletal Malignancies** · IS PYKA 41 **Site Specific Tumours** · WK 702/703/803/804 35/36/37/38 **Psychosocial Oncology**
5:00 pm	

JKMR - James Kung Meeting Room (2nd Floor)
LPYLT - Lim Por Yen Lecture Theatre (Ground Floor)
PYKA - Pao Yue Kong Auditorium (Ground Floor)
Room 702&703 (7th Floor)
Room 803&804 (8th Floor)

PROGRAM AT A GLANCE

PSYCHOSOCIAL ONCOLOGY

Working Together for Better Cancer Care

	Friday, 8 December 2000	Saturday, 9 December 2000
8:30 am	**Opening Ceremony**	SYM PYKA 25
9:00 am	HKICC Lecture 13 **Environment & Cancer** W. Au, *U.S.A.*	**Community Care**
10:00 am	**Coffee Break**	
10:30 am	SAL RRSH 14 **Environmental Contamination & Cancer** B.D. Goldstein, *U.S.A.*	SAL PYKA 29 **Consumers as Advocates in Cancer Care** S. Redman, *Australia*
11:10 am	SAL RRSH 15 **Tobacco, Air & Cancer** A.J. Hedley, *H.K.*	SAL PYKA 30 **Stress & Cancer** P.W.H. Lee, *H.K.*
11:50 am	SAL RRSH 16 **Advocacy & Policy** C. Loh, *H.K.*	SAL PYKA 31 **Quality of Life** R. Fielding, *H.K.*
12:30 pm	**Lunch**	
1:30 pm	SYM PYKA 19 **Psychosocial Clinical Guidelines**	Workshop 702/703/803/804 35/36/37/38 **Psychosocial Oncology**
3:00 pm	**Coffee Break**	
3:30 pm	SYM PYKA 22 **Psychosocial Clinical Guidelines**	Workshop 702/703/803/804 35/36/37/38 **Psychosocial Oncology**
5:00 pm		

PYKA - Pao Yue Kong Auditorium (Ground Floor)
RRSH - Run Run Shaw Hall (1st Floor)
Room 702&703 (7th Floor)
Room 803&704 (8th Floor)

SCIENTIFIC PROGRAM

Room / Time	Session	
Function Room	**1**	**Free Paper Session** **5th Research Postgraduate Symposium - Molecular Medicine** Moderators: S.S.M. Chung, *Hong Kong* P.K.H. Tam, *Hong Kong*
9:00 a.m.	1.1	Insulin-Dependent Inhibition of MTP Gene Transcription is Mediated by MAPK Pathway in HepG2 Cells W.S. Au, M.C. Lin, H.F. Kung, *Hong Kong*
9:10 a.m.	1.2	Different Subgroups of H6N1 Influenza Viruses Present in Southeastern China P.S. Chin, K.F. Shortridge, J.S.M. Peiris, *Hong Kong*
9:20 a.m.	1.3	The Expression and Regulation of Endothelin-1 Gene for Craniofacial and Cardiac Development K.W. Chiu, S.K. Chung, *Hong Kong*
9:30 a.m.	1.4	Investigating the Function of Sox9 in Development Y.H. Geng, K.S.E. Cheah, *Hong Kong*
9:40 a.m.	1.5	Aldose Reductase-Deficient Mice are Protected from Motor Nerve Conduction Deficit Associated with Diabetes E.C.M. Ho, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
9:50 a.m.	1.6	A Study of the Molecular Mechanism and Pathogenesis of Schmid Metaphyseal Chondrodysplasia in Transgenic Mice S.P. Ho, K.S.E. Cheah, D. Chan, *Hong Kong*
10:00 a.m.	1.7	The Molecular Basis of G6PD Variants, Plymouth and Mahidol Y.X. Huang, V.M.S. Lam, D.M.Y. Au, *Hong Kong*
10:10 a.m.	1.8	Molecular Epidemiology of Melioidosis in an Oceanarium in Hong Kong R.E. Kinoshita, D.A. Higgins, P.L. Ho, *Hong Kong*
10:30 a.m.	1.9	The Role of Endothelin-1 on the Homeostasis of Vascular Tone in the ET-1 Transgenic Mice H.W. Koon, S.K. Chung, *Hong Kong*
10:40 a.m.	1.10	Association of Polymorphisms in the NRAMP1 Gene and Host Susceptibility to Tuberculosis Y. Lam, S.W.K. Im, W.C. Yam, *Hong Kong*
10:50 a.m.	1.11	Generation and Characterization of Sodium/myo-inositol Cotransporter Knockout Mice M.K. Lee, S.K. Chung, S.S.M. Chung, *Hong Kong*
11:00 a.m.	1.12	*AFMP1* Encodes an Antigenic Cell Wall Galactomannoprotein in *Aspergillus Fumigatus* S.P. Leung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
11:10 a.m.	1.13	Regulation of Gene Expression in Hypertrophic Chondrocytes V.Y.L. Leung, K.S.E. Cheah, *Hong Kong*
11:20 a.m.	1.14	Relationships between Epidermal Growth Factor Precursor and IGFs *In Vivo* K.K.L. Mak, S.Y. Chan, *Hong Kong*
11:30 a.m.	1.15	The Clinical Association of Mannose Binding Lectin with Hepatitis B Infection Y.F. To, Y.L. Lau, C.L. Lai, *Hong Kong*
11:40 a.m.	1.16	Feedback Inhibition of Redox-Responsive Transcription Factors Yap1p and Skn7p in *Sacchromyces Cerevisiae* by Peroxiredoxins Tsa1p and Tsa2p C.M. Wong, D.Y. Jin, H.F. Kung, *Hong Kong*
11:50 a.m.	1.17	3' Region of the *Xenopus* GATA-1B Transcript is Responsible for the Antineurogenic Effect of GATA-1B G.W. Wong, H.F. Kung, M.C. Lin, *Hong Kong*
12:00 noon	1.18	DNA Engineering Utilizing Thymidylate Synthase A (THY A) Selection System in *Escherichia Coli* Q.N.Y. Wong, H.F. Kung, J.D. Huang, *Hong Kong*
12:10 p.m.	1.19	PDZ Domain Containing Factors and Regulation of Insulin Gene Transcription M.L. Yeung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
12:20 p.m.	1.20	Adeno-Associated Virus (AAV) Mediated CTLA4Ig Transfer into Rat Orthotopic Liver Transplant Z.F. Yang, J. Luk, S.T. Fan, *Hong Kong*
Room 702-3	**2**	**Free Paper Session** **5th Research Postgraduate Symposium - Neuroscience / Musculoskeletal System** Moderators: P.K.Y. Chiu, *Hong Kong* J. Hugon, *Hong Kong*
9:00 a.m.	2.1	Caspase Inhibitors Prevent Spinal Motoneurons from Death Following Root Avulsion in Neonatal Rats Y.M. Chan, W. Wu, H.K. Yip, *Hong Kong*
9:10 a.m.	2.2	Neuroprotective Effects of Extracts from American Gingseng, Ginkgo Biloba and St. John's Wort on Striatal Dopaminergic Neurons against 1-Methyl-4-Phenyl- 1,2,4,6-Tetrahydropyrdine (MPTP)-Induced Toxicity V.W.Y. Chan, H.K. Yip, K.F. So, *Hong Kong*
9:20 a.m.	2.3	Neuropeptide Y and Related Compounds can Modulate Nitric Oxide Production during Focal Cerebral Ischemia in the Rat: An Electron Paramagnetic Resonance Study S.H. Chen, Z. Pei, R.T.F. Cheung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
9:30 a.m.	2.4	Mixture of American Ginseng, *Ginkgo Biloba* and St. John's Wort Extracts Enhances the Survival of Axotomized Retinal Ganglion Cells Z.H.Y. Cheung, K.F. So, H.K. Yip, *Hong Kong*
9:40 a.m.	2.5	Maximal Isometric Muscle Strength of the Cervical Spine in Healthy Volunteers T.T.W. Chiu, T.H. Lam, A.J. Hedley, *Hong Kong*
9:50 a.m.	2.6	Design of Implant Plate for Distal Radius Fracture H.P.H. Ho, *Hong Kong*
10:00 a.m.	2.7	Neurochemical and Behavioral Studies on Transgenic Mice Carrying Human Presenilin-1 Gene X.G. Huang, *Hong Kong*
10:10 a.m.	2.8	Ciliary Neurotrophic Factor Prevents the Death of Retinal Ganglion Cells in a Rat Glaucoma Model J.Z. Ji, *Hong Kong*
10:30 a.m.	2.9	Expression of Chondroitin Sulfate during Embryonic Hindbrain Development C.F. Kwok, D.K.Y. Shum, M.H. Sham, *Hong Kong*
10:40 a.m.	2.10	Trinucleotide CAG Repeats in X-Linked Spinal and Bulbar Muscular Atrophy: An *In Vitro* Model to Examine the Role of Neuromuscular Interdependency H.Y. Law, P.T. Cheung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
10:50 a.m.	2.11	Bilirubin Induces Apoptosis in Glial Cells through Caspase Activation X.H. Liang, C.Y. Yeung, P.T. Cheung, *Hong Kong*
11:00 a.m.	2.12	Melatonin Abolishes the Increase in Nitric Oxide Production during Cerebral Ischemia in the Rat Z. Pei, S.H. Chen, R.T.F. Cheung, *Hong Kong*
11:10 a.m.	2.13	The Effect of Electrical Vestibular Stimulation of the Labyrinth on Baroreflex Response in Anesthetized Rats B. Sun, Z.L. Guan, Y.S. Chan, *Hong Kong*
11:20 a.m.	2.14	Studying the Role of Mouse *Sox10* in Schwann Cell Development by Conditional Gene Targeting W.H. Tsang, M.H. Sham, *Hong Kong*
11:30 a.m.	2.15	Moved to P22
11:40 a.m.	2.16	Intraoperative Correction Force Measurements in Adolescent Idiopathic Scoliosis K.W.K. Yeung, K.M.C. Cheung, W.W. Lu, *Hong Kong*
11:50 a.m.	2.17	Effect of Eccentric Contractions on Force and Intracellular pH Regulation in Rat Soleus Muscles E.W. Yeung, H.J. Ballard, J.P. Bourreau, *Hong Kong*
12:00 noon	2.18	Spontaneous Activity of Primary Vestibular Afferent Neurons during Postnatal Development of the Rat Y.K. Zhang, Y.S. Chan, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 803-4	**3**	**Free Paper Session** **5th Research Postgraduate Symposium - Cardiovascular System, Endocrinology & Reproduction** Moderators: A.W.C. Kung, *Hong Kong* H.Y.S. Ngan, *Hong Kong*
9:00 a.m.	3.1	Sequence Comparison of Human and Mouse Oviduct-Specific Glycoprotein Promoters A. Agarwal, K.F. Lee, *Hong Kong*
9:10 a.m.	3.2	Effect of Magnesium Tanshinoate B on Protein Kinases K.W. Au Yeung, Y.L. Siow, D.Y. Zhu, *Hong Kong*
9:20 a.m.	3.3	Ginkgolides and Bilobalide Selectively Inhibit Inducible Nitric Oxide Synthase F. Cheung, Y.L. Siow, K. O, *Hong Kong*
9:30 a.m.	3.4	Pretreatment with U50488H Restores the Calcium Content in the Sarcoplasmic Reticulum in the Rat Ventricular Myocyte Following Metabolic Inhibition J.C.S. Ho, T.M. Wong, S. Wu, *Hong Kong*
9:40 a.m.	3.5	Effects of Estrogen on Human Catechol-O-Methyltransferase H. Jiang, Z.H. Feng, S.L. Ho, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
9:50 a.m.	3.6	Acute Inhibition of Contraction in Porcine Coronary Arteries by 17β-Estradiol Involves Both the Cyclic AMP and the Cyclic GMP Pathways W. Keung, R.Y.K. Man, *Hong Kong*
10:00 a.m.	3.7	Galactosemia and Rat Granulosa Cell Apoptosis K.W. Lai, L. Cheng, W.S. O, *Hong Kong*
10:10 a.m.	3.8	Blood Pressure is Related to Obesity in Women T.C. Lam, B.M.Y. Cheung, *Hong Kong*
10:30 a.m.	3.9	Effects of Genistein on Porcine Coronary Arterial Contraction *In Vitro* M.Y.K. Lee, R.Y.K. Man, *Hong Kong*
10:40 a.m.	3.10	Adrenomedullin is Involved in the Depressed Ca^{2+} Transients in Myocytes from LPS-Treated Rats Q.X. Shan, J.M. Hyvelin, J.P. Bourreau, *Hong Kong*
10:50 a.m.	3.11	Expression of Monocyte Chemoattractant Protein-1 in Homocysteine-Treated Human Endothelial Cells L. Sung, K. O, Y.L. Siow, *Hong Kong*
11:00 a.m.	3.12	Effect of *Salviae Miltiorrhizae* Extract and the Magnesium Tanshinone B Enriched Fraction on the Vascular Contraction of Porcine Coronary Artery A.K.S. Wan, R.Y.K. Man, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
11:10 a.m.	3.13	An Application of the Stages of Change Model to Increase Calcium Intake of Premenopausal Women F.Y.Y. Wong, *Hong Kong*
11:20 a.m.	3.14	The Hepatocyte Nuclear Factor-1∝ Gene Plays a Significant Role in Southern Chinese Subjects with Early-Onset Type 2 Diabetes J.Y. Xu, V.N.Y. Chan, K.S.L. Lam, *Hong Kong*
Room 903-4	**4**	**Free Paper Session** **5th Research Postgraduate Symposium - Renal System, Respiratory System, Gastrointestinal System & Blood-Related Studies** Moderators: C.H. Cho, *Hong Kong* R.H.S. Liang, *Hong Kong*
9:00 a.m.	4.1	A Rapid Assay to Detect Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency S.H.W. Chan, V.M.S. Lam, D.A. Higgins, *Hong Kong*
9:10 a.m.	4.2	Heparan Sulphate Protection of Neutrophil Elastase Activity in Bronchial Secretions of Patients with Bronchiectasis C.H. Chan, D.K.Y. Shum, M.S.M. Ip, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
9:20 a.m.	4.3	A Study of Health Promotion Behaviors and Lifestyle Factors: Applying the Transtheoretical Model on Healthy Living Survey 1999 B.H.Y. Chan, T.H. Lam, A.J. Hedley, *Hong Kong*
9:30 a.m.	4.4	Effect of Peritoneal Dialysis Fluid (PDF) and Heparin on Proteoglycan Synthesis in Human Peritoneal Mesothelial Cells (HPMC) X.R. Chen, S. Yung, T.M. Chan, *Hong Kong*
9:40 a.m.	4.5	The Production of a Novel Immunosuppressive Fusion Protein $CTLA_4$-Ig and a Study of Its Immunosuppressive Function W.H. Guo, L. Tian, P.K.H. Tam, *Hong Kong*
9:50 a.m.	4.6	AIDBase: G6PD, an Integrated Database for Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency C.J. Kwok, A.C.R. Martin, V.M.S. Lam, *Hong Kong*
10:00 a.m.	4.7	Decreased Yield, Phenotypic Expression and Function of Immature Monocyte-Derived Dendritic Cells in Cord Blood E.M. Liu, Y.L. Lau, H. Law, *Hong Kong*
10:10 a.m.	4.8	Oxidative Effects of Ethanol on Acetic Acid-Induced Gastric Ulcer Formation E.S.L. Liu, C.H. Cho, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
10:30 a.m.	4.9	Involvement of Macrophage Migration Inhibitory Factor in Graft-Versus-Host Disease W.S. Lo, H.Y. Lan, R.H.S. Liang, *Hong Kong*
10:40 a.m.	4.10	Estimation for Effects of Air Pollution on Daily Mortality Using Poisson Regression with an Offset S. Ma, C.M. Wong, A.J. Hedley, *Hong Kong*
10:50 a.m.	4.11	Validation of a Disease-Specific Health-Related Quality of Life Questionnaire for Sleep Apnea: Chinese Version of Calgary Sleep Apnea Quality of Life Index (SAQLI) W.Y.W. Mok, M.S.M. Ip, I.J. Lauder, *Hong Kong*
11:00 a.m.	4.12	IGF-I Gene Expressions are Altered in Nutritionally Perturbed Rat Pups H.B. Ng, L.C. Balonan, H.P. Sheng, *Hong Kong*
11:10 a.m.	4.13	The Effects of Pseudomonas Aeruginosa 1-Hydroxyphenazine on iNOS and eNOS Expression in Human Nasal Epithelium Culture Model I.H.Y. Shum, K.W.T. Tsang, W.K. Lam, *Hong Kong*
11:20 a.m.	4.14	Glial Cell Line-Derived Neurotrophic Factor and Neurturin Share Signaling Pathways of Ret W.L. Wong, *Hong Kong*
11:30 a.m.	4.15	Moved to 1.20

SCIENTIFIC PROGRAM

Room / Time	Session	
Function Room	**5**	**Free Paper Session** **Young Investigators' Awards** **Psychosocial Oncology** Adjudicator: P. Simpson, *Hong Kong*
1:30 p.m.	5.1	Quality of Life after Gynecologic Cancer Treatment Y.M. Chan, B.Y.G. Li, H.Y.S. Ngan, *Hong Kong*
1:42 p.m.	5.2	Patients' Support Network: Implications and Challenges for a Self Help Organization S.K. Choi, *Hong Kong*
1:54 p.m.	5.3	The Nurses' Knowledge, Attitude and Behavior Towards Traditional Chinese Medicine in Hong Kong: An Initial Exploration C. Kwan, O.N. Li, L. Sinclair, *Hong Kong*
2:06 p.m.	5.4	Unheard Little Voices: The Needs of Children When Their Parents are Seriously Ill B.W.S. Koo, A.Y.M. Chow, A.F. Tin, *Hong Kong*
2:18 p.m.	5.5	The Meaning of Social Support in Coping with Breast Cancer W.W.T. Lam, R. Fielding, *Hong Kong*
2:30 p.m.	5.6	Sharing Tears and Gaining Support: Unfolding of Bereavement Groups A.F. Tin, A.Y.M. Chow, E.W.K. Koo, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
2:42 p.m.	5.7	The Experiences of Caring and Support of Caregivers for Terminally Ill Patients E. Yeung, V. Chan, E. Mok, *Hong Kong*
James Kung Meeting Room	**6**	**Free Paper Session** **Young Investigators' Awards - Medical I** Adjudicators: R.J. Mayer, *U.S.A.* Y.L. Kwong, *Hong Kong*
1:30 p.m.	6.1	Identification and Cloning of Downstream Target Genes of LMP-1 in Nasopharyngeal Carcinoma Cells K.F. Lo, Y. Liu, S.W. Tsao, *Hong Kong*
1:40 p.m.	6.2	Effect of Air Supply in Phonation: A Comparison between Esophageal and Tracheoesophageal Speech in Cantonese Laryngeal Cancer Patients M.W. Ng, I.C.L. Kwok, *U.S.A. & Hong Kong*
1:50 p.m.	6.3	Hypermethylated Promoter of p16 Gene as a Promising Blood Marker in Chinese Patients with Invasive Ductal Breast Cancer X.C. Hu, L.W.C. Chow, *Hong Kong*
2:00 p.m.	6.4	E-Cadherin Expression is Silenced by DNA Methylation in Cervical Cancer Cell Lines and Tumors C.L. Chen, S.S. Liu, H.Y.S. Ngan, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
2:10 p.m.	6.5	Profiling Differential Gene Expressions in Radiosensitive and Radioresistant Cervical Cancer Cell Lines S.S. Liu, A.N.Y. Cheung, H.Y.S. Ngan, *Hong Kong*
2:20 p.m.	6.6	Recurrent Chromosome Changes in 31 Primary Ovarian Carcinomas Detected by Comparative Genomic Hybridization T.C.M. Tang, J.S.T. Sham, Y. Fang, *Hong Kong*
2:30 p.m.	6.7	Screening Ovarian Cancer Related Genes by Differential Displayed PCR Method W. Yue, L.Y. Sun, C.H. Li, *China*
2:40 p.m.	6.8	Upregulation of ID-1, TRPM-2 and MMP-7 during Sex Hormone-Induced Prostate Carcinogenesis in the Noble Rat X.S. Ouyang, X.H. Wang, Y.C. Wong, *Hong Kong*
2:50 p.m.	6.9	Biopanning and Identification of the Binding-Peptide of MUC1/Y Protein L.X. Zhang, C.H. Li, L.Y. Sun, *China*

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 702-3	7	**Free Paper Session** **Breast and Obstetrics & Gynaecology** Chairpersons: D.K.L. Cheng, *Hong Kong* M.C.M. Chan, *Hong Kong*
1:30 p.m.	7.1	Effect of Flutamide and Tamoxifen on Sex-Hormone Induced Mammary Carcinogenesis in Noble Rats G.C.W. Leung, Y.C. Wong, *Hong Kong*
1:40 p.m.	7.2	To Screen or Not to Screen: Mammography for Chinese Women G.M. Leung, T.H. Lam, A.J. Hedley, *Hong Kong*
1:50 p.m.	7.3	Management of Non-Palpable Breast Cancer F.H.F. Tsang, L.N. Wong, L.W.C. Chow, *Hong Kong*
2:00 p.m.	7.4	Results of Treating Patients with Advanced Metastatic Breast Cancer by Capecitabine as a Single Agent S.C. Chan, L.W.C. Chow, *Hong Kong*
2:10 p.m.	7.5	Attenuation of Epidermal Growth Factor (EGF)-Stimulated LNCaP Prostate Cancer Cell Proliferation by Melatonin W.F. Siu, S.Y.W. Shiu, *Hong Kong*
2:20 p.m.	7.6	Possible Association between Carcinoma of Breast, Carcinoma of Fallopian Tube and Tamoxifen Use S.K. Lam, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
2:30 p.m.	7.7	Results of Treatment (Rx) of Primary Ovarian Germ Cell Tumors (OGCT): Local Experience in 17 Years R.K.Y. Wong, R.K.C. Ngan, V.C. Sin, *Hong Kong*
2:40 p.m.	7.8	Recurrent BRCA2 Mutation is Found in Chinese Ovarian Cancer Patients K.Y. Fung, *Hong Kong*
2:50 p.m.	7.9	Differential Expression and Allelic Loss of BRCA1 and BRCA2 Genes in Sporadic Ovarian Cancer Y.K. Chan, *Hong Kong*
3:00 p.m.	7.10	Telomerase Activity in Ovarian Epithelial Carcinomas and Their Clinical Significance H.X. Li, C.H. Li, M.M. Ye, *China*
Room 803-4	**8**	**Free Paper Session** **NPC and Cancer Genetics** Chairpersons: X.Y. Guan, *Hong Kong* U.S. Khoo, *Hong Kong*
1:30 p.m.	8.1	*N*-(4-Hydrxoyphenyl) Retinamide Induces Up-Regulation of GADD153 in a Nasopharyngeal Carcinoma Cell Line Y.H. Xia, N.S. Wong, H. Tideman, *Hong Kong*
1:40 p.m.	8.2	Inverse Planning by Conventional Beam Optimisation in 3-Dimensional Radiotherapy of Nasopharyngeal Carcinoma V.W.C. Wu, J.S.T. Sham, D.L.W. Kwong, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
1:50 p.m.	8.3	Comparative Genomic Hybridization Analysis of Nasopharygeal Carcinoma: Consistent Patterns of Genetic Aberrations and Clinicopathological Correlations P.W. Yuen, G. Chien, Y.L. Kwong, *Hong Kong*
2:00 p.m.	8.4	Management of Extensive Cervical Nodal Metastasis in Nasopharyngeal Carcinoma after Radiotherapy: A Clinicopathologic Study K.H. Li, W.I. Wei, L.K. Lam, *Hong Kong*
2:10 p.m.	8.5	Immune Escape Mechanisms of Nasal T/NK-Cell Lymphoma A.K.S. Chiang, L. Shen, G. Srivastava, *Hong Kong*
2:20 p.m.	8.6	Expression and Clinical Significance of Drug-Resistance Genes Associated Marker in Carcinoma C.H. Li, G.M. Chen, G.J. Chen, *China*
2:30 p.m.	8.7	Withdrawn
2:40 p.m.	8.8	Reduction of ATM Induction Z.M. Fang, R.A. Clarke, J.H. Kearsley, *Australia*
2:50 p.m.	8.9	Withdrawn
3:00 p.m.	8.10	Local Experience with High Grade Astrocytoma K.K. Chau, Y.T. Fu, P.F. So, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Function Room	**9**	**Free Paper Session** **Psychosocial Oncology** Chairperson: C. Tosen, *Hong Kong*
3:30 p.m.	9.1	Beyond Boundaries: An Attempt of Using Adventure-Based Therapy to Help Long-Term Cancer Survivors S.F. Chow, K.F. Wong, *Hong Kong*
3:45 p.m.	9.2	The Health Care Needs of the Families with Cancer Children S.Y. Chiu, C. Wu, I. Martinson, *Hong Kong*
4:00 p.m.	9.3	Sexual Rehabilitation Program for Cancer Patient W.Y. Lam, *Hong Kong*
4:15 p.m.	9.4	Cross-Cultural Validation of McGill Quality of Life Scale in Palliative Care for Hong Kong Chinese: Final Analysis R.S.K. Lo, J. Woo, K. Zhoc, *Hong Kong*
4:30 p.m.	9.5	The Process of Empowerment among Chinese Cancer Patients in Hong Kong E. Mok, *Hong Kong*
4:45 p.m.	9.6	A Practical Model of Collaboration between Hospice Bereavement Team and Community Bereavement Centre in Provision of Bereavement Care: Experience in Hospice Unit of Caritas Medical Centre M.H.P. Suen, A.Y.M. Chow, A.C.N. Ip, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
James Kung Meeting Room	**10**	**Free Paper Session** **Young Investigators' Awards - Medical II** Adjudicators: Y.L. Kwong, *Hong Kong* R.J. Mayer, *U.S.A.*
3:30 p.m.	10.1	High-Density Allelotyping on Chromosome 8p in Hepatocellular Carcinoma: Allelic Losses Associated with Tumor Progression K.L. Chan, I.O.L. Ng, *Hong Kong*
3:40 p.m.	10.2	Mutation and Expression of β-Catenin Gene in Hepatocellular Carcinoma: Clinicopathological and Prognostic Significance J.C.M. Wong, S.T. Fan, I.O.L. Ng, *Hong Kong*
3:50 p.m.	10.3	Comparison of Modified Colorimetric MTT Assay and Sulforhodamine B Assay for Tumor Chemosensitivity Testing Y.H. Wang, B.R. Davidson, *China and United Kingdom*
4:00 p.m.	10.4	Correlation of p53 Status and Pathologic Complete Response in Locally Advanced Rectal Cancer Patients Treated by Pre-operative Chemo-Radiation R. Chan, M. Reddy, N. Popnikolov, *U.S.A.*
4:10 p.m.	10.5	Overexpression of Protein Kinase C-β1 Isoenzyme Suppresses SC-236-Induced Apoptosis in Gastric Epithelial Cells X.H. Jiang, B.C.Y. Wong, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
4:20 p.m.	10.6	BCL10 Somatic Mutations Rarely Occur in B-Cell Non-Hodgkin's Lymphomas of Gastric Origin: Detection of High Frequency of Polymorphisms in *BCL10* Coding Region Y.W. Chen, G. Srivastava, R.H.S. Liang, *Hong Kong*
4:30 p.m.	10.7	Intensive Chemotherapy with Peripheral Blood Stem Cell Support for Leukemia and Lymphoma Relapse after Allogeneic Bone Marrow Transplantation: Clinical Results and Chimerism Findings W.Y. Au, Y.L. Kwong, A.K.W. Lie, *Hong Kong*
4:40 p.m.	10.8	CT-Pathologic Correlation of Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) in Non-Small Cell Lung Cancer: A Pilot Experience R. Chan, A. Haque, J. Zwischenberger, *U.S.A.*
4:50 p.m.	10.9	Differential Gene Expression in Gestational Trophoblastic Disease Using cDNA Array P.Y. Fong, A.N.Y. Cheung, G.S.W. Tsao, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 702-3	**11**	**Free Paper Session - Liver and Lung** Chairpersons: R.T.P. Poon, *Hong Kong* K.W.T. Tsang, *Hong Kong*
3:30 p.m.	11.1	The Use of Intraductal Ultrasound in the Management of Biliary Stricture C.N. Tang, K.H. Fung, M.K.W. Li, *Hong Kong*
3:40 p.m.	11.2	Genome-Wide Expression Profiling of Hepatocellular Carcinoma by cDNA Microarray Technology S.T. Cheung, S.T. Fan, X. Chen, *Hong Kong*
3:50 p.m.	11.3	Hepatocellular Carcinoma: Mn-DPDP Enhanced MRI Verus Contrast Enhanced Helical CT; Preliminary Results Y.C. Ho, K.S. Tai, W.K. Tso, *Hong Kong*
4:00 p.m.	11.4	Study on Relative Risk of Anti-HBe and Hyaluronic Acid in HCC Patients X.R. Zhu, K.L. Zhu, P.S. Yang, *China*
4:10 p.m.	11.5	The Antitumor Effect of a Traditional Chinese Herbal Medicine Injection Produced by Membrane Filtration S.Z. Li, X.Y. Li, *Hong Kong*
4:20 p.m.	11.6	Result of Pulmonary Metastectomy in Grantham Hospital from 1984-2000 L.C. Cheng, C.L. Yeung, S.W. Chiu, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
4:30 p.m.	11.7	Dual Effects of Cigarette Smoke Extracts on Cell Proliferation in Cancer Cells V.Y. Shin, C.H. Cho, *Hong Kong*
4:40 p.m.	11.8	Repeated Pulmonary Metastectomy: Grantham Hospital Experience from 1984-2000 L.C. Cheng, S.W. Chiu, *Hong Kong*
4:50 p.m.	11.9	Video-Assisted Thoracic Surgery (VATS) Lobectomy for Lung Cancer W.S. Chau, S.W. Chiu, L.C. Cheung, *Hong Kong*
5:00 p.m.	11.10	Positron Emission Tomography in Non-Small Cell Lung Cancer W.S. Chau, S.W. Chiu, L.C. Cheung, *Hong Kong*
5:10 p.m.	11.11	Non-Small Cell Lung Cancers from Smokers and Non-Smokers Show Different Genetic Aberrations in Chromosome 3p M. Wong, M.Y. Lee, L.P. Chung, *Hong Kong*
5:20 p.m.	11.12	The Clinical Observation for Treating Advanced Lung Cancer by Inhaling Gasficatic Preparation of Immunotherapy X.H. Yu, Y.X. Weu, X.D. Keu, *China*
5:30 p.m.	11.13	A Clinical Audit on the Management of Cancer Dyspnoea in the Setting of an Acute Clinical Oncology Center C. Leung, K.H. Wong, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 803-4	**12**	**Free Paper Session** **Gastric and Head & Neck** Chairpersons: L.K. Lam, *Hong Kong* B.C.Y. Wong, *Hong Kong*
3:30 p.m.	12.1	Hypermethylation of the E-Cadherin Promotor Region in Esophageal Carcinoma H.X. Si, *Hong Kong*
3:40 p.m.	12.2	Molecular Markers and Prognosis in Colorectal Cancer L. Chieco-Bianchi, G. Esposito, M. Lise, *Italy*
3:50 p.m.	12.3	Prospective Randomized Study of Post-Operative Chemotherapy with Levamisole and UFT for Head and Neck Carcinoma K.Y. Lam, P.W. Yuen, C.M. Ho, *Hong Kong*
4:00 p.m.	12.4	Radiotherapy for Major Salivary Gland Carcinoma: A Single Institution Experience T.S. Choy, R.K.C. Ngan, K.H. Au, *Hong Kong*
4:10 p.m.	12.5	Pharyngolaryngo-Oesophagectomy with Pharyngogastric Anastomosis: A Meta Analysis K.Y. Lam, W.I. Wei, *Hong Kong*
4:20 p.m.	12.6	Clinicopathological Significance of bcl-2 Expression in Patients with Surgery for Laryngeal Carcinoma W.K. Ho, P.W. Yuen, J.T.H. Choy, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
4:30 p.m.	12.7	Assessment of Chromosomal Gains and Losses in Oral Squamous Cell Carcinoma by Comparative Genomic Hybridization L. Sun, X.Y. Guan, H. Tideman, *Hong Kong*
4:40 p.m.	12.8	E-Cadherin and Catenins (α, β, γ) in Oral Tongue Carcinoma B.Y.H. Wong, P.W. Yuen, W.I. Wei, *Hong Kong*
4:50 p.m.	12.9	Malignant Tumours in the Head and Neck Region in Childhood: Good Outcome with Current Therapeutic Approach G.C.F Chan, K.L. Chan, S.Y. Ha, *Hong Kong*
5:00 p.m.	12.10	Is Deltopectoral Flap Reliable for Head and Neck Reconstruction? W.M. Ng, L.K. Lam, S.Y. Wong, *Hong Kong*
5:10 p.m.	12.11	Special Allometric Kinetics in MTT Assay for Quantitative Assessment of Cell Viability Y.H. Wang, B.R. Davidson, *China & United Kingdom*

SCIENTIFIC PROGRAM

Room / Time	Session	
Run Run Shaw Hall	**13**	**HKICC Lecture** **Environment and Cancer** Chairperson: T.K. Chan, *Hong Kong*
9:00 a.m.		Genetic Susceptibility to Environmental Cancer W. Au, *U.S.A.*
Run Run Shaw Hall	**14**	**State-of-the-Art Lecture** **Psychosocial Oncology** Chairperson: W.M. Ko, *Hong Kong*
10:30 a.m.		Environmental Contamination and Cancer B.D. Goldstein, *U.S.A.*
Run Run Shaw Hall	**15**	**State-of-the-Art Lecture** **Tobacco, Air and Cancer** Chairperson: W.M. Ko, *Hong Kong*
11:10 a.m.		Smoke Kills in Hong Kong: Environmental Priorities in Cancer Prevention A.J. Hedley, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Run Run Shaw Hall	**16**	**State-of-the-Art Lecture** **Psychosocial Oncology** Chairperson: W.M. Ko, *Hong Kong*
11:50 a.m.		Advocacy and Policy C. Loh, *Hong Kong*
Lim Por Yen Lecture Theatre	**17**	**Symposium** **Colorectal Cancer and Environment** Chairpersons: J. Boey, *Hong Kong* H. Yuen, *Hong Kong*
1:30 p.m.	17.1	Colorectal Carcinogenesis S.T. Yuen, *Hong Kong*
1:50 p.m.	17.2	Risk Factors for Colorectal Cancer J.W.C. Ho, *Hong Kong*
2:10 p.m.	17.3	Colorectal Cancer Screening J.D. Hardcastle, *United Kingdom*
2:30 p.m.	17.4	Chemoprevention B.C.Y. Wong, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
James Kung Meeting Room	**18**	**Educational Symposium** **From Laboratory to Clinical Practice** Chairpersons: H. Kung, *Hong Kong* D.Y.M. Lo, *Hong Kong*
1:30 p.m.	18.1	Plasma DNA in Health and Disease: A New Tool for Molecular Diagnosis D.Y.M. Lo, *Hong Kong*
1:55 p.m.	18.2	Recent Advances in the Use of Tumour Markers in Clinical Practice E.Y.T. Chan, *Hong Kong*
2:20 p.m.	18.3	Effective Use of Microbiological Investigations in Cancer Management W.H. Seto, *Hong Kong*
Pao Yue Kong Auditorium	**19**	**Symposium - Psychosocial Oncology** **Psychosocial Clinical Guidelines** Chairperson: S.H. Liu, *Hong Kong*
1:30 p.m.	19.1	Psychosocial Clinical Guidelines for Breast Cancer S. Redman, *Australia*
2:20 p.m.	19.2	A Case Presentation: How Psychosocial Guidelines would have Influenced the Care of Angie V. Chan, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Lim Por Yen Lecture Theatre	**20**	**Symposium** **Hormonal Related Cancer** Chairpersons: D.L.W. Kwong, *Hong Kong* P.C. Tam, *Hong Kong*
3:30 p.m.	20.1	Hormone Replacement Therapy and Breast Cancer C.S. Huang, *Taiwan*
3:55 p.m.	20.2	New Understanding of Prostate Cancer S.Y.L. Leung, *Hong Kong*
4:20 p.m.	20.3	Oral Contraceptives and Ovarian Cancer T.Y. Ng, *Hong Kong*
James Kung Meeting Room	**21**	**Symposium** **Brain and Skull Base Tumour** Chairpersons: D.T.S. Fong, *Hong Kong* C. Schold, *U.S.A.*
3:30 p.m.	21.1	Imaging of Skull Base F.L. Chan, *Hong Kong*
3:50 p.m.	21.2	Brain Tumour and Mobile Phone Y.W. Fan, *Hong Kong*
4:10 p.m.	21.3	Surgical Approaches to the Inferior Skull Base: Their Indications and Limitations S. Kishimoto, *Japan*

SCIENTIFIC PROGRAM

Room / Time	Session	
4:30 p.m.	21.4	Skull Base Surgery: Hong Kong Experience W.I. Wei, *Hong Kong*
Pao Yue Kong Auditorium	**22**	**Symposium - Psychosocial Oncology Psychosocial Clinical Guidelines** Chairperson: V. Wong, *Hong Kong*
3:30 p.m.	22.1	Psychosocial Guidelines in Hong Kong: How can We Make It Work? P.W.H. Lee, Y.F. Wu, S.M. Fung, *Hong Kong*
4:10 p.m.	22.2	The Hospital Authority's Vision for Psychosocial Care H. Fung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Lim Por Yen Lecture Theatre	**23**	**Symposium** **Blood Cancer** Chairpersons: E.K.W. Chiu, *Hong Kong* K.I.K. Lei, *Hong Kong*
8:30 a.m.	23.1	The WHO Classification for Lymphomas J.K.C. Chan, *Hong Kong*
8:55 a.m.	23.2	Distinguishing between Phenotype and Genotype in Non-Hodgkin's Lymphoma (NHL) R.D. Gascoyne, *Canada*
9:20 a.m.	23.3	Acute Promyelocytic Leukemia: A Unique Subtype of Acute Leukemia R.J. Mayer, *U.S.A.*
James Kung Meeting Room	**24**	**Symposium** **Basic Science II: Cancer Genetics** Chairpersons: X.Y. Guan, *Hong Kong* N. Wong, *Hong Kong*
8:30 a.m.	24.1	Alterations at Early Stage of Human Lung Carcinogenesis S.J. Cheng, Y.N. Gao, Q. An, *China*
8:55 a.m.	24.2	Use of Biomarkers for Understanding Cancer Risk W. Au, *U.S.A.*

SCIENTIFIC PROGRAM

Room / Time	Session	
9:20 a.m.	24.3	New Molecular Cytogenetic Techniques in Leukaemia E.S.K. Ma, *Hong Kong*
Pao Yue Kong Auditorium	**25**	**Symposium - Psychosocial Oncology Community Care** Chairperson: C.L.W. Chan, *Hong Kong*
8:30 a.m.	25.1	"Voices of Caregivers": The Experience of CancerLink S.F. Chow, *Hong Kong*
9:00 a.m.	25.2	The Interface of Palliative Care in Acute Care Setting R. Liu, *Hong Kong*
9:30 a.m.	25.3	Working Model of Community Psychosocial Care F. Chu, *Hong Kong*
Lim Por Yen Lecture Theatre	**26**	**State-of-the-Art Lecture** **Microarrays** Chairperson: D. Higgins, *Hong Kong*
10:30 a.m.		Tissue Microarray Technology for Translating Molecular Discoveries to Clinical Applications O. Kallioniemi, *U.S.A.*

SCIENTIFIC PROGRAM

Room / Time	Session	
Lim Por Yen Lecture Theatre	27	**Hong Kong Anti-Cancer Society Lecture** **New Development in Cancer Therapy** Chairperson: A.W.M. Lee, *Hong Kong*
11:10 a.m.		Colorectal Cancer: From Molecular Pathogenesis to Multimodality Management R.J. Mayer, *U.S.A.*

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Lim Por Yen Lecture Theatre	28	**State-of-the-Art Lecture** **Gastric Cancer** Chairperson: K.M. Chu, *Hong Kong*
11:50 a.m.		Gastric Cancer M.S. Karpeh, Jr., *U.S.A.*
Pao Yue Kong Auditorium	29	**State-of-the-Art Lecture** **Psychosocial Oncology** Chairperson: S. Lum, *Hong Kong*
10:30 a.m.		Consumers as Advocates in Cancer Care S. Redman, *Australia*

SCIENTIFIC PROGRAM

Room / Time	Session	
Pao Yue Kong Auditorium	**30**	**State-of-the-Art Lecture** **Psychosocial Oncology** Chairperson: S. Lum, *Hong Kong*
11:10 a.m.		Is Stress Carcinogenic? P.W.H. Lee, *Hong Kong*
Pao Yue Kong Auditorium	**31**	**State-of-the-Art Lecture** **Psychosocial Oncology** Chariperson: S. Lum, *Hong Kong*
11:50 a.m.		Duration of Cancer Survival Relates to QOL R. Fielding, C.L.W. Chan, C. Yu, *Hong Kong*
Lim Por Yen Lecture Theatre	**32**	**Symposium** **Basic Science I: Microarrays** Chairpersons: Y.L. Kwong, *Hong Kong* I.O.L. Ng, *Hong Kong*
1:30 p.m.	32.1	Microarray Technologies for Basic, Translational and Clinical Cancer Research O. Kallioniemi, *U.S.A.*
2:10 p.m.	32.2	Gene Expression Profiling of Chemotherapeutic Response in Lymphoma L.T. Lam, E.A. Sausville, L.M. Staudt, *U.S.A.*

SCIENTIFIC PROGRAM

Room / Time	Session	
James Kung Meeting Room	**33**	**Educational Symposium** **Environment / Communication** Chairpersons: D.V.K. Chao, *Hong Kong* D.K.T. Li, *Hong Kong*
1:30 p.m.	33.1	Occupational Cancer I.T.S. Yu, *Hong Kong*
1:55 p.m.	33.2	Smoking and Cancer Mortality in Hong Kong T.H. Lam, S.Y. Ho, A.J. Hedley, *Hong Kong*
2:20 p.m.	33.3	Breaking Bad News: A Chinese Perspective C.Y. Tse, *Hong Kong*
Pao Yue Kong Auditorium	**34**	**Debate** **Colorectal Cancer** Chairpersons: G.K.H. Au, *Hong Kong* J.W.C. Ho, *Hong Kong*
1:30 p.m.		Colorectal Cancer: Place of Surgery, Chemotherapy and Radiotherapy Panelists: J. Boey, *Hong Kong* J.D. Hardcastle, *United Kingdom* L.P.K. Li, *Hong Kong* W.M. Sze, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 702	35	**Workshop - Psychosocial Oncology** **Approaches to Research in Psychosocial Care**
1:30 p.m.		Approaches to Research in Psychosocial Care S. Redman, *Australia*
Room 703	36	**Workshop - Psychosocial Oncology** **Families and Cancer:** **A Family Systems Perspective**
1:30 p.m.		Families and Cancer: A Family Systems Perspective P. Simpson, *Hong Kong*
Room 803	37	**Workshop - Psychosocial Oncology** **It's about Living: Possibility of Anticipatory Grief Work in Hospitals**
1:30 p.m.		Making Good Use of the Precious Moment: Possibility of Anticipatory Grief Work in Hospitals A.Y.M. Chow, *Hong Kong*
Room 804	38	**Workshop - Psychosocial Oncology** **Working with Difficult Emotions**
1:30 p.m.		Working with Difficult Emotions L. Chung, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
Lim Por Yen Lecture Theatre	**39**	**Symposium** **Paediatric Cancers:** **Aetiology and Pathogenesis** Chairpersons: Y.L. Lau, *Hong Kong* C.K. Li, *Hong Kong*
3:30 p.m.	39.1	Molecular Model of Leukaemogenesis A.T. Look, *U.S.A.*
3:55 p.m.	39.2	Timing of Infections and Risk of Childhood Leukaemia L.C. Chan, *Hong Kong*
4:20 p.m.	39.3	Immunodeficiency and Childhood Malignancy G.C.F. Chan, Y.L. Lau, S.Y. Ha, *Hong Kong*
James Kung Meeting Room	**40**	**Symposium** **Musculoskeletal Malignancies** Chairpersons: P. Chien, *Hong Kong* J.W.K. Wong, *Hong Kong*
3:30 p.m.	40.1	Surgical Strategies in Soft Tissue Sarcomas R. Capanna, G. Beltrami, P.D. Biase, *Italy*
3:50 p.m.	40.2	The Role of Pathologist in the Management of Musculoskeletal Tumours T.W.H. Shek, *Hong Kong*

SCIENTIFIC PROGRAM

Room / Time	Session	
4:10 p.m.	40.3	Imaging of Soft Tissue Tumours L.L.S. Wong, *Hong Kong*
4:30 p.m.	40.4	The Role of Radiotherapy & Chemotherapy in the Modern Management of Soft Tissue Sarcoma R.T.T. Chan, *Hong Kong*
Pao Yue Kong Auditorium	**41**	**Interactive Session** **Site Specific Tumours**
3:30 p.m.		Site Specific Tumours: Carcinoma of Prostate, Nasopharyngeal Carcinoma and Ovarian Tumor Panelists: W.K. Kwong, *Hong Kong* A.W.M. Lee, *Hong Kong* T. Leung, *Hong Kong* R.K.Y. Lo, *Hong Kong* P.M.L. Teo, *Hong Kong* L.C. Wong, *Hong Kong* Case Writers: 1) Carcinoma of Prostate P.C. Tam 2) Nasopharyngeal Carcinoma D.T.T. Chua 3) Ovarian Tumour D.K.L. Cheng

SCIENTIFIC PROGRAM

Room / Time	Session	
Room 702	35	**Workshop - Psychosocial Oncology (con't)** **Approaches to Research in Psychosocial Care**
3:30 p.m.		Approaches to Research in Psychosocial Care S. Redman, *Australia*
Room 703	36	**Workshop - Psychosocial Oncology (con't)** **Families and Cancer:** **A Family Systems Perspective**
3:30 p.m.		Families and Cancer: A Family Systems Perspective P. Simpson, *Hong Kong*
Room 803	37	**Workshop - Psychosocial Oncology (con't)** **Making Good Use of the Precious Moment:** **Possibility of Anticipatory Grief Work in Hospitals**
3:30 p.m.		Making Good Use of the Precious Moment: Possibility of Anticipatory Grief Work in Hospitals A.Y.M. Chow, *Hong Kong*
Room 804	38	**Workshop - Psychosocial Oncology (con't)** **Working with Difficult Emotions**
3:30 p.m.		Working with Difficult Emotions L. Chung, *Hong Kong*

Carcinoma of Prostate

Case Writer: P.C. Tam, Department of Surgery, University of Hong Kong Medical Centre, Queen Mary Hospital, Hong Kong

Case History

- Mr. Chen, a 66-year-old gardener, presented with LUTS (Lower Urinary Tract Symptoms) for 2 years
- DRE
  - 30g prostate
  - 1cm nodule over R lobe
- Serum PSA 8.2 ng/c.c.
- TRUS (prostate)
  - ill-defined hypoechoic lesion at R lobe, near base
  - overlying capsule ill-defined, ? invasion
- Prostatic sextant biopsy
  - R mid-zone
  - adenocarcinoma, Gleason grade 3 + 4

Points for Discussion

1. Role of staging investigations, including bone scan and CT scan / MRI
2. Treatment options
3. Role of neoadjuvant hormonal therapy

SCIENTIFIC PROGRAM

INTERACTIVE SESSION: CASE SUMMARY

Nasopharyngeal Carcinoma

Case Writer: Daniel T. T. Chua, Department of Clinical Oncology, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Case History

- A 35-year-old gentleman presented with bilateral neck mass for 2 months.
- Examination revealed bilateral upper cervical lymphadenopathy largest 4 cm in diameter
- Endoscopy revealed tumor in the nasopharynx and biopsy showed undifferentiated carcinoma
- CT showed tumor in nasopharynx with extension to right parapharyngeal space and bilateral enlarged upper cervical nodes.
- Diagnosis: Nasopharyngeal Carcinoma, Ho's stage II (T2N1)/ AJCC stage III T2bN2
- Patient received radiotherapy to 68Gy concomitant with 3 cycles of CDDP 100mg/m2. After completion of chemoirradiation patient received 1 cycle of adjuvant chemotherapy with CDDP 80mg/m2 D1 and 5FU 1G/m2 D1-4, and was scheduled to receive 2 more cycles.
- On week 6 after completion of RT, endoscopy however still revealed irregular mucosa in left roof of nasopharynx and biopsy showed residual tumor. There were no palpable residual neck nodes.
- Repeated biopsies still showed persistent disease and patient subsequently received transpalatal gold grain implant.
- Nine months later, patient noticed pain in the low back and X-ray showed lytic lesion in lumbar spine. Bone scan was performed and showed abnormal uptake in thoraco-lumbar spine, pelvis and multiple ribs.

Issues for Discussion

1 What is the recommended primary treatment for this patient? Radiotherapy alone or combined modality treatment?

2 What is the optimal time for assessing local disease status after primary treatment? What salvage options are available for locally persistent disease?

3 What is the role of chemotherapy in metastatic NPC? Any effective second-line chemotherapeutic agents in patients previously treated by cisplatin-based regimen?

SCIENTIFIC PROGRAM

INTERACTIVE SESSION: CASE SUMMARY

Ovarian Tumour

Case Writer: D.K.L. Cheng, Division of Gynaecological Oncology, Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Case History

- 25 year old previously healthy, nulliparous, sexually inactive businesswoman
- October 1999 - admitted to Hong Kong Sanatorium and Hospital for nausea and vomiting
- Incidental finding of LLQ mass. Leiomyoma diagnosed on pelvic ultrasound scan. Scheduled to have myomectomy January 2000, due to business commitment.
- December 1999 - 2 day history of abdominal pain ➡ prompted laparotomy

Operative Findings

- 15x12x10 cm tumour replacing left ovary
- Mass adherent to omentum, which in turn contained 2 tumour masses measuring 11.5x7x2.5 cm and 4x3x2 cm, respectively
- Enlarged matted para-aortic lymph nodes from left renal vein to aortic bifurcation

Procedure

Left salpingo-oophorectomy, partial omentectomy, appendicectomy

Frozen Section

Anaplastic necrotic carcinoma

FIGO Staging

a) IIIa
b) IIIb
c) IIIc
d) IV

Management Options

1) hysterectomy and right salpingo-oophorectomy
2) multiple peritoneal biopsies
3) debulk para-aortic nodes
4) close up abdomen

a) 1
b) 1 & 2
c) 1,2, & 3
d) 4

Paraffin Section

Left ovarian tumour infiltrating outer coat of fallopian tube. It is composed of islands of tumour cells separated by fibrous bands. Focally, these bands are densely infiltrated by lymphocytes. The tumour cells contain uniform round nuclei with mild nuclear pleomorphism and prominent nucleoli. Mitotic figures are frequently seen.

Immunohistochemical Staining

Some of the tumour cells display positive membranous staining for placental-like alkaline phosphatase (PLAP). They are negative for epithelial markers or hCG.

Serum Tumour Markers

CA-125 = 34.7 IU/ml
hCG < 5 mIU/ml
AFP = 2 ng/ml
CEA = 1.5 ng/ml

Final Diagnosis

a) anaplastic carcinoma with clear cell differentiation
b) adult granulosa cell tumour
c) immature teratoma
d) pure dysgerminoma

Metastatic Survey

Matted chain of para-aortic lymph nodes, with central necrosis, from L3 to L5. The largest node measures 2.8 x 3.9 cm.

Adjuvant Therapy

a) radical debulking of para-aortic nodes
b) 25 Gy whole abdominal irradiation + 2 Gy pelvic boost
c) chemotherapy alone
d) chemo-irradiation because of bulky nodes

Treatment Toxicity

- Leucopenia G4, no neutropenic fever
- Thrombocytopenia G3

Treatment Results

- June 2000, CT Scan - 1.5 cm diameter left sided para-aortic node at L5
- June 2000, PET scan -

Salvage Therapy

BEP chemotherapy

Points for Discussion

1. Intraoperative management -
    - Extent of staging & debulking
    - Reliability of frozen section
    - Fertility sparing surgery in advanced disease
2. Indications for & adjuvant therapy regimens
3. The role of second look laparotomy
4. Available salvage therapies

SCIENTIFIC PROGRAM

POSTER SESSIONS

P1 Establishment and Characterization of a New Xenograft-Derived Human Esophageal Squamous Cell Carcinoma Cell Line SLMT-1 of Chinese Origin
J.C.O. Tang, G. Srivastava, A.K.Y. Lam, *Hong Kong*

P2 Detection of Genetic Alterations in Esophageal Squamous Cell Carcinoma Tumor Specimens and Adjacent Normal Epithelia by Comparative DNA Fingerprinting Using Inter-Simple Sequence Repeat PCR
J.C.O. Tang, G. Srivastava, A.K.Y. Lam, *Hong Kong*

P3 Intraoperative Radiation Therapy for Bile Duct Cancer
G.X. Chen, D.J. Wu, I.J. Zhao, *China*

P4 Yeast One-Hybrid System Identifies the Binding Proteins for Rat Glutathione S-Transferase P Enhancer I
F.D. Fang, M.X. Liao, D.Y. Liu, *China*

P5 Local Recurrence after Resection for Rectal Cancer
S. Maksimovic, *Bosnia & Hercegovina*

P6 Reduction of Murine Mammary Tumor Metastasis by Conjugated Linoleic Acid
K.L. Erickson, N.E. Hubbard, D. Lim, *U.S.A.*

P7 Primary Study for the Expression of Human Tissue Inhibitor of Metalloproteinase-4 in *Pichia Pastoris* Yeast System
K.Q. Li, E.Y.N. Shi, C.H. Li, *China and U.S.A.*

P8 Fludarabine, Mitoxantrone and Dexamethasone (FND) in the Treatment of Indolent Lymphoid Malignancies
W.Y. Au, Y.L. Kwong, C.S. Chim, *Hong Kong*

P9 Non-TBI Conditioning Regimens were Associated with Less Transplant-Related Morbidity and Mortality in Patients who Received BMT from Matched-Unrelated Donors
A.Y.H. Leung, A.K.W. Lie, R.H.S. Liang, *Hong Kong*

P10 Unmanipulated Bone Marrow Transplantation from One-HLA Antigen Mismatched Siblings Carries High Transplant-Related Mortality Compared with the HLA-Identical Counterparts
A.Y.H. Leung, A.K.W. Lie, W.Y. Au, *Hong Kong*

P11 Clostridium Difficile-Associated Diarrhoea (CDAD) in Bone Marrow Transplantation
A.Y.H. Leung, N.L.S. Lee, C.K. Yeung, *Hong Kong*

P12 Herpes Zoster Virus Infection after Bone Marrow Transplantation
A.Y.H. Leung, K.Y. Yuen, A.K.W. Lie, *Hong Kong*

P13 The 23-Valent Polysaccharide Pneumococcal Vaccination is not Useful in BMT Patients at Risk of Pneumococcal Bacteremic Sepsis
A.Y.H. Leung, A.K.W. Lie, Y.L. Kwong, *Hong Kong*

P14 A Comparative Study of Hysteroscopic Dissemination of Endometrial Carcinoma Using Carbon Dioxide and Normal Saline
W.K. Lo, T.H. Cheung, S.F. Yim, *Hong Kong*

SCIENTIFIC PROGRAM
POSTER SESSIONS

P15 Detection of *p53* Gene Mutations in Human Epithelial Ovarian Cancer
S.M. Ip, L.C. Wong, H.Y.S. Ngan, *Hong Kong*

P16 A Prospective Study of the Microbiological Environment of the Genital Tract in Women Diagnosed to have High Grade or Low Grade Squamous Intraepithelial Lesions
S.F. Yim, T.H. Cheung, W.K. Lo, *Hong Kong*

P17 Effect of Diet on IGF-I and IGFBP-3 in Middle-Aged and Older Chinese in Singapore
H. Wang, A. Seow, V.H.H. Goh, *Singapore*

P18 The Fine-scale Mapping of NIDDM Susceptibility Genes in Northern Chinese Han Population
W.N. Du, H.X. Sun, F.D. Fang, *China*

P19 My Patient Die in Suicide, I Feel .....
H.Y. Wong, S.M. Shiu, S.Y. Poon, *Hong Kong*

P20 Working Together for Better Cancer Care: The Psycho-social Experiences of Patients with Advanced Cancer
W.H. Liu, S.C. Chan, S.Y. Lau, *Hong Kong*

P21 Acupuncture for the Relief of Breathlessness in Hospice Patients
C. Kwan, E.C.M. Wu, J. Wong, *Hong Kong*

P22 Kinematic Analysis of Rotation Pattern of ACL Deficient Knee, ACL Reconstructed Knee and Normal Knee during Single Leg Hop and Pivot Shift Test
Y.H. Wong, P. Chien, J.C.Y. Leong, *Hong Kong*

SOCIAL PROGRAM

OPENING CEREMONY

Friday 8 December 2000 8:30 am - 9:00 am

The Opening Ceremony of the Congress will take place at the Run Run Shaw Hall, Hong Kong Academy of Medicine Building.

ACCOMPANYING PERSONS PROGRAM

Two local half-day tours are organized for accompanying persons.

HONG KONG ISLAND TOUR

Friday 8 December 2000 9:00 am - 1:00 pm

An excellent orientation tour - the city changes so rapidly that it will refresh "old memories" and delight "first timers". The tour starts with a drive up to Victoria Peak for a panoramic view of Hong Kong Island, Kowloon and the surrounding islands. It proceeds next to Stanley market for great shopping. You will also visit picturesque Repulse Bay and the fishing village of Aberdeen to see the "Floating Community" - still very much a part of Hong Kong's society. Here an opportunity to join an optional "Sampan" ride is available, allowing a "close up" view of waterborne life. This is a tour not to be missed.

KOWLOON & NEW TERRITORIES TOUR

Saturday 9 December 2000 9:00 am - 1:00 pm

The New Territories, which lie between the Kowloon Hills and the boundary with mainland China. With 150 years of colonial influence, Hong Kong reveals itself subtly. Everything changes, much remains the same. This tour gives you a unique opportunity to explore the culture, heritage and lifestyles in Hong Kong. Sightseeing points include Make Wishes Tree, Tin Hau Temple, Tai Po Market, and Bird Garden.

GENERAL INFORMATION

TIME

Hong Kong time is 8 hours ahead of Greenwich Mean Time.

CLIMATE

Hong Kong enjoys a generally sub-tropical climate. Daytime temperature in December varies between 18 - 23°C. There may be occasional rain.

DRESS

Outside official functions, light winter clothing or informal dress may be worn.

CURRENCY

Most foreign currencies and traveller's cheques are easily exchanged at banks, hotels and money-changers. A passport is required for money exchange services. Exchange rates for US$1 = approx. HK$7.70.

Hong Kong Dollars are available in $10, $20, $50, $100, $500 and $1,000 denominations. Coinage is in 10, 20, 50 cents and $1, $2, $5 and $10.

BANKS

	Business hours
Monday to Friday	9:00 am - 4:30 pm
Saturday	9:00 am - 12:30 pm
Sundays and public holidays	Closed

POSTAL SERVICES

Hotels often provide simple postage service. Post offices open every day except Saturday afternoons and Sundays.

GENERAL INFORMATION

ELECTRICITY

Electricity is supplied as alternating current; the voltage is 220 volts and frequency 50 cycles.

PUBLIC TRANSPORT

For general transport, taxis are plentiful and cheap. In addition, a subway service (MTR) allows easy access throughout the territory. Public bus, tram and ferry services are also frequent. The famous Star Ferry operates from Tsim Sha Tsui to Central District and the Convention Centre. The funicular Peak Tram is a popular tourist attraction with breathtaking views of Victoria Harbour.

RESTAURANTS

Hong Kong has more than 5,000 restaurants specializing in all regional dishes of China and neighbouring Asian countries as well as European and American cuisine.

SHOPPING

Most shops and department stores are open seven days a week until 9:00 pm. Street markets are in business every day until late into the night. Hong Kong is reowned for bargains, speedily made tailored clothing, antiques, jewellery, cameras and electronic equipment. Major credit cards are widely accepted.

INSURANCE

The Organizing Committee is not responsible for personal accidents and/or damage to the private property of participants. Participants should therefore make their own arrangements with respect to personal insurance if they wish.

CONGRESS FACILITIES

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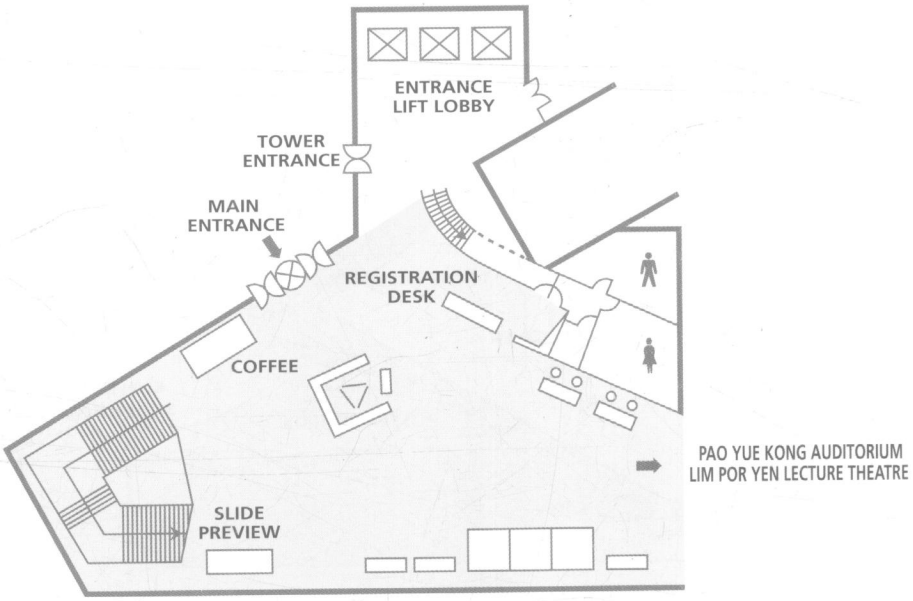
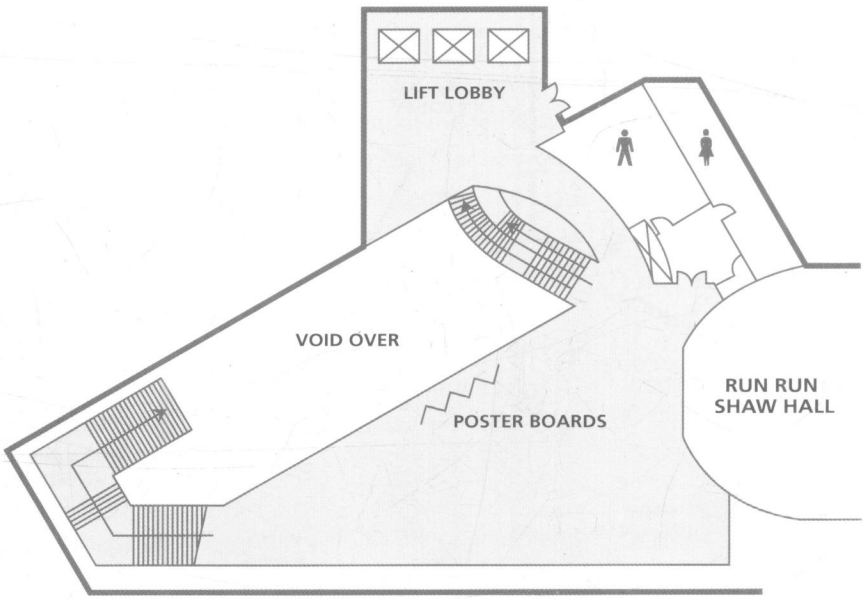


CONGRESS FACILITIES

1ST FLOOR - FOYER



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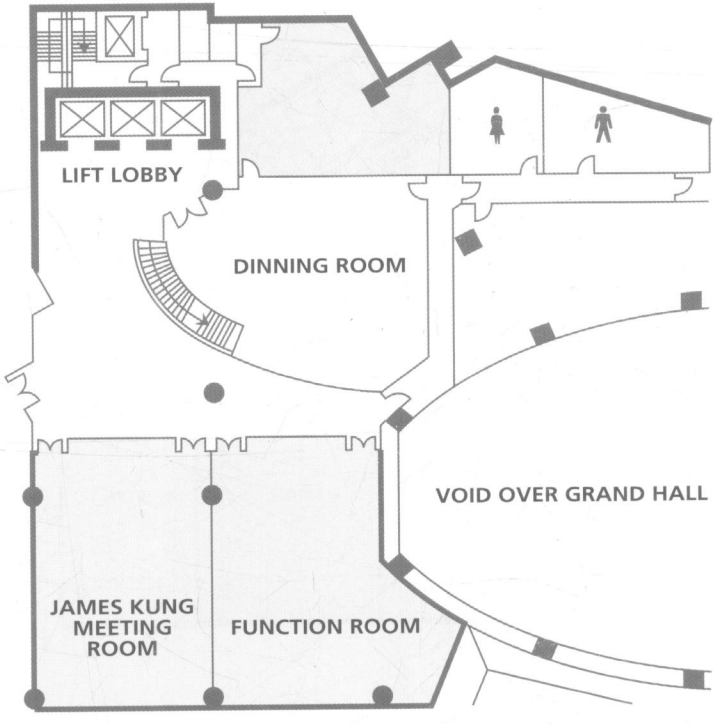

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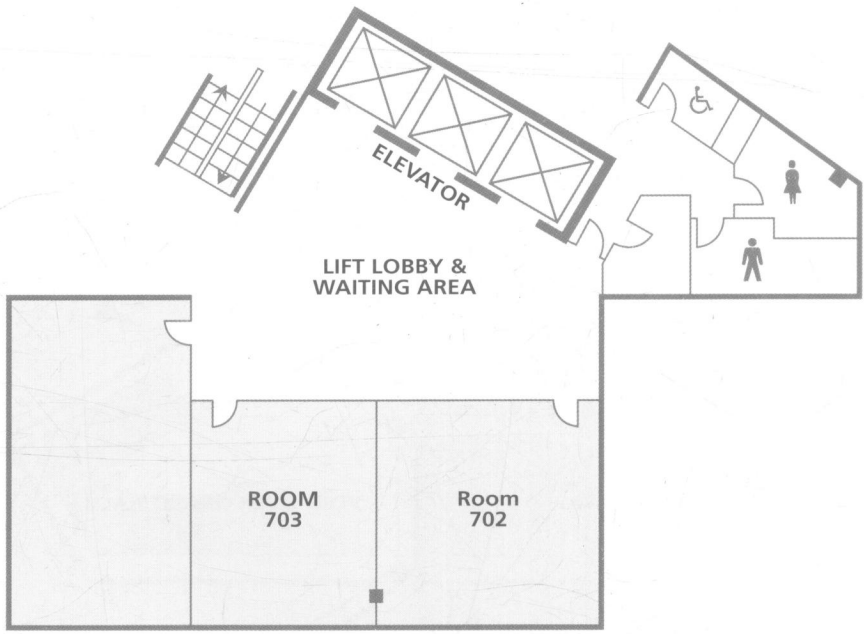

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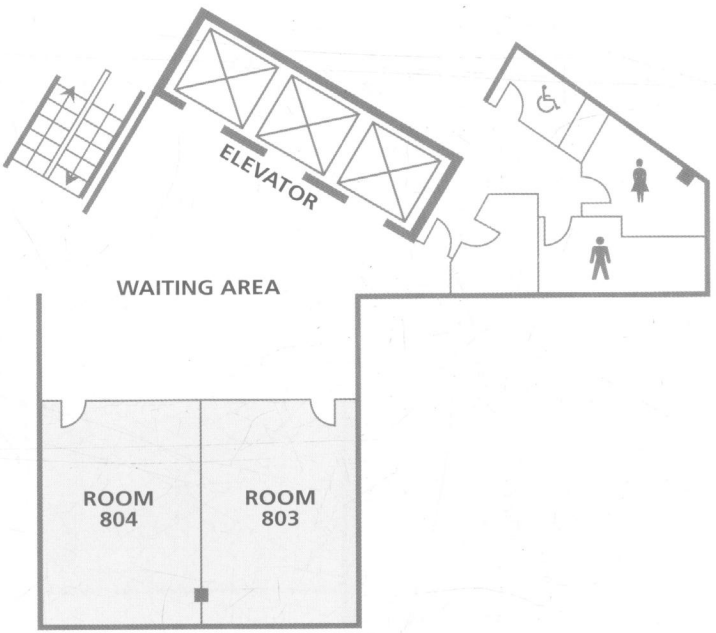

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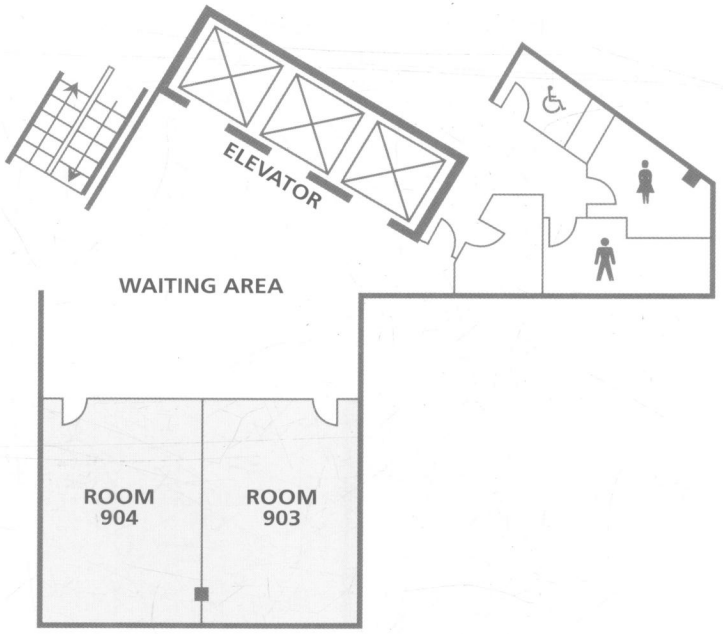
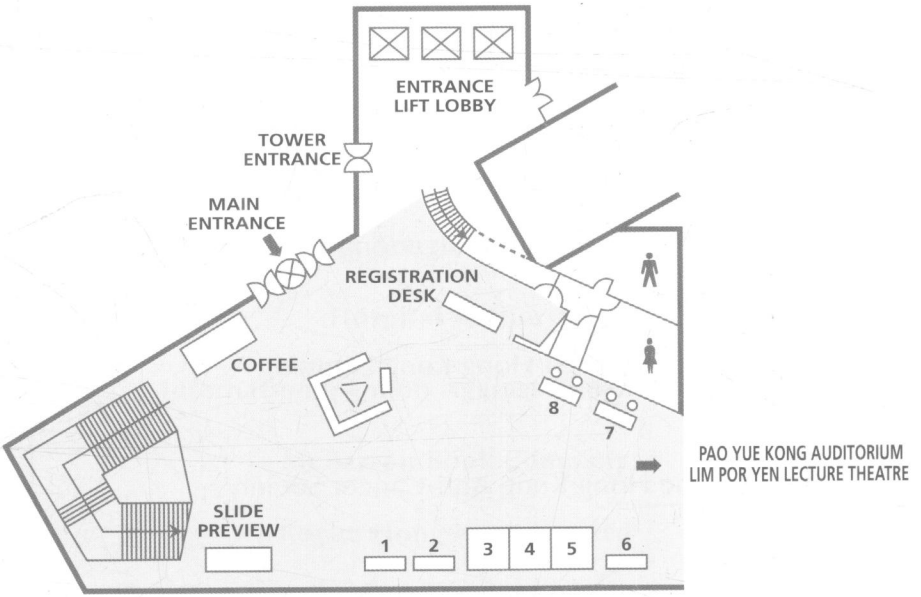


EXHIBITION

GROUND FLOOR



EXHIBITORS' LIST

1. The Society for Promotion of Hospice Care

2. Hong Kong Cancer Fund

3. Children's Cancer Foundation

4. Bristol-Myers Squibb (Hong Kong) Limited

5. AstraZeneca Hong Kong Limited

6. The Hong Kong Anti-Cancer Society

7. McBarron Book Company

8. Springer-Verlag Hong Kong Limited

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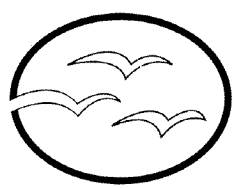

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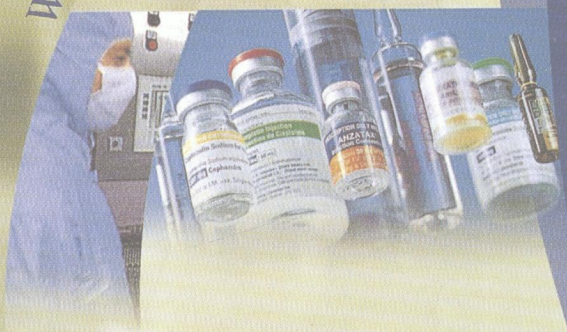

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ABSTRACTS

5TH RESEARCH POSTGRADUATE SYMPOSIUM

1.1

Insulin-dependent inhibition of MTP gene transcription is mediated by MAPK pathway in HepG2 cells

W.S. Au, H.F. Kung, M.C. Lin
Institute of molecular biology, HKU

The microsomal triglyceride transfer protein (MTP) is essential for the assembly and secretion of the apolipoprotein B (ApoB) containing lipoproteins.[1] Emerging evidence has clearly demonstrated a link between hepatic MTP level and diseases of lipogenic abnormalities. Previously we have shown that insulin inhibits MTP gene transcription via a novel insulin responsive element. However, the underlying mechanism is not known. Insulin signals are mediated mainly through Mitogen-activating protein Kinase (MAPK), Phosphoinositol-3-Kinase (PI3-K). We, herein, investigate the responsible signaling pathway in HepG2 cells by specific inhibitors. We find that (PI-3K) inhibitor, LY294002 and its downstream p70S6 kinase inhibitor, rapamycin pose no change on insulin effect. Whereas, MAPK pathway inhibitor, PD98059 effectively abolishes the insulin induced inhibition in a dose dependent manner. This is the first evidence demonstrating that the insulin-dependent inhibition of MTP gene transcription is transduced through MAPK pathway and hence may provide a new mechanism ultimately for insulin dependent regulation of plasma ApoB containing low dense lipoprotein.

1. Wetterau JR, Lin MC, Jamil H (1997) *Biochim Biophys Acta* 1345:136-50

1.2

Different Subgroups of H6N1 Influenza Viruses Present In Southeastern China

P.S. Chin, J.S.M. Peiris, K.F. Shortridge, Department of Microbiology, The University of Hong Kong, Hong Kong Special Administrative Region, P.R. CHINA.

During the H5N1 incident in Hong Kong Special Administrative Region (SAR) in 1997, the most prevalent influenza virus subtypes in the retail poultry markets were H5N1, H9N2 and H6N1. Studies on one of the H6N1 viruses, viz. a teal isolate, found that all internal genes as well as its neuraminidase gene were closely related to those of the 1997 H5N1 viruses isolated from human and avian hosts. Virus surveillance studies carried out in poultry markets in the SAR from 1998 to 2000 revealed that H6N1 influenza viruses are still present in poultry in southeastern China at low level. Nine H6N1 and nine H6N2 influenza viruses were isolated from different types of land-based and aquatic poultry. Genetic analysis of the haemagglutinin gene of these and earlier H6 isolates indicate that they are of Euroasian origin and comprise three subgroups: (1) isolates from the 1970's (with various neuraminidase subtypes) from aquatic birds; (2) ten recent H6N1 isolates from aquatic birds; (3) two recent H6N1 isolates from aquatic birds and eight recent H6N1 isolates from land-based birds. These findings show the diversity of H6 virus subgroups in this region and highlight the need for further genetic and epidemiological studies in this region.

1.3

THE EXPRESSION AND REGULATION OF ENDOTHELIN-1 GENE FOR CRANIOFACIAL AND CARDIAC DEVELOPMENT

K.W. Chiu, S.K. Chan,S.K. Chung

Institute of Molecular Biology, Faculty of Medicine, The University of Hong Kong

Large number of human congenital syndromes, such as CATCH-22, Treacher Collins, Pierre-Robin sequence, with the characterics of craniofacial and cardiac defects are thought to be result of abnormal craniofacial neural crest development. Recently, it has been shown that mice without prepoendothlin-1 (ET-1) die at birth with the severe craniofacial and cardiac defects similar to those of above mentioned human congenital syndromes (1). We have shown that ET-1 is expressed by branchial epithelial and paraxial mesodermal core cells and subsequently, ETA receptor has been shown to be expressed by the neighboring neural crest-derived ectomesenchymal cells. ETA receptor knockout mice also have the similar phenotype to that of ET-1 knockout mice. In order to understand the expression and regulation of ET-1 during the critical period for craniofacial and cardiac development, we searched for regulatory sequences in the 5'- and 3'- regiouf ET-1 gene that may govern branchial arch specific ET-1 expression in vivo by making use of transgenic mice carrying the lacZ reporter gene under the control of ET-1 genomic sequences (mPPET-1). We have identified thebranchial arch specific element (192bp) in the 3'-untranslated region (UTR) of ET-1genomic sequence. To investigate the *in vivo* function of this branchial mesodermal core-specific element of the ET-1 gene, we decided to knockout this element by conditional (loxP/cre system) knockout approach. The knockout construct was created by usinga 8.5kb fragment subcloned from the mouse ET-1 phage clone. We inserted loxP flanking the selection marker pGKneo to delete 242bp, which included the 192 bp branchial arch specific element, of the 3'UTR of the ET-1genomic sequences by linking 2.63 kb of the 5'fragment and 3.31 kb of the 3' fragment to the corresponding ends of thdoxP-tk-neo-pGK-loxP marker fragment. The resulting construct (9.44kb) is now being transfected into ES cells. After neo selection, thdoxP flanked portion will be Cre out by transient transfection and the chimeric mice will be generated. Three different genotype embryos from the F1 hetero and hetero mating will be collected at various stages to determine the ET-1 expression in thebranchial mesodermal core and to study its contribution to the craniofacial and cardiac development.

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1.4

Investigating the Function of Sox9 in Development

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SOX9 is a high mobility group (HMG) domain transcription factor, a member of the SOX family of proteins related to the mammalian Y-linked testis-determining factor SRY. During chondrogenesis in the mouse, *Sox9* is coexpressed with *Col2a1*, the gene encoding type-II collagen, the major component of cartilages. SOX9 has been shown to activate *COL2a1* directly. Mutations in human *SOX9* have been shown to be associated with autosomal dominant congenital disease, campomelic dysplasia (CD). CD is commonly characterised by malformation of the skeleton such as shortened and bowed limbs and retarded bone formation. CD is also characterised by nonskeletal anomalies affecting development of the olfactory system, brain ventricles, lung, heart and the urinogenital organs. In addition male to female sex reversal is associated with CD. The disease is usually lethal in the neonatal period. SOX9 may therefore be important for the development of the skeleton and a variety of other developmental processes.

Sox9 is expressed very strongly and early in the notochord which plays the key role in the development of skeleton. To study the function of Sox9 in the notochord, we have reproduced the mouse equivalent of one of the human CD mutations, in which there is a point mutation in the transcription activation domain. An enhancer *Hoxa1 EIII* was used to target expression of control and mutant *Sox9* constructs. Transgenic embryos expressing mutant *Sox9* show developmental abnormalities for example retardation of growth, abnormal heart and open neural tube. The analysis of those mutant phenotypes can gain insight into the function of SOX9 in early development.

1.5

ALDOSE REDUCTASE-DEFICIENT MICE ARE PROTECTED FROM MOTOR NERVE CONDUCTION DEFICIT ASSOCIATED WITH DIABETES

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Exaggerated flux through the polyol pathway during hyperglycemia is thought to be the major cause of lesions in the peripheral nerve. The polyol pathway consists of aldose reductase (AR), which converts glucose to sorbitol with the aid of NADPH as a co-factor, and sorbitol dehydrogenase (SDH), which oxidizes sorbitol to fructose using NAD^+. Numerous evidence supporting the role of AR comes from the animal studies showing that treatment with AR inhibitors lead to the prevention of sorbitol accumulation and improvement in MNCV deficits[1] although the efficacy of ARIs *in vivo* have been questioned. Alternately, blocking SDH activity by treating the animals with SDH inhibitor also prevented MNCV deficits although conflicting results has been obtained [2-3]. To clarify the role of these two enzymes in diabetic neuropathy, we adopted molecular genetics approach by making use of SDH-deficient mice. Previously, we have shown that the exaggerated sorbitol metabolism by SDH and the levels of sorbitol and fructose do not contribute to MNCV deficit in SDH-deficient mice[4]. We suggested that the exaggerated flux through AR causing the depletion of NADPH may be the major culprit in the pathogenesis of diabetic neuropathy. To confirm such notion, we introduced AR mutation into the SDH deficient mice creating complete deletion of polyol pathway. AR/SDH double mutant, AR deficient and wild type control mice were induced to become diabetic by streptozotocin injection (200mg/kg body weight) and compared the MNCV reduction. Similar to SDH deficient mice, there was no difference in MNCV between untreated AR/SDH deficient, AR deficient and wild type mice. The wild type diabetic mice showed significant MNCV reduction compared to the normoglycemic littermates ($P<0.001$, One-way ANOVA). However, the AR/SDH or AR deficient diabetic mice did not show reduction in MNCV and was not different from those of normoglycemic AR/SDH or AR deficient mice. The present data suggest that the exaggerated flux through AR may contribute more to the pathogenesis of diabetic neuropathy.

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1.6

A study of the molecular mechanism and pathogenesis of Schmid Metaphyseal Chondrodysplasia in transgenic mice

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Type X collagen is the major extracellular matrix component synthesized by hypertrophic chondrocytes in growth plates of long bones during endochondral ossification. It is a homotrimer of three $\alpha1(X)$ chains. Each $\alpha1(X)$ chain consists of a triple helical domain, flanked with globular domains, NC2 and NC1, at the N- and C-termini, respectively. Clusters of mutations in the NC1 domain of collagen X are associated with Schmid metaphyseal chondrodysplasia (SMCD), a human disorder with primary growth plate abnormalities. *In vitro* studies provide molecular mechanisms for these SMCD mutations, but there is a lack of in vivo data for the understanding of the pathogenesis of SMCD. Therefore transgenic mice (*col10-13del*) expressing a SMCD mutation were created. The mutation is a frameshift deletion of 13 nucleotides in the NC1 domain resulting in the production of 52 non-endogenous peptide sequence. *Col10-13del* are dwarf mice with expansion of hypertrophic zone. In addition, they exhibit progressive increased bone density that was not observed in human SMCD patients. Aiming to investigate whether these phenotypes are common with transgenic mice expressing other SMCD mutation and thus establishing a mouse SMCD model, transgenic mice expressing another SMCD mutation were created. The mutation selected is a nonsense mutation. Compared with the 13 nucleotides deletion, this mutation results in a truncation in the NC1 domain at the region of the 13 nucleotides deletion, but without the non-endogenous peptide predicted for the *col10-13del* mouse. Therefore, in addition to the SMCD phenotype, we can address whether the increased-bone phenotype of *col10-13del* is due to the presence of the non-endogenouse peptide to provide insights into the mechanism of increased bone formation.

1.7

THE MOLECULAR BASIS OF G6PD VARIANTS, PLYMOUTH AND MAHIDOL

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Among the 127 different human Glucose-6-phosphate dehydrogenase (G6PD) deficient mutations so far identified, it is surprising to find that the two mutants, $G6PD_{Plymouth}$ G163D and $G6PD_{Mahidol}$ G163S, which have different amino acid substituted at the exactly same polypeptide chain position, residue 163, manifest very different clinical severity. In order to obtain insights into the molecular mechanism underlying G6PD deficiency, these two naturally occurring mutants were constructed by site-directed mutagenesis of the G6PD WT Clone (pTrc99A/G6PD), which were expressed in *E.coli* and the proteins purified. By changing the conditions used and also co-expressing the recombinant with $G6PD_{Plymouth}$ in the presence of GroEL, the expression yield was increased by 50 fold for $G6PD_{Plymouth}$. This suggests that $G6PD_{Plymouth}$ appears to have difficulty in folding properly *in vivo* and this could be one of the factors that contribute towards enzyme deficiency. Preliminary characterisations (electrophoretic mobility, Michaelis constants for substrates and utilisation of substrate analogues) suggest that these two recombinant mutants are similar to their naturally occurring counter-parts. Stability in the presence and absence of $NADP^+$, heat-induced inactivation, urea-induced inactivation and reactivation studies were carried out for these mutants and the WT. These results, which may shed light on the different behaviour of the two mutants under differing conditions, will be discussed.

1.8

MOLECULAR EPIDEMIOLOGY OF MELIOIDOSIS IN AN OCEANARIUM IN HONG KONG

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Introduction. Melioidosis is a disease of animals and man caused by the bacterium *Burkholderia pseudomallei* and is endemic to South East Asia and Northern Australia. The organism is a free-living environmental saprophyte and can be isolated from soil and/or water. Melioidosis was first reported in Hong Kong in 1975 after dolphins died suddenly at a local oceanarium, Ocean Park. Other animals that have succumbed to melioidosis at this park, include pinnipeds, birds, a lesser panda and a llama.
Methods. A total of 30 environmental and clinical isolates of *B. pseudomallei* from various species, collected from Ocean Park, plus one human isolate from Hong Kong provided by a local hospital, were molecularly characterized. The genetic inter-relatedness of these isolates was compared by ribotype analysis and pulse field gel electrophoresis (PFGE) after digestion by *Xba*I, which is highly discriminatory.
Results. All isolates belonged to one ribotype pattern classified as Group I out of 44 known ribotype groups. Electrophoresis of the *Xba*I digested restriction fragments by PFGE demonstrated only two patterns (A and B) with one (pattern A) predominating and representing 87% of isolates from Ocean Park.
Conclusions. Our findings suggest that one strain of *B. pseudomallei* has been responsible for the vast majority of clinical cases at Ocean Park, indicating clonality of the organism. The earliest isolate in the collection belonging to this predominant strain was isolated in 1976. There may be a reservoir of this strain which is surviving in soil at the park over many years or infected animals may be contaminating their environment and creating a cycle of persistence. The isolates from the park should be compared with those outside the park to provide a wider epidemiological picture.

1.9

THE ROLE OF ENDOTHELIN-1 ON THE HOMEOSTASIS OF VASCULAR TONE IN THE ET-1 TRANSGENIC MICE

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Endothelin-1 (ET-1), a potent vasoconstrictor, is known to contribute to various cardiovascular disorders such as pulmonary and systemic hypertension, chronic heart failure and atherosclerosis based on the pharmacological and molecular studies. Pharmacological approach has been questioned due to its short half-life. On the other hand, homozygous ET-1 knockout mice die soon after birth with the unexpected craniofacial defect and whereas heterozygous ET-1 knockout mice showed unexpected hypertension. Therefore, we generated transgenic mice with endothelial cell-specific ET-1 over-expression by linking the ET-1 cDNA with endothelial specific transmembrane receptor tyrosine kinase (Tie-1) promoter. Two lines of Tie-1/ET-1 transgenic mice with transgene expression in number of tissues such as lung, brain, kidney, liver, etc by RT-PCR were chosen for further analysis (line 3771 and 3796). The level of ET-1 peptide in various organs was measured by enzyme immunoassay (ELISA). The ET-1 peptide level in lung of homozygous Tie-1/ET-1 mice is about 2 times higher than those of wild-type mice whereas the ET-1 peptide levels in brain, heart and kidney was not significantly different between transgenic and wild-type mice. In-situ hybridization was performed to determine the ET-1 mRNA expression at the cellular level using antisense ET-1 (mouse ET-1 specific) and SV40 (transgene-specific) riboprobe. ET-1 mRNA was more prominently expressed in the mesenchyme of the lung which appears to be endothelial cells of both line 3771 and 3796. The effects of ET-1 over-expression was studied by measuring systemic blood pressure of the Tie-1/ET-1 mice was measured in anesthetized 8-9 weeks old mice. The systemic blood pressure of homozygous Tie-1/ET-1 (both line 3771 and 3796) mice is significantly higher than those of wild-type mice (91 mmHg vs. 80 mmHg). At present, we are investigating the cause of hypertension in those transgenic mice with significant over-expression of ET-1 by electrocardiography and measurement of heart weights.

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1.10

Association of polymorphisms in the NRAMP1 gene and host susceptibility to tuberculosis

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Evidence for the genetic factor, human natural-resistance-associated-macrophage-protein 1 (NRAMP 1) gene to have a role in susceptibility to tuberculosis was found in West Africans and Koreans.The objective of the study is to investigate whether the polymorphisms in the four regions of the NRAMP 1 gene: 5'microsatellite, Intron4, D543N and 3'UTR are associated with susceptibility to tuberculosis among Chinese population in Hong Kong SAR.

Polymorphisms in NRAMP1 gene were investigated in a case-control study of tuberculosis in Hong Kong SAR, China. Polymerase Chain Reaction—Restriction Fragment Length Polymorphism (PCR-RFLP) analysis was used to type the polymorphisms and to determine the allelic frequencies of different regions of the gene among patients and controls. Patients suffering from tuberculosis were diagnosed by positive findings in chest X-ray, and sputum culture, while the controls were healthy blood donors with no history of tuberculosis. Relationship of the polymorphisms in the NRAMP 1 and the host susceptibility to tuberculosis among Chinese population in Hong Kong SAR will be highlighted and discussed.

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1.11

Generation and characterization of Sodium/myo-inositol cotransporter knockout mice

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Cells that experience prolonged hypertonic environment undergo various adaptations. One of these changes is the accumulation of small organic osmolytes which do not perturb the behavior of key metabolic enzymes. These osmolytes include sorbitol, betaine, glyceraldehyde phosphate and myo-inositol. Mammalian cells accumulate myo-inositol through an active transporter, the Sodium/Myo-inositol cotransporter (SMIT), which is also called SLC5A3 for solute carrier family 5, number 3 protein. Previous observations suggest that SMIT may have several physiological functions besides osmoregulation. Although inhibitors against SMIT can be used to understand its function, the in vivo efficacy and specificity of these drugs are not clear. On the other hand, mouse genome can be readily manipulated. We generated SMIT knockout mice which enable us to delineate the role of SMIT under both normal and disease conditions. Northern blot hybridization and RT-PCR analysis showed that the 12kb transcript of SMIT mRNA is absent in the tissues of homozygous knockout mice that express high level of SMIT, such as brain, kidney, testis and intestine. Osmolytes analysis using HPLC showed that there was approximately 70% reduction in tissue myo-inositol in the brain and kidney of homozygous knockout mice. We are testing whether the residual amount of tissue myo-inositol is due to blood myo-inositol, transporters other than SMIT or de novel synthesis of myo-inositol. Totally 37 litters of F2 mice were born from heterozygous to heterozygous F1 mice mating pairs and only 25% homozygous mice survive into adulthood (+/+:+/-:-/- = 22:161:90). In order to determine whether the mice die in utero or after birth, we sacrificed 8 pregnant heterozygous females, which mated with heterozygous male, at embryonic day 18.5 (E18.5). The average litter size was 9.4 and the genotypic ratio followed mandellian ratio (16 homozygous : 41 heterozygous : 18 wildtype). This indicates all homozygous SMIT knockout can survive up to E18.5 but died after birth. Postnatal death of homozygous knockout mice were rescued by feeding the pregnant female with 1% myo-inositol at the day of plug suggesting the death of neonates is related to myo-inositol depletion. Furthermore, a detailed characterization of knockout mice to understand the cause of lethality is in progress.

1.12

AFMP1 ENCODES AN ANTIGENIC CELL WALL GALACTOMANNOPROTEIN IN *ASPERGILLUS FUMIGATUS*

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We cloned the *AFMP1* gene, which encodes the first antigenic cell wall galactomannoprotein in *Aspergillus fumigatus*. *AFMP1* codes for a protein, Afmp1p, of 284 amino acid residues, with a few sequence features that are present in Mp1p, the antigenic cell wall mannoprotein in *Penicillium marneffei* that we described previously, as well as several other cell wall proteins of *Saccharomyces cerevisiae* and *Candida albicans*. It contains a serine- and threonine-rich region for O glycosylation, a signal peptide, and a putative glycosylphosphatidylinositol attachment signal sequence. Specific anti-Afmp1p antibody was generated with recombinant Afmp1p protein purified from *Escherichia coli* to allow further characterization of Afmp1p. Afmp1p has high affinity for *Galanthus nivalis* agglutinin, a characteristic indicative of a mannoprotein. Furthermore, it was recognized by a rat monoclonal antibody against the galactofuran side chain of galactomannan, showing that it is a galactomannoprotein. Ultrastructural analysis with immunogold staining indicated that Afmp1p is present in the cell walls of the hyphae and conidia of *A. fumigatus*. Finally, it was observed that patients with invasive aspergillosis due to *A. fumigatus* develop a specific antibody response against Afmp1p, suggesting that the recombinant protein and its monoclonal antibody may be useful for serodiagnosis in patients with aspergilloma or invasive aspergillosis, and the protein may represent a good cell surface target for host humoral immunitiy.

1.13

Regulation of gene expression in hypertrophic chondrocytes

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In the growth plate of hyaline cartilage, chondrocytes undergo a program of proliferation and differentiation. Hypertrophic chondrocytes are the terminally differentiated cells in cartilage and are defined by the expression of a particular set of genes different from the immature chondrocytes, such as type X collagen as well as others like EGF, p57kip2, and CRYBP1. We have utilized a hypertrophic chondrocytic cell line MCT to study the regulation of genes expressed in hypertrophic chondrocytes. Collagens and nuclear factors expression in MCT cells have been examined. We reported that MCT cells are expressing osteogenic markers, suggesting the cell line has attained a terminal hypertrophic or osteoblastic phenotype. By using 3H-proline labeling assay, we also observed that the cells are capable of expressing high level of type I, III, and X but low level of type II collagen under growth arrest condition. Furthermore, MCT cells are able to express an exogenous type X collagen reporter construct, suggesting the cells can acquire a hypertrophic phenotype upon growth arrest and are suitable to our study. We are now aiming to establish an ecdysone inducible gene expression system in MCT cells. To date we have succeeded in producing lines expressing the functional ecdysone receptors (VgRXR), which is a regulatory component of the system. The expression of an inducible LacZ reporter in these lines is responsive to the administration of hormone. Such induction system in MCT cells will provide means to study gene regulation in hypertrophic chondrocytes in vitro.

1.14

RELATIONSHIPS BETWEEN EPIDERMAL GROWTH FACTOR PRECURSOR AND IGFs *IN VIVO*

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Epidermal growth factor (EGF) is a strong mitogen that stimulates cell proliferation in cell culture systems and in intact animals. However, its physiological roles are still unclear. The mature form of EGF (53 amino acids) is generated from a much larger precursor (EGFP) of 1217 amino acids. The EGFP is a transmembrane molecule with 8-EGF like repeats N-terminal to mature EGF. The mid portion shares a 33% homology with the low density lipoprotein receptor which suggests that EGFP could function as a membrane-bound receptor. And its unprocessed form present in kidney further suggests that such a receptor function could be operative in the distal convoluted tubules of kidney, most probably taking some roles in transportation of sodium and hydrogen ions. In order to get insight for the role of EGF and find out the relationships between EGF signaling and other growth factor systems, transgenic models should be made for detailed analysis *in vivo*. Our recent findings suggested that widespread overexpression of a shortened form of EGFP in mice causes growth retardation. Serum IGFBP-3 in these transgenic animals was significantly reduced. It is widely studied that growth rate is majorly controlled by growth hormone and insulin-like growth factor (IGF) family and most of the circulating IGFs are produced by hepatocytes. Therefore, we are going to generate transgenic mice that overexpress EGFP confined to liver only in order to elucidate the specific effect of EGF on the IGF system and growth. We have made a construct with the mouse EGFP cDNA driven by a ubiquitous cytomegalovirus (CMV) promoter in order to investigate the physiological functions in mice generally. Another liver-specific construct was also made with the cDNA driven by a α-fetoprotein enhancer and a basal β-globin promoter for detailed analysis between EGF and IGF system and find out their relationships *in vivo*.

1.15

THE CLINICAL ASSOCIATION OF MANNOSE BINDING LECTIN WITH HEPATITIS B INFECTION

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Background : Hepatitis B virus (HBV) infection is common in the Chinese population. After HBV infection, the patients may be either asymptomatic (carrier of HBV and do not have clinical symptoms) or symptomatic (patients with clinical symptoms: cirrhosis, hepatocellular carcinoma or ascites spontaneous bacterial peritonitis). Human immune system has different ways in responding to HBV infection. Mannose binding lectin (MBL) is one of the components that may have a role in responding to HBV infection. The mannose residues in the middle envelope of the HBV may be a target of the MBL. MBL may recognizes the target residue and activate opsonization or lectin complement pathway to eliminate the virus. Serum MBL level can be affected by the polymorphisms in exon 1 (codon 52, 54 and 57) and promoter polymorphism (H/L alleles at –550 and X/Y alleles at –221). The polymorphisms in exon and promoter haplotypes LX lead to low serum MBL level. Previous studies show that codon 52 and 54 polymorphisms are related to chronic hepatitis B virus (HBV) infection in Caucasian and progression of HBV liver disease in Chinese patients respectively[1,2].
Aim : In this study, the significance of codon 54 polymorphism and promoter haplotypes of *MBL* in HBV infection of Hong Kong Chinese is being investigated.
Method : The serum MBL level, frequencies of codon 54 polymorphism and promoter haplotypes between the control group and patients group were compared. Different groups of patients were collected:

1. asymptomatic HBsAg carriers that were not treated with lamivudine (n=112)
2. symptomatic HBsAg positive patients with hepatocellular carcinoma, cirrhosis and spontaneous bacterial peritonitis (n=28)

Results : The serum MBL level of the HBsAg carriers group (1307 ug/litre, n=112) is significantly lower than the control group (2214 ug/litre, n=109) where $P<0.013$. The gene frequency of the codon 54 polymorphism is lower in control group (0.09, n=83) as compared to the HBsAg carriers (0.15, n=112), but not yet significant. Further work is in progress and results relating to the other groups will be presented.
Conclusion : Low serum MBL level leads to a higher probability to become HBV carriers. Codon 54 polymorphism, which leads to low serum MBL level, may be a risk factor for HBV carriers. The importance of promoter polymorphism of MBL in preventing HBV carriers state and disease is being studied.

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1.16

Feedback inhibition of redox-responsive transcription factors Yap1p and Skn7p in *Sacchromyces cerevisiae* by peroxiredoxins Tsa1p and Tsa2p

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Peroxiredoxins (PRXs) are a family of antioxidant enzymes conserved from bacteria to humans. In this study, we set out to characterize yeast PRXs using genetic and molecular biological approaches. Among the five PRXs in yeast, Tsa2p has not been extensively studied albeit its striking homology with the well characterized Tsa1p.

We constructed and characterized Δtsa2 and Δtsa1Δtsa2 strains. The double deletant was much more susceptible to oxidants than Δtsa1/Δtsa2 strain. Notably, the tsa1/2-null mutants exhibited a hypersensitivity to nitric oxide donors GSNO and diethylamine NONOate. Thus we have the first evidence that eukaryotic PRXs play important roles in the protection against reactive nitrogen species.

We also documented a compensational activation of Yap1p and Skn7p in Δtsa2 and Δtsa1Δtsa2 strains. Several Yap1p- and Skn7p-dependent genes (TSA1, TSA2 and TRX2) were activated 3-5-fold as shown in LacZ reporter assay and Northern blotting. Results from gel mobility shift assay indicate that Yap1p is hyperactive in the Δtsa1Δtsa2 strain. All of this suggests that loss of Tsa1p/Tsa2p may have de-repressed Yap1p and Skn7p.

We then constitutively overexpressed Tsa1p and/or Tsa2p in yeast using a GAL1 promoter. Surprisingly, these strains were hyper-susceptible to H_2O_2. An inhibition of Yap1p and Skn7p was confirmed by LacZ reporter assay and Northern blotting. Taken together, our findings support a feedback control of Yap1p and Skn7p by Tsa1p and Tsa2p.

1.17

3' REGION OF THE *XENOPUS* GATA-1B TRANSCRIPT IS RESPONSIBLE FOR THE ANTINEUROGENIC EFFECT OF GATA-1B

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The erythroid transcription factor GATA-1 in *Xenopus* has been cloned as a pair of presumably duplicated genes designated as xGATA-1a and xGATA-1b. Previously we showed that although both xGATA-1a and xGATA-1b are able to stimulate erythropoiesis, only xGATA-1b is capable of inhibiting neurogenesis in *Xenopus* embryos[1]. In this study we constructed chimeras of these two genes by swapping corresponding parts of their coding region and their 3' untranslated region (UTR). The neural inhibitory ability of the chimeras was then assayed in animal cap (AC) induced to neuralize by dominant negative BMP-4 receptor(DNBR). Of the chimeras tested so far, all those containing the last three condons of xGATA-1b and its 3'UTR are able to inhibit neurogenesis. The effect of the 3'UTR is not on the stability of the mRNA. Further experiments using deletion constructs demonstrated that most of the middle region of 3'UTR is dispensable for the neural inhibitory function. These observations suggest the influence of 3'UTR in xGATA-1 on the inhibition of neurogenesis. The minimum sequence for the GATA-1b 3'UTR to exert the effect is currently under investigation.

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1.18

DNA ENGINEERING UTILIZING THYMIDYLATE SYNTHASE A (THY A) SELECTION SYSTEM IN *ESCHERICHIA COLI*

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The bacteriophage λ recombination system in *Escherichia coli* (the *red* system) is a useful tool for DNA engineering.[1-3] The red system allows DNA cloning and modification without DNA restriction enzymes and ligase. A single selectable marker has been developed to further improve the *red* system. This improvement not only allows one to efficiently perform point mutations by homologous recombination at very high frequency, it also provides a selection system for easy identification of the desired clone. The strategy is to utilize the same marker for both positive and negative selection. This selectable system involves the synthesis of thymine coupled by the consumption of tetrahydrofolate as a substrate of the reaction mediated by thymidylate synthase A.[4] The selection procedure requires trimethoprim and thymine as selective reagents. A *thyA*- λ phage *Red* strain was created by homologous recombination, which will be used to repair 3 point mutations in the promoter region of pGK-neo, a plasmid frequently used for gene targeting experiments in mammalian cells. Next, this *thyA* system will be used to create a point mutation in a mouse homolog of the human collagen gene COL10A1, which is known to cause Schmid metaphyseal chondrodysplasia.

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1.19

PDZ DOMAIN CONTAINING FACTORS AND REGULATION OF INSULIN GENE TRANSCRIPTION

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PIN-1 is a novel PDZ-domain factor isolated in a yeast two-hybrid screen for E12-interacting protein in the insulinoma cell line, INS-1. E12 as a basic helix-loop-helix transcription factor activates insulin gene expression by binding to upstream E-box sequences. PIN-1 may, therefore, play a role in regulating insulin gene expression through its interaction with E12. Sequence comparison reveals that C-terminus of PIN-1 has high homology with that of pro-IL-16, 33.3% identity and 52.1% similarity. Pro-IL-16 has to be processed post-translationally before the bioactive IL-16 is secreted. The modification takes place at the site that is highly homologous to PIN-1's C-terminal, suggesting that PIN-1 might also undergo the same or similar modification before it changes into its bioactive form. Experiments were designated to study possible post-translational processing of PIN-1 and its subcellular localization by epitope tagging. Functional assay will be done to study the function of PIN-1 in the regulation of insulin gene expression.

1.20

Adeno-associated virus (AAV) mediated CTLA4Ig transfer into rat orthotopic liver transplant

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Background and Objectives: Gene transfer technique has been increasingly used in organ transplantation. Adeno-associated vector has recently become an attractive tool for gene therapy in transplantation because of its non-pathogenicity, broad host range of infectivity, including non-dividing cells. Acute rejection is one of the most severe post-transplantation complications that lead to graft loss and recipient death. Costimulatory pathway plays an important role in T cell activation and proliferation during rejection. CTLA4Ig, an immunoglobulin fusion protein, has been proven to be able to block costimulatory pathway by its potent combination with receptor on antigen presenting cells (APC). The purpose of this study is to transfer CTLA4Ig into orthotopic liver graft by a recombinant adeno-associated vector (rAAV) and detect its protein expression.
Materials and Methods: Inbred male Lewis rats are donors and recipients. rAAV-CTLA4Ig was constructed according to two plasmids homogenous methods. Viral vectors were administrated by portal vein perfusion of isolated whole liver graft. The graft was preserved in 4°C Ringer's solution for 2 hours, and then implanted orthotopically into recipient's abdominal cavity. The recipients were sacrificed 3, 5 and 7 days after transplantation. Immunohistochemistry and ELISA were done to detect CTLA4Ig expression in the graft and its soluble form in serum.
Results: No CTLA4Ig expression and soluble CTLA4Ig were found in day 3 graft and serum. CTLA4Ig expression was seen in 1.5 % hepatocytes and endothelial cells in day 5 graft, and detectable soluble CTLA4Ig was found in the same day. 2% hepatocytes and endothelial cells showed positive CTLA4Ig expression in day 7 graft and serum soluble CTLA4Ig level was doubled compared to day 5. In addition, the AAV-transduced syngeneic liver graft maintained normal structure.
Conclusion: AAV is a stable and safe vector that can direct gene interest into liver graft, and help its protein expression. Further study should be done to detect long term protein expression.

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2.1

CASPASE INHIBITORS PREVENT SPINAL MOTONEURONS FROM DEATH FOLLOWING ROOT AVULSION IN NEONATAL RATS

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In neonatal rats, the loss of motoneurons following root avulsion is mediated by apoptosis. Caspases are important mediators of apoptosis. The present study examined the effects of caspase inhibition on the survival of spinal motoneurons in neonatal rats. On the day of birth, C7 spinal root was avulsed and the animals were treated by either a general caspase inhibitor, benzyloxycarbonyl-Asp(OMe) fluoromethylketone (Boc-D-FMK), or a specific caspase-3 inhibitor, N-acetyl-Asp-Glu-Val-Asp aldehyde (Ac-DEVD-CHO). In control animals, virtually all motoneurons died 7 days after root avulsion. Treatment with either 0.5μg Boc-D-FMK or 1μg Ac-DEVD-CHO enhanced the survival of motoneurons by 80% and 85% of controls, respectively, for up to 14 days post-injury. Lower concentrations resulted in less motoneuron survival. Long-term survival effect of caspase inhibitors and the capacity to regenerate from these rescued motoneurons are now under investigation.

2.2

Neuroprotective effects of extracts from American gingseng, ginkgo biloba and St. John's Wort on striatal dopaminergic neurons against 1-methyl-4-phenyl-1,2,4,6-tetrahydropyrdine (MPTP)-induced toxicity

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Parkinson's disease is an idiopathic disease characterized by a depletion of neurotransmitter and loss of dopaminergic (DA) neurons in basal ganglia. It has been suggested that some herbal extracts, e.g. ginkgo biloba, can enhance the survival of injured CNS neurons. We examined the neuroprotective action of several herbal extracts, which have been standardized by ChemBioPrint ™ (CV Technologies, Inc., Canada) procedure, on MPTP-induced neurotoxicity in striatal DA neurons. C57Bl/6N mice (6-9 months old) were given 4 i.p. injections of MPTP (10mg/kg, 2 hrs interval) on day 1. Animals were fed orally with either vehicle or different types of herbal extracts (AD-FX, Remember-FX, Menta-FX, Cold-FX, from CV Technologies, Inc., Canada) from day 1 to day 14, and were sacrificed on day 15. DA neurons in substantial nigra (SN) were visualized by tyrosine hydroxylase (TH) immunocytochemistry. TH-positive neurons were counted under light microscope. A reduction of 37% of DA neurons in SN was observed after treatment with MPTP. Daily administration of Remember-FX (North Amercian Ginseng extract) rescued 77% ($p<0.05$) of the neurons from MPTP-induced neurotoxicity. However, other herbal extracts have no significant effect on the survival of the neurons. The result indicated that extracts of American ginseng could provide neuroprotective effects for the striatal dopaminergic neurons against MPTP-induced neurotoxicity.

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2.3

NEUROPEPTIDE Y AND RELATED COMPOUNDS CAN MODULATE NITRIC OXIDE PRODUCTION DURING FOCAL CEREBRAL ISCHEMIA IN THE RAT. AN ELECTRON PARAMAGNETIC RESONANCE STUDY

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Background and Purpose: In a rat endovascular middle cerebral artery occlusion (MCAO) model, we previously showed that intracerebroventricular (ICV) injection of NPY or a Y1 agonist increased the infarct volume. Nevertheless, ICV injection of a NPY Y1 antagonist, BIBP3226, dramatically reduced the infarct volume. Nitric oxide (NO) is a key mediator of tissue damage during cerebral ischemia. In this study, we examined the modulating effects of NPY and the related compounds on NO production during MCAO.

Methods: Male Sprague-Dawley rats were anaesthetised with sodium pentobarbital to undergo ipsilateral endovascular MCAO with a 4-o nylon suture. NPY (10μg/kg), [Leu31, Pro34]-NPY (30μg/kg, a Y1 agonist), BIBP3226 (15μg/kg, a Y1 antagonist), NPY3-36 (15μg/kg, a Y2 agonist) or vehicle was administered by a slow ICV injection at 2 minutes after onset of ischemia. The rats were decapitated at 15 minutes after MCAO. The brains were sliced into 2mm coronal sections between Bregma levels +6 and –8 mm. NO measurement was made in the brain slices between Bregma levels +2 and –4 mm. NO trapping reagents, diethyldithiocarbamate (DETC) and Fe-citrate, were administered by intraperitoneal and subcutaneous injection, respectively, at 15 minutes prior to MCAO. Tissue concentration of NO was measured using electron paramagnetic resonance (EPR) spectroscopy. Results from the ischemic side were expressed as a percentage of the non-ischemic side and compared among groups using two-tailed Student's t test.

Results: After 15 minutes of focal ischemia, the relative NO concentration increased to 131.9±8.0% (mean±SEM; n=8). NPY treatment significantly increased the NO signal (250.9±50.5%; n=8, $P<0.05$), whereas BIBP3226 dramatically reduced the NO signal (69.6±8.8%; n=8, $P<0.05$). Treatment with [Leu31, Pro34]-NPY and NPY3-36 produced no change in NO signal (133.4±13.3%, n=8; 129.2±21.8%, n=8).

Conclusions: Exogenous NPY enhances the NO production at 15 minutes of focal cerebral ischemia, whereas BIBP3226 reverses this effect. Our results can explain the exacerbation of infarction by ICV injection of NPY during cerebral ischemia.

2.4

MIXTURE OF AMERICAN GINSENG, *GINKGO BILOBA* AND ST. JOHN'S WORT EXTRACTS ENHANCES THE SURVIVAL OF AXOTOMIZED RETINAL GANGLION CELLS

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Recent evidence suggests that free radicals play a role in the delayed death of axotomized retinal ganglion cells (RGCs). Extracts of American ginseng (AG), *Ginkgo biloba* (GB) and St. John's Wort (SJW), all being shown to exhibit free radical scavenging ability, should be able to offer neuroprotection in a model of optic nerve (ON) transection. Transection of the ON 1.5 mm from the optic disc was performed on adult hamsters. Starting on the day of operation, the animals received daily oral administration for 7 days of : (1) vehicle (0.01M PBS), (2) GB extract (2, 6 or 12 mg), (3) AG extract (10, 20 or 30 mg), (4) SJW extract (10, 20 or 30 mg), (5) 30 mg of AD-FX, a mixture consisted of 80% AG and 20% GB extracts by weight or (6) 30 mg of Menta-FX, a mixture composed of 30.8% AG, 7.7% GB and 61.5% SJW extracts by weight. AD-FX and Menta-FX were purchased from CV Technologies, Canada. RGCs survival 7 days post axotomy was quantified by applying 6% FluoroGold to the transected ON to retrogradely label the surviving RGCs 2 days before the animals were killed. The retinae were dissected and the number of fluorescent labeled RGCs was counted. We found that only treatment with Menta-FX can significantly augment the number of surviving RGCs 7 days after axotomy ($p<0.01$, one way ANOVA). We therefore showed for the first time that a mixture of GB, AG and SJW extracts, but not each of the extracts alone, significantly enhanced axotomized RGCs survival 7 days after ON transection.

2.5

MAXIMAL ISOMETRIC MUSCLE STRENGTH OF THE CERVICAL SPINE IN HEALTHY VOLUNTEERS

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Background: Despite its high incidence, studies on neck pain are relatively sparse. Mayer (1994) suggested that normative data regarding the strength of the cervical musculature in healthy individuals are required for comparative evaluation of patients with neck pain. **Objective**: To describe the maximal isometric strength of the cervical musculature measured by a Multi Cervical Rehabilitation Unit, in different directions in 91 (45 male, 46 female, aged 19-84) subjects without neck pain. **Methods**: During the measurement the subject sat in an adjustable chair, the trunk was secured with the shoulder restraint system. An adjustable head brace fitted with a load cell, was secured around the head of the subject. After 2-3 practice trials the subject was instructed to do three consecutive steady contractions as hard as they could, with 10 seconds rest in between each contraction and 2 minutes rest between different directions. The peak isometric strength for each of the six directions (flexion, extension, lateral flexions, protraction and retraction) was calculated. **Results:** Neck muscles exhibited twice the maximal strength relative to the mass of the head-neck complex. No significant difference was found in muscle strength between different age groups except for extension at 20° (p=0.03-0.93). Isometric strength in all directions in men was 1.2-1.7 times that in women (p=0.00-0.02). For example the maximal extensor strength in men was 98.1 Newtons (10kg) while that in women was 65.6 Newtons (6.7kg). Correlations between physical measurements (height and weight) and strength values were all insignificant in both genders. **Conclusion:** Both men and women can maintain high levels of cervical muscle strength up to the seventh decade. In accordance with other muscle groups, men have approximately 20% to 70% greater strength than women. As the cervical musculature exhibits high strength levels simple antigravity training would be insufficient for the strengthening of neck muscles.

2.6

Design of Implant Plate for distal radius fracture

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Objectives:
This project seeks to develop a plate for distal radius fractures that provide:
- Rigid fixation on complicated distal radius fractures.
- Anatomical profile for accurate reduction and to provide stability.
- Low-profiled for the minimization of the soft tissue irritation.
- Limited contacted on the bone surface.
- Fine contouring can be perform in situ

Background of research:
Fractures of the distal end of radius have been estimated to account for 1/6 of all fractures that are seen and treated in emergency rooms. Open reduction and rigid internal fixation have been the treatment choice for unstable articular and periarticular fractures. However, if there is an inappropriate reduction, malalignment results in limitation of movement (Fernandez 1993), changes in load distribution (short et al 1987), midcarpal instability (Taleisnik and Watson 1984) and an increased risk of osteoarthritis of the radiocarpal joint.

Nowadays, there are a number of internal fixation implants available in the market like the T-plates and the Pi-Plates. However, there are still no properly designed implants such that it can cope with the complex fracture perfectly. For instance, the most popular internal fixation that the surgeons used is the AO-ORIF T-Plate. Owning to the protruding screw heads and the sharp edge of the implant, these factors contributed the problem of soft tissue irritation. For a consistent irritation, the patient who received the implant may result tenosynovitis especially the area of the radial wrist extensor tendon. Moreover, the new Titanium Distal Radius Plate System (Pi-Plate) was developed as an new generation, however, there was a report revealed that there were complications on tendon rupture as well as the plate breakage.

The aims of the present study are to provide a device that should have components that can be reliably fixed to the skeletal structure of patients, and shaped to allow early wrist movement. With the integration of the concepts of an anatomical design, low profile, and accurate reduction accessories, it is believed that a new generation of the implant plate will be developed. Of course, this will need further development in design and biomechanical testing, after which it will be ready for human trial.

2.7

NEUROCHEMICAL AND BEHAVIORAL STUDIES ON TRANSGENIC MICE CARRYING HUMAN PRESENILIN-1 GENE

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Wild-type and mutant human presenilin-1 transgenic mice have been generated with conventional microinjection method. Expression of human presenilin-1 mRNA in brains of the transgenic mice was confirmed by RT-PCR and further restriction digestion of RT-PCR products. Using a specific monoclonal antibody Western blotting analysis was performed to demonstrate protein expression of human presenilin-1 in brains of these mice. These transgenic mice together with their respective non-transgenic littermates were tested in a series of behavioral experiments including open field activity, object recognition task, water maze reference memory task, water maze working memory task and anxiety test. Behavioral data are being processed from videotapes and neurochemical tests on the ratio of Abeta42 to Abeta40 and ChAT activity levels are in progress.

2.8

CILIARY NEUROTROPHIC FACTOR PREVENTS THE DEATH OF RETINAL GANGLION CELLS IN A RAT GLAUCOMA MODEL

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The protective effect of ciliary neurotrophic factor (CNTF) on retinal ganglion cells (RGCs) in a rat glaucoma model with increased intraocular pressure (IOP) was investigated. Elevated IOP (about 1.5 times above normal) of the right eye in 36 SD rats was induced by laser photocoagulation of the episcleral and limbal veins. The laser treatments were done twice with 7 days separation. On the next day after the second laser treatment, the animals were divided into two groups. CNTF group (n=18): 2 μg CNTF (PeproTech Inc) in 2μl of vehicle was injected into the right eye. Control group (n=18): 2 μl of PBS was injected into the right eye. IOP of both eyes of each animal was measured once a week. One week before killing the animals, a piece of gelfoam soaked with 6% Fluoro-Gold was placed on the surface of both superior colliculi. After a survival of 2, 4 or 8 weeks following the first laser treatment, the left and right eyes were enulceated and flat-mounted retinas were prepared. The number of labelled RGCs was systematically counted in four quadrants of all the retinas. In all groups, the changes in the densities of RGCs were expressed as percent loss of RGCs comparing the laser treated and contralateral, control eyes from the same animal. (%RGC loss = 1 – [RGC density in eye with elevated IOP/RGC density in eye with normal IOP] X 100%). There was a significant difference in the %RGC loss in the two weeks or 4 weeks groups between the CNTF and PBS animals. (2 weeks- CNTF: -7.4% and PBS: 12.6% ($p<0.01$); 4 weeks- CNTF: 4.6% and PBS: 21.2%($p<0.01$)). However, there was no significant difference in the RGC loss in the 8 weeks CNTF and PBS groups (CNTF: 19.6% and PBS: 25.8%, $p>0.05$). The IOP in the CNTF or PBS animals maintained at an elevated level up until 8 weeks. We concluded that CNTF injected intravitreally may provide protection against glaucoma–induced RGC death in rats up to 4 weeks. This effect was not due to a decrease in IOP.

2.9

EXPRESSION OF CHONDROITIN SULFATE DURING EMBRYONIC HINDBRAIN DEVELOPMENT

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During early development of the mouse, the hindbrain region is segmented into repetitive segments, known as rhombomeres. These segments are found to be important in patterning subsequent hindbrain development. Positive staining of chondroitin sulfate (CS) epitopes in the rhombomere boundaries suggests that CS-containing isoforms may be involved. To locate CS expression in mouse embryos at stages 9.5 dpc and 10.5 dpc when rhombomere formation actively takes place, we used the monoclonal antibody CS-56. The epitopes were found in the boundaries between the neuroepithelium and mesenchyme, with stronger signals in 10.5 dpc than in 9.5 dpc. As chondroitin 6-sulfate was found to neutralize CS-56 immunoreactivity, we hypothesisd that cells that produce the CS epitope in the boundary environment are upregulated in expression of chondroitin 6-sulfotransferase (C6ST). *In situ* hybridization was therefore performed with a riboprobe specific for C6ST. Signals were found in mesenchymal tissue rather than in the neuroepithelium of both 9.5 dpc and 10.5 dpc preparations. These results can be interpreted in one of 2 ways: (1) C6ST found in the mesenchyme was not responsible for the synthesis of the CS epitope found in the neuroepithelial boundaries; (2) migratory cells that were upregulated in C6ST deposited CS-56 positive glycoforms along their paths, thus resulting in the observed accumulation of the glycoforms in the boundaries. Further work will be performed to identify the migratory cells that are upregulated in C6ST expression.

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2.10

TRINUCLEOTIDE CAG REPEATS IN X-LINKED SPINAL AND BULBAR MUSCULAR ATROPHY: AN *IN VITRO* MODEL TO EXAMINE THE ROLE OF NEUROMUSCULAR INTERDEPENDENCY

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X-linked spinal and bulbar muscular atrophy (SBMA or Kennedy's disease) is a neurodegenerative disease that is characterized by loss of motor neurons in the spinal cord and brainstem in adulthood. The underlying defect in SBMA is the CAG trinucleotide repeat expansion in the first exon of the androgen receptor gene which leads to an elongation of the polyglutamine tract present in the N-terminal transactivation domain of the encoded protein. Motor neurons and skeletal muscle are intimately linked in term of mutual dependency during development and maintenance of postnatal functional units. We hypothesized that muscle plays an important role in the pathogenesis of SBMA, in which genetically affected motor neurons degenerate only when their dependency on the nurturing and protective mechanisms subserved by their target muscles are disrupted. In the present study, a co-culture model of neuronal cell line NG108-15 and muscle cell line C_2C_{12} is used to examine the above hypothesis. Constructs encoding the human androgen receptor containing normal and mutated CAG repeats driven under general (CMV) and neural cell specific (thy1.2) promoters were generated. Stability of the CAG repeat was determined by fluoroescent-based PCR genotyping. The instability of the number of CAG repeats during the cloning process was overcome by the using special *E.coli* strain (TOP10). Immunocytochemical and immunoblotting studies demonstrated the expression of human androgen receptor in C_2C_{12}, confirming the successful transfection and expression of the androgen receptor constructs. The effect of such mutant human androgen receptor transgene on the expression levels of insulin-like growth factor-1, neutrotrophin-3 and glial-derived neurotrophic factors and other functional characteristics of these cells will be examined. The results of this study will contribute to the understanding of the pathogenetic mechanisms involved in SBMA.

2.11

BILIRUBIN INDUCES APOPTOSIS IN GLIAL CELLS THROUGH CASPASE ACTIVATION

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The cytotoxicity of bilirubin has been proved in neural cells and glial cells, but the mechanism is not clear until now. We have found that bilirubin induced apoptosis in cultured glial cells before. In this study, we tested the mechanism in bilirubin-induced apoptosis and the possible effect of caspase inhibitor.

We used mouse primary glial cell culture to examine the mechanism of bilirubin insult. Two weeks old neonatal astroglial culture was treated with 0.72 mM bilirubin and 0.6 mM albumin (Ratio 1.2) from 0 to 12h. Apoptosis was tested by TUNEL/DAPI staining and nuclear size was measured using Stereo Investigator analysis system (version 3.0). Caspase-3 was tested by immunoblotting. A general caspase inhibitor BOC-Asp(Ome)-Fluoromethyl Ketone (B-D-FMK) was added to some bilirubin-treated cells at 100μM from 0h of insult for its ability of inhibiting apoptosis.

Immunoblotting analysis showed that proform of caspase-3 (32kDa) was processed into the 17kDa active form by 7h of insult. With B-D-FMK treatment, apoptosis was decreased from 24.3±4.7% (mean±SD) to 11.6±3.2% at 9h and 53.8±4.0% to 36.7±4.2% at 12h ($p<0.01$). Nuclear diameters of bilirubin-treated cells were significantly smaller than those of control cells (5.4±1.5μM at 9 hr and 4.9±1.2μM at 12 hr of treatment versus 7.8±0.1μM in control; $p<0.001$). With B-D-FMK treatment, surviving cells had larger diameters, 6.4±1.7μM at 9h and 5.9±1.5μM at 12h, that those without B-D-FMK ($p<0.01$) but did not achieve the healthy nuclear sizes as in control cells ($p<0.01$). We concluded that bilirubin induced apoptosis in glial cells through the activation of caspases. Caspase inhibitor has a potential treatment role in bilirubin-induced cell damage.

2.12

MELATONIN ABOLISHES THE INCREASE IN NITRIC OXIDE PRODUCTION DURING CEREBRAL ISCHEMIA IN THE RAT

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Excessive production of nitric oxide (NO) is an important mediator of excitotoxic necrosis in severe ischemia. Melatonin, the neurohormone secreted predominantly by the pineal gland, has been shown to inhibit nitric oxide (NO) production in the brain via suppression of nitric oxide synthase. Our previous results indicated that exogenous melatonin protects against focal cerebral ischemia in a middle cerebral artery occlusion (MCAO) model. In this study, we used electron paramagnetic resonance (EPR) spectroscopy to explore the effect of exogenous melatonin on NO production in the MCAO model.

Methods: Adult male Sprague-Dawley rats were anaesthetised with sodium pentobarbital to undergo reversible endovascular MCAO for 15minutes. Melatonin (at 1.5, 5, 15, or 50 mg/kg) or the vehicle was given as a single intraperitoneal (IP) injection at 0.5 hour before the MCAO. The NO production was measured using NO trapping reagents and EPR spectroscopy. Body temperature was maintained constant, and hemodynamic parameters were continuously monitored during anaesthesia. The rats were decapitated after 15 minutes of ischemia, and specimens of brain tissue were placed in an EPR tube to measure the NO concentration. Results from the ischemic side were expressed as a percentage of the non-ischemic side.

The relative NO concentration was 132.64±7.96% (mean±SEM; n=8 rats) with vehicle, and the results with 1.5, 5, and 50 mg/kg melatonin were 104.20±11.4% (n=8 rats), 55.67±5.57% (n=11 rats), and 104.86±12.56% (n=9 rats), respectively. The NO production was significantly reduced with melatonin at 5mg/kg ($P < 0.05$, 2-tailed Student's t test). There was no significant difference in the hemodynamic parameters among all the groups.

Exogenous melatonin at 5 mg/kg but not lower or higher doses abolishes the increase in NO production during ischemia, when given as a single IP dose at 0.5 hour before 15 minutes of MCAO. This inhibitory effect of melatonin on NO production during ischemia and the ability of melatonin to scavenge free radicals may be responsible for its neuroprotective effect in the MCAO model.

2.13

THE EFFECT OF ELECTRICAL VESTIBULAR STIMULATION OF THE LABYRINTH ON BAROREFLEX RESPONSE IN ANESTHETIZED RATS

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To investigate the influence of the vestibular system on cardiovascular control, the cardiovascular responses before and after electrical stimulation of the vestibular end organs were examined in urethane anesthetized female adult Sprague Dawely rats. Train pulses (500-800 μA) of either 10 min (short) or 120 min (long) duration was delivered to the labyrinth through two silver-silver chloride electrodes that were implanted into the round and oval windows on the left side. Cardiovascular parameters monitored included: basal mean blood pressure (MBP), heart rate (HR) as well as phenylephrine-induced baroreflex response and its sensitivity index (ΔHR/ΔMBP). These cardiovascular responses were evaluated at 3 time points: 30 min before electrical stimulation (control), immediately after and 30 min after the termination of electrical stimulation. The basal MBP and HR remained unaltered in both the short and long duration groups. In the short duration group, the bradycardia induced by phenylephrine decreased from −30 bpm (control) to −38 bpm immediately after the electrical stimulation ($P<0.05$) while the sensitivity index increased from 1.04 to 1.43 bpm/mmHg ($P<0.01$). Baroreflex response and its sensitivity returned to their original levels at 30 min after electrical stimulation. After long duration electrical stimulation, the change in MBP induced by phenylephrine increased from 28.33 mmHg (control) to 31.17 mmHg immediately after the electrical stimulation ($P<0.05$). Further, the bradycardia induced by phenylephrine was comparable to that of the short duration group. These changes were still observed at 30 min after electrical stimulation. In addition, an increase in the baroreflex sensitivity index was observed at 30 min after the stimulation. In the sham operated group (i.e. without electrical stimulation), however, there was no change in all the cardiovascular parameters measured. These findings suggest that vestibular activation might participate in the regulation of baroreflex response.

2.14

STUDYING THE ROLE OF MOUSE *Sox10* IN SCHWANN CELL DEVELOPMENT BY CONDITIONAL GENE TARGETING

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Schwann cells are originated from the neural crest. During development the neural crest cells develop as immature Schwann cells which at postnatal stages differentiate into myelinating and non-myelinating Schwann cells[1]. Several transcription factors, including *Krox-20*, *SCIP*, *Pax 3* and *Sox 10*, have been implicated in Schwann cell development. The *Sox10* gene encodes a HMG domain transcription factor which has been shown to be important for neural crest development. At later stages of development, *Sox10* expression is restricted to the glial cell lineage in both the CNS (the oligodendrocytes) and the PNS (the Schwann cells)[2], suggesting that *Sox10* probably play an important role in glial cell determination. The *Dominant megacolon* mutant, caused by a point mutation in the *Sox10* gene, has phenotypic defect on neural crest derivatives including Schwann cells[3]. However, homozygous *Dom* mutation is embryonic lethal, making it important to examine Schwann cell development in this mutant. To study the role *Sox10* in Schwann cell development in mice, a mutant model will be produced in which mutation of *Sox 10* will be triggered in a tissue-specific manner. To achieve this, we created a targeting vector in which exon 5 of *Sox10*, which encodes the transactivation domain, is flanked by a pair of *loxP* sites. Using the green fluorescent protein as a reporter, upon *cre* recombinase mediated targeted deletion of exon 5, GFP will be expressed to mark the cells with mutant *Sox10*. The mutant mice carrying this targeted allele will express *Sox10* normally. However, when they are crossed with other transgenic mouse lines which express *cre* recombinase in a specific tissue, e.g. in developing Schwann cells, *cre*-mediated deletion will produce the desired tissue-specific knock out mutant.

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2.16

INTRAOPERATIVE CORRECTION FORCE MEASUREMENTS IN ADOLESCENT IDIOPATHIC SCOLIOSIS

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Introduction: Severe Scoliosis (Cobb angle measurement is more than 50°) requires operation to straighten the spine by implanting the spinal instrumentation. This correction is typically achieved by use of a rod bent into an appropriate "C" or "S" shape. This rod is then fitted to the spine and rotated from the coronal plane to the sagittal plane, thereby reducing the scoliotic curve and restoring a normal lordosis and kyphosis. To analyze the force required to correct the scoliotic spine we have developed a device to measure and record the rotational torque applied to the rod during surgery.

Methodology: The spinal torque-measuring device consists of an adapter fitted with strain gauges and a data acquisition system. This adapter fits to a standard rod holder, allowing the torsion applied to correct the spine be recorded and plotted on a PC. The correction of the scoliotic curve cannot be achieved by a single rotation, and so the data normally consists of torsion measurements from some 4 to 5 turns of the rod. Between turns, the rod is held in place by another rod holder while the rod holder fitted with the adapter is repositioned. Following data collection, all data are reduced and plotted on standard spreadsheet software.

Results: Preliminary results have been obtained successfully from six patients (1M and 5F). The peak torques were found to be in the range 0.6 to 4.0 Nm. The maximum torque was normally found at the third or fourth turn. The force magnitude seemed inversely proportion to the fulcrum flexibility[1]. No previous work has recorded values for the mechanical properties of the rotation of long sections of the spine as a whole.

Summary: The aim of this series of experiments is to establish values for an appropriate torsional correction force to the scoliotic spine. These values will be used in the design parameters for a *superelastic* rod which will use this property to achieve a gradual correction of the scoliotic curvature. Measurements are still continuing, and we aim to collect data from approximately 30 patients to ensure that the results are statistically significant.

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2.17

Effect of eccentric contractions on force and intracellular pH regulation in rat soleus muscles

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The effect of eccentric contraction on force, intracellular pH was studied in rat soleus muscle fibers. Muscle bundles consisting of 3-5 muscle cells were isolated, placed in the Krebs' solution equilibrated with 95% O_2 and 5% CO_2. The muscle fiber was then mounted for isometric force recording while $[pH]_i$ was measured with pH-dependent fluorescent indicator, 2',7'-bis-(2-carboxyethyl)-5-(and-6)-carboxyfluorescein, BCECF.

The force-frequency relationship of the muscle fibers (n =6) was determined before and immediately after they had been stretched by 30% of the optimal length (11.08 ± 0.52mm) during a series of 10 tetani (the eccentric contraction). Following the eccentric contraction, there was an increase in the optimal length by 4.47% ($p < 0.001$), in support of the popping-sarcomere hypothesis as proposed in the literature, and force was reduced to less than 25.78% of control at all stimulation frequencies ($p < 0.05$).

Intracellular pH regulation was examined (n = 4) by inducing an acute intracellular acid load with a brief prepulse of 20mM NH4Cl, and then observing the time course of pH_i recovery back to the initial level. The pH_i recovered from 6.35 ± 0.12 to 6.75 ± 0.18 in 30 minutes prior to eccentric contraction, and from 6.17 ± 0.12 to 6.18 ± 0.12 in 30 minutes post-eccentric contraction.

We conclude that following eccentric contraction, there is a significant reduction in the force and an impairment in the ability of the muscle cell to correct its intracellular pH following acid loading.

2.18

SPONTANEOUS ACTIVITY OF PRIMARY VESTIBULAR AFFERENT NEURONS DURING POSTNATAL DEVELOPMENT OF THE RAT

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To examine the maturation profile of primary vestibular afferents, their activities at the horizontal stationary position were studied in young (ranging from P8 to P28) and adult rats. With the use of glass micropipettes, the extracellular activities of neurons within the superior Scarpa's Ganglion were recorded *in vivo* in rats decerebrated under halothane anesthesia. Based on the coefficient of variation of their interspike intervals (ISI) and the ISI histograms, the spontaneous activities of vestibular afferents were categorized into regular and irregular neurons. From P8 to P9, the vestibular afferents fired in bursts with varying periods of silence. No regular afferent was observed in this period. In P10-P12, both regular and irregular afferents were observed, with a mean spontaneous firing rate of 10.5 spikes/s. Neurons exhibiting multiple discharges were also observed in this postnatal period. After the second postnatal week, the spontaneous activity increased gradually with age ($P<0.001$): from 29.2 spikes/s (P14) to 60.4 spikes/s (adult). The proportion of regular afferents also increased with age from 21% in P14 to 54% in adult. Our results indicate that the primary vestibular afferents undergo progressive changes in spontaneous discharge patterns during postnatal development. The physiological implications of these changes will be discussed with reference to the development of postural and vestibulocollic reflexes.

3.1

Sequence Comparison of Human and Mouse Oviduct-Specific Glycoprotein Promoters

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The oviduct-specific glycoprotein (OGP) is expressed in the oviduct of many mammalian species and it is postulated to have a role in fertilization and early embryonic development. In order to understand the regulation and expression of the OGP, we cloned the human (HOGP) and mouse (MOGP) OGP promoters and studied their trans-activities on various cell lines under estrogen stimulation. The 5' flanking sequences of HOGP and MOGP were isolated from genomic DNA using a PCR based GenomeWalker kit and their respective sizes are 2.5kbp and 3.6kbp. Both have partial coding sequences (exon 1 and exon 2)and DNA sequence analysis for both reveals a number of consensus binding sites for known transcriptional factors such as AP1, AP2, LBP1 and TATA-like sequences. Interestingly, several half-estrogen responsive elements (5'-TGACC-3') were found throughout the promoter sequence and intron 1 of HOGP and MOGP, whereas they were present only 5' to the exon 1 in the hamster OGP promoter sequence. All three had an imperfect ERE site (5'-GGTCANNNTGACT-3') located upstream of the transcriptional start sites. The transcriptional start site for HOGP was found to be 31 bp upstream of the translational start site. The HOGP and MOGP promoters were cloned into pBlue-TOPO reporter vector in both orientations and transfected into CHO-K1, MCF-7 and immortalized human oviduct epithelial (OE_{89} E6E7) cell lines. Our preliminary data has shown that HOGP fragments can trans-activate reporter constructs in OE_{89} E6E7 cells under estrogen stimulation, but not on other cell lines. Interestingly, the intron 1 of both HOGP and MOGP promoters has intrinsic trans-activation activity in CHO-K1 cells, the mechanisms of which are not clearly understood. These findings shall facilitate our understanding of the role of OGP in the process of fertilization.

This project is partially supported by a CRCG grant (HKU) to KFL. Sequence data for HOGP and MOGP have been deposited with the GenBank under Accession nos. AF 189710 and AF 148876 respectively.

3.2

EFFECT OF MAGNESIUM TANSHINOATE B ON PROTEIN KINASES

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Magnesium tanshinoate B is a purified compound from Radix Salviae Miltiorrhizae, a Chinese herbal medicine. Our laboratory has shown that MTB has a significant inhibitory effect on stress-activated protein (SAP) kinase. The objective of the present study was to investigate the effect of MTB on protein kinases other than SAP kinase. p38 mitogen-activated protein kinase (p38 MAPK) and SAP kinase belong to family of kinases activated by stress factors. Therefore, the effect of MTB on p38 MAPK was first studied. In our model system, it was found that the activation of p38 MAPK was transient with a peak after 15 min of ischaemia. If 20 min reperfusion was introduced after global ischaemia, there was a significant activation of p38 MAPK. This increased p38 MAPK activity was maintained for up to 60 min of ischaemia with 20 min reperfusion. Although MTB had significant inhibitory effect on SAP kinase activity, it did not have any significant effect on p38 MAPK activity. It was also found that although there was an increase in the Ca^{2+}-dependent PKC activity after ischaemia/reperfusion, MTB did not have any effect on the activity of this kinase. The Ca^{2+}-independent PKC activity was unaffected in the absence or presence of MTB following ischaemia/reperfusion. The *in vitro* effect of MTB (10 nM to 10 mM) on other protein kinases was also studied. At these concentrations of MTB, there was no significant effect on the activity of both cAMP-dependent protein kinase and p42 MAPK. A significant inhibition of calcium/calmodulin-dependent protein kinase II was only observed at 1 mM of MTB. In conclusion, MTB is demonstrated to have some specificity towards its inhibition of SAP kinase. (This study is supported by the RGC and NSFC/RGC)

3.3

GINKGOLIDES AND BILOBALIDE SELECTIVELY INHIBIT INDUCIBLE NITRIC OXIDE SYNTHASE

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Nitric oxide (NO) is a principal mediator in many physiological and pathological processes. NO produced by constitutive nitric oxide synthase in endothelial cells (eNOS) acts as a vasodilator while excess NO production due to elevated expression of inducible nitric oxide synthase (iNOS) may pose cytotoxic effects to cells in the vascular wall. We demonstrated in our previous study that the extract of ginkgo biloba leaves (EGb) inhibited the iNOS-mediated NO production. The objective of the present study was to investigate the effect of several active EGb components on the iNOS-mediated NO production in human monocytic cell (THP-1) derived macrophages. Ginkgolide A, ginkgolide B or bilobalide (0.25 – 1.0 μg/mL) caused a 30 – 65% reduction in the levels of NO metabolites released by THP-1 macrophages after 4 hr incubation with a corresponding decrease in the iNOS activity. Such inhibitory effect was due to a reduction in iNOS mRNA levels. Taken together, these results suggest that ginkgolide A, ginkgolide B and bilobalide may contribute to the selective inhibitory effect of EGb on iNOS expression.

3.4

PRETREATMENT WITH U50488H RESTORES THE CALCIUM CONTENT IN THE SARCOPLASMIC RETICULUM IN THE RAT VENTRICULAR MYOCYTE FOLLOWING METABOLIC INHIBITION

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κ-opioid receptor (OR) restores the contractility in ventricular myocytes subjected to metabolic inhibition (MI), one of the consequences of ischemia. This is accompanied by electrically-induced intracellular calcium ($[Ca^{2+}]_i$) transient, which is directly proportional to contraction of the ventricular myocyte. Since the electrically induced $[Ca^{2+}]_i$ transient represents influx of Ca^{2+} upon electrical stimulation and Ca^{2+} release from the sarcoplasmic reticulum (SR), the intracellular Ca^{2+} store, triggered by the influx of Ca^{2+}. The restoration of the $[Ca^{2+}]_i$ transient may be due to restoration of the Ca^{2+} release from the intracellular Ca^{2+} store. To test the hypothesis, we measured $[Ca^{2+}]_i$ and its transients induced by electrical stimulation or caffeine in single ventricular myocytes with a spectrofluorometric method employed using fura 2/AM as calcium indicator. Caffeine depletes Ca^{2+} of SR and thus the caffeine-induced $[Ca^{2+}]_i$ transient represents the content of the intracellular Ca^{2+} store. Single ventricular myocytes, isolated from rat heart with a collagenase method, were preconditioned with U50, 488H(U_{50}), a selective κ-OR agonist, at a concentration ($3x10^{-5}$ M) known to be blocked by nor-BNI, a selective κ-OR antagonist, for 3 cycles of 1 min each. This was followed by 3 min of reperfusion and MI with 10mM 2-deoxy-D-glucose (2-DOG) and 10 mM sodium hydrosulphite ($Na_2S_2O_4$) for 9 min. It was found that MI decreased the amplitudes of electrically-and caffeine-induced $[Ca^{2+}]_i$ transients. The effects were attenuated with preconditioning with U_{50}, a result similar to preconditioning with MI with 10mM 2-DOG and 10 mM $Na_2S_2O_4$ for 3 cycles of 3 min each. In conclusion, results confirm that both pretreatment with a κ-OR agonist and preconditioning with MI, which is mediated by κ-OR agonist, restore the electrically-induced $[Ca^{2+}]_i$ transient and thus the contractility. This may be mainly due to reduced release of Ca^{2+} from the intracellular Ca^{2+} store. (Supported by the Research Grants Council, Hong Kong)

3.5

EFFECTS OF ESTROGEN ON HUMAN CATECHOL-O-METHYLTRANSFERASE

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Catechol-*O*-methyltransferase (COMT, EC 2.1.1.6) is crucial to the metabolism of catechols and catecholamines. Two isoforms of COMT exist: soluble- (S-COMT) and membrane-bound (MB-COMT) that are encoded by two transcripts (1.3-kb and 1.5-kb in human) regulated by proximal and distal promoters respectively. We previously reported physiologic concentrations of 17β-estradiol (E2) down-regulated the 1.3-kb transcript in a dose-dependent manner in MCF-7 cells. We also showed that a 280-bp COMT proximal promoter fragment containing two half-palindromic estrogen response elements (ERE) was important in mediating this effect. Using a radioenzymatic assay, we now report that E2 (10^{-9} to 10^{-7} M) reduced COMT activity in MCF-7 cells in a dose-dependent manner. E2 similarly reduced S-COMT protein levels using Western analysis. A specific estrogen receptor (ER) antagonist (ICI 182780) blocked these estrogenic effects on COMT protein expression and enzyme activity. Our gelshift assays showed that ER in nuclear proteins extracted from MCF-7 cells, which were pretreated with E2 (10^{-9} M) for 48 hr, bound directly to half-palindromic EREs in the 280-bp COMT proximal promoter fragment. E2 (10^{-9} to 10^{-7} M) increased this binding in a dose-dependent manner. Hence, we propose that E2 decreased COMT activity through down-regulation of its gene and protein expression mediated via the ER in a dose-dependent manner, associated with a parallel increase in direct ER-DNA binding. Our study may shed an important insight in the pathophysiology of estrogen-related human disorders.

3.6

ACUTE INHIBITION OF CONTRACTION IN PORCINE CORONARY ARTERIES BY 17β-ESTRADIOL INVOLVES BOTH THE CYCLIC AMP AND THE CYCLIC GMP PATHWAYS

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Over the years, it has been established that the cardioprotective effects of estrogen are attributed to its genomic actions through its favorable alteration of lipid metabolism and its antioxidant effects. Only recently has it been suggested that estrogen also exerts rapid non-genomic actions on the vasculature. Previous studies from our laboratory demonstrate that short-term (20 min) exposure of porcine coronary arteries to a physiological level of 17β-estradiol (1 nM) enhances endothelium-independent relaxation via a cyclic AMP-dependent pathway and inhibits agonist-induced contraction. The present study aims to investigate the mechanism of inhibition of contraction by 17β-estradiol in porcine coronary arteries. In particular, the possibility of involvement of cyclic AMP and cyclic GMP pathways was explored. Our results showed that the cyclic AMP analogue 8-Br-cAMP, the protein kinase A activator Sp-cyclic AMPS and the cyclic GMP analogue 8-Bromo-cyclic GMP mimicked the inhibition of U46619-induced contraction by 17β-estradiol (1 nM). The inhibition was not further increased by the co-incubation of 8-Br-cyclic AMP or 8-Br-cyclic GMP with 17β-estradiol. The effect of 17β-estradiol was abolished by pre-incubating the porcine coronary arterial rings with the cyclic AMP antagonist Rp-8-Br-cAMPS and the cyclic GMP antagonist Rp-8-Br-cGMPS. These results suggest that the inhibition of contraction by 17β-estradiol, at least in porcine coronary arterial model, involves both the cyclic AMP and the cyclic GMP pathways.

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3.7

Galactosemia and rat granulosa cell apoptosis

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Galactosemia is a genetic disease with deficiency of an galactose-1-uridyltransferase resulting in the accumulation of galactose or galactose-1-phosphate in the blood and tissues. Clinical consequences include mental retardation, visual cataract and ovarian failure. A galactosemic rat model has developed to study ovarian dysfunction in galactosemia. We postulate that there is an extensive apoptosis of growing follicles which may be due to an imbalance of cell death inducers and survial signals . Fas and Fas Ligand (FasL) are cell death inducer and they can induce apoptosis in various tissues. It has been found that they mediated granulosa cell apoptosis during follicular atresia (1-2). On the other hand, the inhibitor of apoptosis protein (IAP) is the survial signal and it can suppress apoptosis and IAP expression was very low in atretic follicles (3). In this study, control and galactosemic rats were killed at different time points after hCG injection to assess granulosa cell apoptosis, Fas/FasL and IAP (Riap) expression by in situ TUNEL and Western blot, respectively. Fas and FasL contents and apoptosis were significantly higher in the galactosemic group than in the control. On the other hand, the Riap expression of the galactosemic group were lower. These findings support our hypothesis that ovarian dyfunction in galactosemic subjects is due to increased apoptosis in granulosa cells of maturing follicles.

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3.8

BLOOD PRESSURE IS RELATED TO OBESITY IN WOMEN

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Objective: We have previously found that hypertension is strongly related to obesity. The aim of the present investigation is to explore further indices of obesity associated with blood pressure.
Methods: Thirty-six hypertensive patients (16 men, 20 women; age 55 ± 10 yrs) not on antihypertensive drugs were screened prior to participation in a clinical study of qigong. The medical history was obtained and the subjects were examined with special attention to blood pressure and indices of obesity. Body fat was assessed using bioelectrical impedence (Body Fat Analyzer, Tanita).
Results: Fat mass, waist circumference and body mass index were intercorrelated. In hypertensive men, blood pressure was not significantly related to any of the variables examined. In hypertensive women, the systolic blood pressure was related to age ($r = 0.55$, $p = 0.01$), waist circumference ($r = 0.53$, $p = 0.04$) and waist-hip ratio ($r = 0.63$, $p = 0.004$). Multiple regression analysis suggested that only the waist-hip ratio was an independent predictor of systolic blood pressure in hypertensive women.
Conclusions: Our findings suggest that blood pressure is related to obesity in women more than men. The waist-hip ratio accounted for 39% of the variance in systolic blood pressure in hypertensive women. Although obesity may be partly influenced by genes, it is modifiable. Avoidance of obesity or weight reduction in these patients may help to decrease their blood pressure.

3.9

EFFECTS OF GENISTEIN ON PORCINE CORONARY ARTERIAL CONTRACTION *IN VITRO*

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Recent studies have implicated the involvement of tyrosine kinase in regulating the contractile responses in vascular smooth muscle to certain agonists. Inhibition of tyrosine kinase activities by genistein directly reduces the ET-1-induced Ca^{2+} response in vascular smooth muscle suggesting a critical role played by tyrosine kinase (1). However, the concentration used is usually as high as 30 μM that can directly produce up to 70% relaxation and is usually physiological irrelevant. On the other hand, it is a bioactive component found in soybeans and can be obtained from plant-based diets. Hence, this study was focused on the effect of genistein at physiological achievable concentration on vascular contraction. Porcine coronary artery was used in the organ bath experiments and genistein was allowed to incubate for 30 minutes before performing the dose-response curve for various agonists. The effects of genistein on various constricting agents were investigated and the role of endothelium was also studied. In this study, 3 μM genistein with little direct effect was selected for incubation. Genistein reduced receptor-mediated vasoconstriction induced by U46619, 5-HT and ET-1 to a greater extend when compared to the voltage-gated vasoconstriction induced by KCl. Use of nitric oxide synthase inhibitor and the removal of endothelium were unable to eliminate the reduced contraction in the presence of genistein. Contribution of tyrosine kinase activities was further investigated by tyrphostin 23, a structurally different tyrosine kinase inhibitor. At 30 μM, it was also unable to reduce contraction to U46619. This suggested that other mechanism(s) might be involved. In summary, genistein at 3 μM can reduce vasoconstriction mediated by receptor-gated vasoconstrictors through endothelium-independent mechanism. Furthermore, such reduction in contraction does not mediated through tyrosine kinase inhibition.

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3.10

ADRENOMEDULLIN IS INVOLVED IN THE DEPRESSED Ca^{2+} TRANSIENTS IN MYOCYTES FROM LPS-TREATED RATS

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Background: Adrenomedullin is a novel hypotensive peptide that was originally isolated from human pheochromocytoma (1). The main actions of ADM are a potent and long-lasting vasodilation, diuresis and natriuresis. Increased circulating ADM levels have been reported in the patients with heart failure, including septic shock (2). However, the direct effect of ADM on cardiac function remains unknown. **Methods:** An animal model of septic shock was established by intraperitoneal injection of lipopolysaccharide (LPS) to Sprague-Dawley rats. Plasma and cardiac levels of ADM were determined by radioimmunoassay. Electrically induced Ca^{2+} transients were measured with the Ca^{2+} indicator Fura-2. **Results:** A marked increase of ADM was observed both in plasma and heart from LPS-treated rats. In ventricular myocytes isolated from LPS-treated rats, the Ca^{2+} transients induced by electrical field stimulation were significantly depressed when compared with those recorded from myocytes from sham control rats. Pretreatment of these cells with ADM (22-52), a specific ADM-receptor antagonist, increased the Ca^{2+} transients in response to electrical stimulation to values similar to those obtained in myocytes isolated from sham control rats. In ventricular myocytes from control rats, ADM decreased the amplitude of electrically induced Ca^{2+} transients. This effect was blocked by ADM (22-52), which itself had no effect on Ca^{2+} transients. **Conclusion:** These data indicate that the overproduction of ADM plays an important role in regulating Ca^{2+} homeostasis in cardiac myocytes from LPS-treated rats and suggest a potentially therapeutic effect of blockade of ADM receptors during septic shock.

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3.11

EXPRESSION OF MONOCYTE CHEMOATTRACTANT PROTEIN-1 IN HOMOCYSTEINE-TREATED HUMAN ENDOTHELIAL CELLS

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Hyperhomocysteinemia has been identified as an independent risk factor for atherosclerosis. The infiltration of monocytes into the arterial wall is one of the key events during atherogenesis. Monocyte chemoattractant protein-1 (MCP-1) is a potent chemokine that stimulates the migration of monocytes into the intima of the arterial wall. The mechanism by which increased monocyte infiltration occurs in atherosclerotic lesions in patients with hyperhomocysteinemia has not been delineated. The objective of this study was to investigate the effects of homocysteine on MCP-1 production in human endothelial cells. Cells were treated with various concentrations of homocysteine. MCP-1 secretion into culture media was analyzed by ELISA. MCP-1 mRNA levels in cells were detected by RT-PCR methods. Chemotactic activity of media collected from homocysteine-treated cells was examined by a chemotaxis assay. Results from this study suggested that MCP-1 secretion and mRNA levels were enhanced in homocysteine-treated endothelial cells which resulted in an enhanced monocyte chemotaxis. This may partly explain the increased risk of atherosclerosis in hyperhomocysteinemic patients.

3.12

EFFECT OF *SALVIAE MILTIORRHIZAE* EXTRACT AND THE MAGNESIUM TANSHINONE B ENRICHED FRACTION ON THE VASCULAR CONTRACTION OF PORCINE CORONARY ARTERY

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Salviae miltiorrhizae (Dan Shen) is a medicinal herb which has been used in the Chinese community to treat cardiovascular diseases. It has been reported that this herb processes various pharmacological effects in the cardiovascular system. One of the major effects is reduction of blood pressure. (Kamata *et al.* 1994 and Lei and Chiou 1986). The focus of the present study is to investigate the effect of the herb in modulating vascular contraction.

The vascular effect of an extract of *Salviae miltiorrhizae* (SME) and a magnesium tanshinone B enriched fraction of *Salviae miltiorrhizae* (MTB75) was investigated with porcine coronary arterial rings. Magnitude of dose response vasoconstriction to U46619, 5-hydroxytryptamine (5-HT) and endothelin-1 (ET-1) was suppressed by pre-incubation of the arterial rings with SME (3 mg/ml and 6 mg/ml) for 30 minutes. While the minimal dose of SME required for suppressing the KCl induced vasoconstriction was 6 mg/ml. Pre-incubation of MTB75 at the dosage of 0.5 mg/ml and 1 mg/ml inhibited the dose response vasoconstriction to U46619 but not to KCl. The effect of SME is not endothelial dependent since removing the endothelium of arteries failed to abolish the contraction suppressive effect of SME. However, the slowly developed vasoconstriction induced by phorbol ester was significantly attenuated by pre-incubation of SME (1 mg/ml and 3 mg/ml)

Therefore, *Salviae miltiorrhizae* suppresses vasoconstriction induced by U46619, 5-HT, ET-1 and KCl. The inhibitory effect of *Salviae miltiorrhizae* on the vasoconstriction induced by the contracting agonists is greater than that induced by depolarization. Protein kinase C related pathway may be involved in the vasoconstriction inhibitory effect.

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3.13

AN APPLICATION OF THE STAGES OF CHANGE MODEL TO INCREASE CALCIUM INTAKE OF PREMENOPAUSAL WOMEN

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The Stages-of-Change Model provides a theoretical framework that may increase the effectiveness of a behavior change program. Intervention that matches the stages of change of the subjects is more effective than the traditional intervention program which provides knowledge alone. Low calcium intake is one of the factors related to the risk of osteoporosis. Women's bone density begins to decrease in the fifties. Compared with the calcium value of 800 mg/day of China RDA, Hong Kong women aged 45 -55 and older had a significant low intake of calcium of 573.3 mg/day (1). The objectives of this study are to develop and evaluate the effectiveness of a psychoeducational program to help subjects to increase calcium intake, and to study the calcium intake of Hong Kong Chinese premenopausal women. 400 premenopausal Hong Kong Chinese women will be recruited and randomly divided into control or intervention group. Knowledge, beliefs and attitudes on osteoporosis and calcium will be studied by a questionnaire. An algorithm will be used to measure the stages of change. Practices of consuming dietary calcium and the confirmation of stage placement will be measured by a three-day dietary record. A psychoeducational program will be provided to the intervention group. Subjects will be divided into the preaction stage group or the action/maintenance stage group. The intervention program will be tailored to meet the needs of the groups. The goal of the subjects is to consume 800 mg or more c+alcium a day. The same questionnaires and food record will be administered and completed by both the control and intervention groups at 6 months after the intervention. The progress of stages of change of the intervention group will be measured. Factors associated with the change of calcium intake will be measured by multiple regression. Differences between the intervention and control groups will be determined using t-test or chi-square. Paired t-test will be used to identify changes of knowledge, attitudes, beliefs and practices after the intervention. Results are important in establishing effective intervention programs to lower the risk of osteoporosis of premenopausal women.

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3.14

THE HEPATOCYTE NUCLEAR FACTOR-1α GENE PLAYS A SIGNIFICANT ROLE IN SOUTHERN CHINESE SUBJECTS WITH EARLY-ONSET TYPE 2 DIABETES

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Maturity-onset diabetes of the young (MODY) is characterized by an early age of onset (<25 years) and an autosomal dominant mode of inheritance [1]. To date, mutations in the hepatocyte nuclear factor (HNF) -4α gene (MODY1), the glucokinase (GCK) gene (MODY2), the HNF-1α gene (MODY3), the insulin promoter factor 1(IPF1) gene (MODY4) and the HNF-1β gene (MODY5) are known to cause MODY [2-6]. The HNF-1α mutations, associated with the usual diabetic complications, have been shown to be the commonest cause of MODY in the UK [3]. In this study, we investigated its importance in early-onset type 2 diabetes in Southern Chinese. We screened 29 unrelated Southern Chinese subjects with early-onset (diagnosed at ≤30 years of age) type 2 diabetes and at least one affected sibling. The 10 exons, flanking introns and promoter region were amplified by polymerase chain reaction using specific primers [3] and were sequenced directly. Four of the 29 (13.8%) unrelated diabetic subjects were found to have mutations, including three reported mutations (frameshift mutation Pro379fsdelCT, nonsense mutation R171X, and missense mutation G20R) and one novel missense mutation (P112L), which was not detected in 100 unrelated subjects with normal glucose tolerance. All these mutations were located in highly conserved regions. In conclusion, mutations in the HNF-1α gene appear to be an important cause of early-onset type 2 diabetes in Southern Chinese.

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4.1

A RAPID ASSAY TO DETECT GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD) DEFICIENCY

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Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common human enzyme deficiency. An estimated 400 million people worldwide are affected by this enzymopathy with the majority from Southeast Asia, the Middle East and Africa. Individuals with the deficiency are likely to develop haemolytic anemia, prolonged neonatal jaundice and other diseases. An immunoassay against normal G6PD could provide a quick, accurate and inexpensive detection system for screening large populations in Asian countries. Four monoclonal antibodies have been isolated thus far, produced by the hybridoma cells from the fusion of P3 myeloma cells and spleen plasma cells from mice immunized with purified human G6PD overexpressed in *E.coli* cells. Western blot analysis showed that all of them react against the purified human G6PD and normal blood lysate, with negative results on other dehydrogenases. The Ig heavy and light chain isotypes of the monoclonal antibodies were determined by immunodiffusion. Polyclonal goat antibodies against human-G6PD were also produced so as to construct a capture assay to enhance binding of the native form of h-G6PD; this will increase the sensitivity of the assay system.

4.2

HEPARAN SULPHATE PROTECTION OF NEUTROPHIL ELASTASE ACTIVITY IN BRONCHIAL SECRETIONS OF PATIENTS WITH BRONCHIECTASIS

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Bronchiectasis is a common airway disease which involves persistent recruitment of neutrophils to inflamed bronchial sites. In the sputum sols of these patients, we observed stimulation of neutrophil-mediated proteolytic activity despite the presence of anti-proteases. To identify the relevant proteases in sputum sols, casein zymography was performed. For each sol sample, a clarified zone suggestive of activity was revealed against a Coomassie blue-stained background; this zone extended from the sample well to a front of nominally 90 kDa. Zymograms stained also with Alcian blue revealed positive staining in the clarified zone, suggesting that polyanionic materials co-migrated with the zone of protease activity. Western blot using antibodies against heparan sulphate, neutrophil elastase or α_1-antitrypsin showed positive result in the region that demonstrated protease activity. This suggests that neutrophil elastase forms aggregate with heparan sulphate and its physiological inhibitor, α_1-antitrypsin in the sputum sols of patients with bronchiectasis. Though exogenuous α_1-antitrypsin can completely inhibit the activity of commercial preparations of neutophil elastase, only 60 % of equivalent activity in sputum sol can be inhibited by the same treatment. Taken together, the results suggest that neutrophil elastase in the sputum sols of patients with bronchiectasis is protected from inhibitors by association with heparan sulphates.

We acknowledge support from Research Grants Council (HK).

4.3

A Study of Health Promotion Behaviors and Lifestyle Factors: Applying the Transtheoretical Model on Healthy Living Survey 1999

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Objectives: To describe the stages of change in health promotion behaviors in Hong Kong based on the information obtained from the Healthy Living Survey 1999, with the use of Transtheoretical Model (TTM) of behavioral change; and to analyze the relationship between lifestyle factors and health promotion behaviors.

Background: The TTM proposes that people change health-related behavior by moving through several stages of change. It has been applied to specific health behaviors, but there appears to be no studies about its application on general health behaviors, e.g. the adoption of health promotion behaviors. Moreover, there are no data of its application in Asian population.

Methods: Cross-sectional telephone survey in 1999 of a random sample of Hong Kong households. A total of 3,270 Chinese Cantonese-speaking adults were successfully interviewed. The response rate was 72%. The respondents' stages of change were assessed for health promotion behaviors, according to their past action and future intention of doing those behaviors to improve health or to prevent diseases. The respondents were classified into three stages: Precontemplation/Contemplation, Preparation/Relapse, and Action/Maintenance, in which individuals in later stages were more willing and committed to do health promotion behaviors. We analyzed the relationship between the stages of change and lifestyle factors, using binary logistic regression adjusted for demographic factors.

Results: Individuals in the Precontemplation/Contemplation stage compared with those in the other two stages were more likely to be older, less educated, have less income, have poorer personal hygiene, have less healthy diet, heavy smokers, have not exercised in past month, have better self-perceived physical and mental health, have no social support, and have poorer health knowledge. The main significant difference between people in Preparation/Relapse stage and those in Action/Maintenance stage was that the latter had experienced fewer barriers when they were doing those health promotion behaviors.

Conclusion: The Transtheoretical Model was found to be applicable to Chinese adults for general health promotion behaviors, since individuals in different stages of change showed different patterns of lifestyle factors. This classification scheme can provide information for the development of stage-matched health promotion programs and fill in the gaps in the literature about the application of the Transtheoretical Model. Furthermore, there is a relationship between lifestyle factors and health promotion behaviors, with those who were more willing and committed to do so also seemed to have a healthier lifestyle.

4.4

EFFECT OF PERITONEAL DIALYSIS FLUID (PDF) AND HEPARIN ON PROTEOGLYCAN SYNTHESIS IN HUMAN PERITONEAL MESOTHELIAL CELLS (HPMC)

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Prolonged exposure of the peritoneum to PDF has been shown to result in both structural and functional deterioration of the peritoneal membrane. Heparin is a highly anionic molecule that may modulate diabetic nephropathy in animal models and peritoneal transport function, but the mechanisms remain unclear. We investigated the effects of spent PDF and heparin on proteoglycan (PG) synthesis in HPMC.

Results: HPMC were stimulated with pooled spent non-infected or infected PDF in the absence or presence of heparin (2U/ml) for up to 96 h. In the presence of PDF, HPMC became elongated, hypertrophic and fibroblastic in appearance. The addition of heparin greatly improved HPMC morphology with the preservation of their cobblestone appearance. Both non-infected and infected spent PDF significantly induced HPMC proliferation in a time-dependent manner. In the presence of heparin, HPMC proliferation was maintained at basal level. Gene expression of TGF-β1 and PGs by HPMC was induced in a time-dependent manner in the presence of PDF. These changes were reversed in the presence of heparin.

Conclusion: These preliminary data suggest that PG synthesis is differentially modulated by spent PDF. Heparin has a potential beneficial role in maintaining the morphology and integrity of HPMC, which has obvious implications in the preservation of peritoneal function.

4.5

THE PRODUCTION OF A NOVEL IMMUNOSUPPRESSIVE FUSION PROTEIN $CTLA_4$-Ig AND A STUDY OF ITS IMMUNOSUPPRESSIVE FUNCTION

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The activation of naïve T cells to allo-antigen requires two signals. The first signal is delivered by the T cell receptor and Ag/MHC engagement. The second, costimulatory signal is delivered by the interaction of Ag-stimulated T cell and antigen presenting cell (APC). B_7 and CD28/$CTLA_4$ ligation is one of the important costimulatory pathways. $CTLA_4$Ig is a novel immunosuppressive reagent which blocks this pathway, however, this fusion protein is not commercially available. In the present study, we have produced fusion protein $CTLA_4$Ig by using the transfected cell culture and tested the immunosuppressive function of the protein. **Materials and Methods:** (1) The production of $CTLA_4$Ig: The plasmid DNA containing mouse CTLA4 sequence and human IgG1 Fc segment was transfected into COS-1 cells and cultured. After 5 days' culture, the culture supernatant containing $CTLA_4$Ig protein was harvested and purified. After the purification, the concentration and the purity of the produced protein were determined. (2) Test of biologic function of the fusion protein: CHO cells which express B_7 molecules were used to test the binding of the produced protein in flow-cytometry analysis(FACS). (3) The immunosuppressive function of the produced protein: one-way allo-response mixed lymphocyte reaction(MLR) and mixed lymphocyte culture (MLC) were used to exam the immunosuuppressive function. **Results:** (1) The purified protein showed the expected size of molecular weight in SDS-PAGE analysis; (2) FACS results showed that > 90% binding of the protein to CHO cells; (3) Results of allo-response MLR study showed that the fusion protein inhibited the cell proliferation in a dose-dependent manner with EC_{50} concentration of 0.2-0.5 ug/ml; and in MLC study, the results showed that the protein significantly suppressed the activation of major T cell populations. **Conclusions**: Novel immunosuppressive protein containing mouse $CTLA_4$ fused with human Ig has been successfully produced in our lab. This fusion protein can significantly suppress the allo-immune reaction. However, its immunosuppressive function is not as potent as the conventional immunosuppressant FK506 which blocks signal 1 pathway when given as a single ageant. The present results laid the foundation of a new treatment regimen with combined therapy targeting at decrease of the dosage of conventional immunosuppressant and induction of donor specific tolerance.

4.6

AIDBase: G6PD, an integrated database for Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency

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AIDBase : G6PD (http://www.rubic.rdg.ac.uk/g6pd/ or http://www.bioinf.org.uk.g6pd/) is a newly created a web-accessible relational database of human Glucose-6-phosphate dehydrogenase (G6PD) deficiency. It integrates mutations at the DNA and protein levels with clinical manifestations, references to biochemical variants originally identified and predictions or crystallographic insights of the structural consequences of the mutations. The database provides a form for submitting additional mutation data and will be linked to other major bioinformatics, mutation, disease and health care databases e.g., OMIM, HGMD, HGBASE and PDD, relevant to understanding G6PD deficiency and its management.

This is one of the first and will be a part of a comprehensive integrated database of 'single amino acid polymorphism' (SAAPs) and related mutations initiated by Dr. A. Martin of a large number of human diseases.

Keyword: glucose-6-phosphate dehydrogenase, deficiency, database, mutations, haemolytic anaemia, tertiary structure

4.7

Decreased yield, phenotypic expression and function of immature monocyte-derived dendritic cells in cord blood

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Background: Neonates are susceptible to infection because of their immature immunity especially T helper type 1 (Th1) function. In order to further understand the mechanism of poor function in Th1, we compared the phenotypic and functional characteristics of monocyte-derived dendritic cells (DCs) that favor Th1 development, from cord blood and adult peripheral blood monocytes.
Methods: We used 3-color flow cytometry for measuring phenotype expression. Results were expressed as mean±SEM.
Results: Our results showed: 1) After culture for 7 days with IL-4 and GM-CSF, cord blood monocytes generated less $CD1a^+$ cells than adult peripheral blood monocytes and the $CD1a^+$ cells percentage decreased thereafter (neonate: 18±2%; adult: 63±6%; $p<0.0001$). 2) Compared with adult blood DCs, cord blood DCs had reduced intensity in the expression of CD1a (neonate: 27±4 MFL; adult: 44±5 MFL, $p=0.02$) and MHC class II molecules (neonate: 397±90 kMESF; adult: 813±94 kMESF; $p=0.012$), but the expression levels of CD11c and CD86 were similar. 3) The endocytotic ability of cord blood DCs was reduced as compared with adult blood DCs (neonate: 90±10 kMESF; adult: 212±36 kMESF; $p=0.0037$) and this function was related to reduced mannose receptor (MR) positive cells (neonate: 81±2%; adult: 93±1%; $p=0.0002$). 4) Furthermore, the ability of cord blood DCs to stimulate $CD3^+$ T cells in an allogeneic mixed lymphocyte reaction was significantly lower than that of adult blood DCs.
Conclusion: These results suggest the dysfunction of cord blood monocytes to differentiate into professional DCs will affect the activation of naïve T cells, especially Th1 development, and may be related to the susceptibility to different infections in particular that due to intracellular pathogens in the neonates.

4.8

OXIDATIVE EFFECTS OF ETHANOL ON ACETIC ACID-INDUCED GASTRIC ULCER FORMATION

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Gastritis plays a role in the pathogenesis of gastric ulcer disease. Concentrated ethanol, a cytotoxic agent via its oxidative effects, can produce hemorrhagic gastritis, causing massive hemorrhage in the gastric mucosa. Yet the relationship between ethanol-induced gastritis and gastric ulcer formation is not well defined. This study aimed to investigate the probable oxidative effects of ethanol and its influence on acetic acid-induced gastric ulcer formation. Male Sprague-Dawley rats were used and were fasted for 24 hours before each oral administration of agents. Acute or sub-chronic gastritis was induced in the rat stomach by oral administration of a single dose or three doses of 80% ethanol respectively. Luminal application of 60% acetic acid was applied to induce gastric ulcer 48 hours after the last addition of ethanol. Mucosal xanthine oxidase (XO), superoxide dismutase (SOD), myeloperoxidase (MPO) levels were determined either 1 hour or 48 hours after the last addition of ethanol. Results showed that both rat ethanol-treated groups had a potentiated gastric ulcer formation, with a larger degree in the sub-chronic gastritis group. Acutely ethanol-treated group had lower XO and SOD activities but a higher MPO activity, when compared to the control, 1 hour after ethanol treatment. Only the difference in MPO activity sustained 48 hours after ethanol treatment. Sub-chronically ethanol-treated group had also a decreased level in SOD and an increased level of MPO 1 hour after treatment, with no change in XO, but the change in MPO were less evident when compared with the acute treated rats, which was accompanied with a lesser lesion area at that moment when compared with the acute one. The decrease of SOD and the increase of MPO sustained 48 hours later in that group, which was followed by an enlarged ulcer formation. These findings indicated that the presence of gastritis potentiated ulcer formation, with SOD depletion probably playing a role in enlarged ulcer formation. Adaptive response to ethanol may be resulted from repeated dosages, which was reflected by a lesser lesion area, together with a less degree of changes of MPO and XO. However, this kind of adaptation did not protect the sub-chronic gastritic animals against ulceration, indicating histological damage and other inflammatory response may be resulted after the chronic treatment, making the mucosa more susceptible to ulcerative damage.

4.9

INVOLVEMENT OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN GRAFT-VERSUS-HOST DISEASE

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Graft-versus-host disease (GvHD) remains the major problem in bone marrow transplantation (BMT) that limits its routine use clinically. The recent finding of macrophage migration inhibitory factor (MIF), a delayed type hypersensitivity-associated cytokine, in mediating both experimental and human renal allograft rejection suggests that MIF may be a key mediator in GvHD. To identify the involvement of MIF in GvHD, skin, colon and lung biopsies from GvHD patients are collected. Local MIF mRNA and protein expression, macrophage and T cell accumulation were examined by in situ hybridization and double immunohistochemistry, while systemic MIF production was measured by ELISA. In normal skin and colon, there is weak, but constitutively, MIF mRNA and protein expression. However, marked upregulation of MIF mRNA and protein by intrinsic skin and colon cells was found with the development of local GvHD response, contributing to prominent T cell and macrophage accumulation. Moreover, MIF is also markedly up-regulated by the infiltrating T cells and macrophages, indicating that they are activated cells responsible for severe tissue damage. Importantly, up to 4 folds of serum MIF was found in the patients with GvHD (1626pg/ml+SD828 vs 369pg/ml+SD304 in normal, $p<0.01$) and this preceded the episode of GvHD clinically, indicating that MIF may be a cause, rather than a consequence, of GvHD. In contrast, in those without evidence of GvHD, there is no increase in MIF expression and production both locally and systemically. In conclusion, we have, for the first time, demonstrated that MIF is markedly upregulated in patients with GvHD. Upregulation of MIF prior to the episode of GvHD strongly suggests that MIF may play a pathogenic role in GvHD.

4.10

ESTIMATION FOR EFFECTS OF AIR POLLUTION ON DAILY MORTALITY USING POISSON REGRESSION WITH AN OFFSET

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Introduction: Short-term effects of air pollution on health have been consistently demonstrated using daily time-series data. The Poisson regression analysis is commonly adopted to obtain the relative risk estimates of air pollution effects. The estimates are adjusted for temporal covariates, such as long-term trend, seasonality and meteorological variable which have been identified from the core model. However, in the modelling it is assumed that the numbers of vulnerable persons are constant throughout the study period.

Objective: The objective of this study is to demonstrate and justify an approach to use OFFSET on log of the expected number obtained from the core model in Poisson regression on daily death counts. In this approach numbers of vulnerable persons are regarded as varying over time and are adjusted for in effect estimation.

Methods: 1) Develop core model according to the APHEA (Air Pollution on Health: a European Approach); 2) Obtain expected number of death from the core model; 3) Perform Poisson regression for daily death counts on pollutant concentrations with OFFSET on log (expected number).

Findings: Effect estimates are more conservative and over-dispersions are smaller in the OFFSET approach compared to those from the APHEA approach.

Conclusion: OFFSET method should be used to adjust for the effects of trend and seasonality and other covariates in the first stage and model effects of air pollution in the second stage of the analysis.

4.11

Validation of a disease-specific health-related quality of life questionnaire for sleep apnea: Chinese version of Calgary Sleep Apnea Quality of Life Index (SAQLI)

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Few disease-specific health-related quality of life (HRQOL) instruments are available to the Chinese patients with sleep apnea to record key elements of the disease that are important to patients, and few from the west have been translated for use with Chinese-speaking patients. The Calgary Sleep Apnea Quality of Life Index (SAQLI) is a well-validated HRQOL instrument that is specific to sleep apnea patients. The index was translated using iterative translation process. Moreover, the psychometric properties of this translated SAQLI(CH) were tested with sleep Apnea patients in Chinese (Hong Kong). Seventy-three diagnosed sleep apnea patients were consecutively recruited from the sleep laboratory in Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital. SAQLI was forward and backward translated by two independent translators. Quantitative and qualitative data were used to assess the cultural equivalence, reliability and validity of SAQLI (Ch) Selected patients who were treated with continuous positive airway pressure (CPAP) treatment for 4-week or above were interviewed again to determinate the impacts of the treatment. The result of the pliot study showed that Cornbach's alpha coefficients of internal reliability were 0.867 for daily functioning, 0.850 for social interactions, 0.922 for emotional functional, 0.825 for symptoms. Construct validity was satisfied as showed by item-scale correlations within each domain. It is also positively correlated with SF-36 of the similar domain. The sensitivity of the instrument was proven by the improvement in scores after CPAP treatment. Thus, the SAQLI (Ch) was seen as a conceptually relevant and sufficient HRQOL for sleep apnea patients as an outcome measure in clinical trials.

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4.12

IGF-I Gene Expressions Are Altered in Nutritionally Perturbed Rat Pups

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Background: Growth hormone (GH) and its mediator, insulin-like growth factor-I (IGF-I) are the primary hormones involved in the growth process and their blood levels are affected by nutritional status. It is not known whether alterations of the GH-IGF-I axis induced by postnatal nutritional environment persists leading to metabolic abnormalities in later life.

Objectives: To investigate the short-term and long-term effects of early postnatal nutritional perturbation on IGF-I gene expressions in the liver.

Methods: Newborn SD rats were reared in litter sizes of 4 (Gp S), 10 (Gp M) and 16 (Gp L) pups to induce different levels of milk intake, thus different growth rates. Pups were then weaned at age 21 days to an *ad libitum* diet until age 90 days. Serum IGF-I levels were measured using a commercially available RIA diagnostic kit. Hepatic IGF-I mRNA and IGFBP-3 levels were assayed by RNase protection assay (RPA) and northern blotting.

Results: Preliminary data showed that pups in Gp L had the lightest, and that those in Gp S had the heaviest body weight at weaning. After weaning to an *ad libitum* diet, pups in Gp L gained weight rapidly but their mean body weight was still lighter than those of the other 2 groups at 90 days of age. There was also a trend for serum IGF-I levels to be the lowest in Gp L at weaning and at 60 and 90 days of age. Mean hepatic IGF-I mRNA levels was higher in Gp L than Gp S: 141.6 for Gp L and 117.5 ± 66.8 for Gp S at 20 days; 220.4 ± 47.8 for Gp L and 132.1 ±33.1 for Gp S at 60 days; and 226.2 ±26.4 for Gp L and 170.0 ± 2.8 for Gp S at 90 days. Changes in hepatic IGFBP-3 mRNA levels paralleled those of IGF-I mRNA: 66.9 ± 9.7 for Gp L and 21.5 ± 15.0 for Gp S at 20 days, 114.4 ± 31.7 for Gp L and 20.5 ± 1.2 at for Gp S at 60 days; and 124.7 ± 33.4 for Gp L and 115.5 ± 10.8 for Gp S at 90 days. Thus, Gp L had the lowest serum IGF-I levels but the highest hepatic IGF-I and IGFBP-3 mRNAs levels.

Conclusion: These preliminary data suggest that nutritionally-induced growth retardation is related to an over-expression of IGF-I mRNA and a low serum IGF-I protein level, which probably involves post-translational defects in hepatic IGF-I synthesis.

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4.13

The effects of Pseudomonas Aeruginosa 1-hydroxyphenazine on iNOS and eNOS expression in human nasal epithelium culture model

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Pseudomonas Aeruginosa frequently colonized the lungs of patients with cystic fibrosis (CF) and severe bronchiectasis. This leads to clinical deterioration, worsening lung function and frequently to death. 1-hydroxyphenazine (1-hp) is a yellow degradation product of the blue phenazine pigment, pyocyanin (pyo), produced by *PA*. 1-hp is known to slow ciliary beat frequency in a dose dependent manner (Muller et al, 1995) and cause rapid onset of ciliary slowing associated with dyskinesia and ciliostasis (Wilson et al, 1987). Nitric oxide is the most abundant free radicals in the body and is well known for its multiple physiological actions and its cytotoxic and cytostatic actions are very important defense mechanisms in the body. In this present study, we investigated the effect of 1-hp on human nasal respiratory epithelium and its effect on inducible and endothelial nitric oxide synthase (iNOS and eNOS) expression in nasal epithelium. Strips of normal human nasal ciliated epithelium obtained from the inferior turbinate of nine different subjects using a cytology brush were decontaminated for 30 minutes in FAD medium containing antibiotics. The cell suspensions were then divided into 2 equal aliquots and incubated in FAD medium containing either saline (control) or 1-hp overnight at 37°C and 5% CO_2. After fixation with 10% neutral buffered formalin, the cells were centrifuged at 3000rpm for 10 min and embedded in 2% agarose gel before the dehydration and infiltration process. 3μm paraffin sections were used for subsequent morphological and iNOS & eNOS immunocytochemistry study. After computer assisted image analysis, it has been shown that the mean iNOS and eNOS intensity of the control and 1-hp groups were 109.86 and 97.74 ($p=0.02$), and 91.64 and 97.74 ($p=0.64$) respectively. Moreover, it has been demonstrated that most of the epithelial cells in the test group were dispersed with loss of cilia and the integrity of the epithelium was disrupted. Our results show that 1-hp causes up-regulation of inducible nitric oxide synthase in respiratory mucosa with destruction of the ciliated respiratory epithelium.

4.14

GLIAL CELL LINE-DERIVED NEUROTROPHIC FACTOR AND NEURTURIN SHARE SIGNALING PATHWAYS OF RET

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The *ret* proto-oncogene enocodes a receptor tyrosine kinase. RET is the functional receptor for the glial cell line-derived neurotrophic factor (GDNF) family ligands. This family consists of GDNF, neurturin (NTN), persephin (PSP) and artemin (ART). The GDNF family ligands bind RET through different members of the GDNF family receptor alpha 1 to 4 (GFRα1-4). Each GDNF family ligand has a preferred co-receptor. These interactions are GDNF-GFRα1, NTN-9GFRα2, ART-GFRα3, and PSP-GFRα4. Alternative interactions such as NTN-GFRα1 and GDNF- GFRα2 are functional.RET is important for the development of enteric nervous system and kidney. Activating mutations of *ret* are found in several cancer syndromes, whereas inactivating mutations of *ret* cause Hirschsprung's disease. Studies on signal transduction pathways of RET will help to understand how RET is involved in normal development and in various diseases. To study the signal transduction pathways of wildtype RET, a cell line derived from human embryonic kidney, 293 and a neuroblastoma/glioma hybrid cell line, NG108-15, were used. NG108-15 cells were found to express high levels of RET and GFRα1, while 293 expressed GFRα1 only. No GFRα2 expression was found in NG108-15 and 293 cells. Thus, we transfected constructs for expressing RET into 293 cells. In NG108-15 cells, tyrosine phosphorylation of RET was induced by GDNF or NTN, followed by the activation of mitogen-activated protein kinase (MAPK) and phosphatidylinositol 3-kinase (PI3K)/Akt pathways. MAPK and Akt phosphorylation was sustained for longer time in NTN-treated cells than in GDNF-treated cells, suggesting that NTN evokes a more prolonged effect than GDNF. Constitutive phosphorylation of RET was observed in 293 cells expressing RET, and RET phosphorylation was not further increased by addition of GDNF or NTN. However, GDNF and NTN stimulation of 293 transfectants resulted in activation of MAPK and PI3K/Akt pathways. Thus, GDNF and NTN share signaling pathways through RET and GFRα1, with different temporal effects.

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ABSTRACTS

7TH HONG KONG INTERNATIONAL CANCER CONGRESS

5.1

Quality of life after gynecologic cancer treatment

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Objective: The objective was to describe the quality of life (QOL) over time and to assess the impact of age, symptoms, disease parameters and treatment on the patients' quality of life.
Method: A longitudinal prospective study of patients with newly diagnosed gynecologic cancer using individual patients as their own control was performed. The questionnaire was the 33-item EORTC QLQ-C30(+3), consisting of a global health status, 5 functional scales and 9 symptom scales. Patients were assessed after confirmation of the diagnosis, after completion of treatment and at 6, 12 and 24 months later. Correlation of factors at different time points and correlation between factors over time were assessed by Spearman correlation analysis. A mixed effect model was fitted into the data. Bonferroni pairwise comparisons were used to analyze the different variables of the significant covariates.
Results: One hundred forty four women completed the study. The overall QOL improved after completion of treatment but remained the same throughout the two years after treatment. The individual patient's QOL before treatment was insignificant while the individual patient's impact of treatment was significant in determining the QOL after treatment. There was a strong correlation for all time points in most factors, indicating that all the global health status, functional scales and symptom scales exhibit a dependent change over time. Patients experiencing improvements in global health status also experience improvements in factors under the functional scale and relief in factors under the symptom scales. Relief in symptoms was associated with improvements in functional scales. The scores on overall QOL were lower for younger patients and for patients treated with chemotherapy than for patients treated with surgery. There were no significant differences in the scores of emotional, cognitive and social functioning for different sites and stages of diseases and treatments.
Conclusion: Regardless of the initial QOL, patients have similar chance of reaching any QOL after treatment. Strategies for supportive care need to focus on symptom management. Psychosocial intervention, if to be effective, should be offered early on during the course of cancer diagnosis and treatment.

5.2

Patients' support network: implications and challenges for a self help organization

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Patients support network has been recognized as an essential element to psychosocial rehabilitation. Identification of major areas initiating support network is needed for health care practice. A cross- sectional study of the quality of life of ostomates was done in Hong Kong in which 559 samples were taken randomly from the member list of Hong Kong Stoma Association. There is a response rate of about 70% in the study. The findings help investigating the said issue in a context of a self help organization.

This presentation outlines the facilitating areas on inducing patients' support network. The implications of service quality and needs in the context of quality of life will be discussed. And it also proposes issues and challenges, which demand increased emphasis on the future psychosocial rehabilitation as well as community collaboration for chronic illness patients. In particular, the growth of mentorship program, the greater involvement of carers, the need for social inclusion and the development of an out-reaching service model are proposed as important future trends.

5.3

The Nurses' knowledge, attitude and behavior towards Traditional Chinese Medicine in Hong Kong - An initial exploration

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Background: Traditional Chinese Medicine (TCM) has a well-established history within China, where equal weight is given to both TCM and Western Medicine in managing health care. In Hong Kong however there is a very different situation in which only 9% of the population consult TCM practitioners as first point of health care (Wan 1995). With the future licensing of TCM practitioners, how is the mode of therapy viewed by Hong Kong Nurses? In particular how does knowledge, working environment and patient's diagnosis influence attitudes towards this therapy? Does TCM offer for those approaching death an accepted last hope?

Objective: To explore how nurses view the use of Traditional Chinese Medicine in relation to their working environment, personal experiences and training. Considering how widely used TCM is within Mainland China, this study proposes that there is a difference in belief and support depending on the person's prognosis.

Methodology: A Quantitative study using postal questionnaire to compare the views of hospice, oncology and acute care nurses towards TCM.

Results: Through this initial exploration of nursing attitudes we hope to discover the impact of the proposed variables in this use of this therapy. Furthermore we hope to explore the support offered to patients using TCM and how this may differ depending on their disease process. As advocates in patient care do nurses offer equal non-judgmental support to patients who may choose this line of therapy?

5.4

Unheard Little Voices :
The Needs of Children when their Parents are Seriously Ill

Brenda Wing Sze KOO, Amy Yin Man CHOW, Agnes Fong TIN, & Elaine Wai Kwan KOO, Bereavement Counsellors
Jessie & Thomas Tam Centre, Society for the Promotion of Hospice Care Ltd.

A Cancer diagnosis affected not only the patient, but also the whole family. Yet, care and attentions are primarily offered to the patient and his spouse, leaving the kids to other available relatives or neighbors. The voices and needs of these children are usually unheard. Even when the child expresses his needs, adults find it difficult to handle. They might use the excuses like "they are too young to understand", "when they grow up, they will be OK" etc to stop further expressions.

In August 2000, the Centre has organized a camp for 23 bereaved children (aged from 4 to 13) and their 19 surviving parents. Part of the programmes is aimed at facilitating the children to express their needs to the surviving parents. The children were being asked, as experts, about their needs when their parents are facing the impending death. The children have generously offered their perspectives in their unique meaning of death, their needs when parents are hospitalized as well as during the moment of death of parents. To our surprise, even young kids have certain degree of understanding of death. Most of them wanted to know about the diagnosis and prognosis of the patients. They even wanted to be involved in the final farewell. In this presentation, we aimed at making the unheard little voices being heard. With the summarization of the ideas from the children, practical implications for health care professionals will be highlighted and discussed.

5.5

THE MEANING OF SOCIAL SUPPORT IN COPING WITH BREAST CANCER

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Objective: The purpose of this study was to explore the meaning of social support in relation to coping with breast cancer.

Method: A phenomenological in-depth study of 17 Chinese women aged 30 to 65 years old with primary BC following surgery and subsequent therapy. Semi-structured interviews were taped transcribed, translated, and analyzed using Colaizzi's method.

Results: Informants' descriptions showed that the possibility of death and changes in physical appearances posed a significant threat to their sense of self and social support was perceived as an important coping resource to help them to re-establish their self-identity. The narrative analysis showed that these women needed social support (1) to cope with the uncertainty over the course of illness, (2) to reduce the threat to one's sense of self, (3) to re-establish self-identity, and (4) to retain normalcy. Spouse, family, friends, and other patients were identified as the desired sources in their social network, but support from non-marital relationships cannot compensate for problematic interactions with the spouses.

Conclusion: This study suggests that being acceptance by others play a significant role of preserving/re-establishing the "normal" identity. This highlights the importance of helping these women to maintain and create their social support across the illness trajectory.

5.6

Sharing Tears and Gaining Support : Unfolding Bereavement Groups

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Society for the Promotion of Hospice Care Ltd.

Groupwork is found to be an effective modality in working with bereaved persons. The Jessie and Thomas Tam Centre, the community based bereavement counselling centre in Hong Kong, has run 16 bereavement groups since its opening in October, 1997, serving over 110 bereaved individuals. Recently, specialized groups like group for widowers, group for widows, group for bereaved adult children, group for bereaved parents as well as group for the aged spouses were run separately. Around half of the participants were referred by health care professionals. Referrers might have no chance to contact with the referred clients after the referral. The lack of knowledge of the development of clients will hinder further referrals. This presentation is aimed to share to all referrers, as well as potential referrers, about the theoretical background of the development, major themes and the major intervention elements of the bereavement groups. Participants showed significant improvement as reflected in the pre- and post measurements. With this presentation, it is hoped that the health care professionals can link potential users of the bereavement services to us, the community partner. Besides, with the sharing of the details of the bereavement groups, health care professionals can re-examine the possibility of running bereavement groups in their hospitals.

5.7

The experiences of caring and support of caregivers for terminally ill patients

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E YEUNG, V CHAN, HK Hospice Nurses' Association
F CHAN, Society for the Promotion of Hospice Care

The purpose of this research was to uncover the meaning of caring and support for relatives of terminally ill cancer patients. Thirty caregivers volunteered to take part in audio-recorded interview to describe their experience of caring and support for their relatives. Data collection, in van Kaam's phenomenological method, consists of written descriptions by participants of the experience being investigated. Themes emerged from the study are the meaning of caring for the terminally, communication among family members, involvement of care, dealing with feelings, considering others and fulfilling roles.

The caregivers focused their concern on the well being of the patients and appreciated nurses' help in instructing them and assisting them in the physical care of the terminally ill patients. Analysis of data also showed that family functioning influenced the caregivers' experience of care and support. Knowledge of family functioning provides nurses with insight and understanding into why it is more difficult to provide optimal care to some caregivers than to others. Nurses need to adjust their care according to the needs of individual family.

6.1

IDENTIFICATION AND CLONING OF DOWNSTREAM TARGET GENES OF LMP-1 IN NASOPHARYNGEAL CARCINOMA CELLS

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Nasopharyngeal carcinoma (NPC) is a common cancer in Hong Kong. Its etiological factors include Epstein Barr Virus (EBV) infection, environmental factors and genetic susceptibility. EBV is thought to be a key factor in NPC development as suggested by the common presence of EBV DNA in NPC tumor cells. Furthermore, elevated titres of antibodies against EBV proteins are frequently observed in NPC patients. Among the EBV proteins, latent membrane protein 1 (LMP-1) is believed to mediate the pathological roles of EBV in NPC development. The LMP-1 protein is expressed in around two thirds of EBV positive cases of NPC. Previous studies have shown that LMP-1 can induce oncogenic transformation of rodent fibroblast cells and alter growth properties of epithelial cells *in vitro*. Morphological changes were also observed in epithelial and fibroblast cells expressing the LMP-1 gene. However, the downstream events of LMP-1 expression are not well understood.

In this study, identification and cloning of downstream target genes of LMP-1 in nasopharyngeal carcinoma cells were performed by suppression subtractive hybridization (SSH). SSH is a PCR-based method commonly used for identifying differentially expressed genes in a specific cell population. By SSH, differentially expressed cDNA libraries were constructed from the NPC cells transfected with LMP-1 gene and the NPC cells with control vector only. Fourteen LMP-1 activated genes and seven LMP-1 suppressed genes in NPC cells were identified. Four of them are unknown sequences. With Northern Blot or RT-PCR, seven of the differentially expressive genes have been confirmed. Four of them are LMP-1 activated gene, and three are LMP-1 suppressed. Further study will be carried out to investigate the significance of these genes in NPC development.

6.2

Effect of air supply in phonation : A comparison between esophageal and tracheoesophageal speech in Cantonese laryngeal cancer patients

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The present study attempted to investigate the aerodynamic differences between esophageal and tracheoesophageal speech in Cantonese laryngeal cancer patients. Six esophageal and six tracheoesophageal male speakers of Cantonese were instructed to complete various speech tasks including: (1) reading a 14-word sentence; (2) sustaining vowels /i/, /a/, /u/, and /ɔ/; (3) producing syllables /pa/ and /p^ha/; and (4) producing the syllable /ipipi/. With careful calibration, airflow rate and air pressure values were measured from the speech samples by using the Aerophone II.

Results indicated that (1) peak flow rates in vowels produced by esophageal speakers were significantly lower than that produced by tracheoesophageal speakers; (2) peak airflow rates in /p/ were significantly lower than /p^h/; (3) esophageal speakers were associated with significantly lower mean peak flow rate during stop production than tracheoesophageal speakers; (4) esophageal speakers were associated with significantly greater sub-pharyngoesophageal pressure than tracheoesophageal speakers. The differences in airflow and air pressure values between esophageal and tracheoesophageal speakers are related to the use of different air supply mechanism. The ability to use pulmonary air supply in tracheoesophageal speech renders a greater airflow in this form of alaryngeal speech.

6.3

Hypermethylated Promoter of p16 Gene as a Promising Blood Marker in Chinese Patients with Invasive Ductal Breast Cancer

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Purpose: The different marker combinations between p16 gene hypermethylation, E-cadherin gene hypermethylation, carcinoembryonic antigen (CEA) and CA15.3 levels in peripheral blood were investigated to determine their values in the prediction of prognosis of Chinese patients with breast cancer.

Patients and Methods: Methylation-specific PCR (MSP) assay was done in the free plasma DNA samples and matched primary tumor samples of 36 patients. The serum levels of CEA and CA15.3 were measured in 33 involved cases.

Results: The percentage of hypermethylated p16 gene was 11.1% (4/36) in primary tumor DNA and 8.3% (3/36) in plasma DNA, while the percentage of hypermethylated E-cadherin gene was 25% (9/36) and 19.4% (7/36) respectively. None of the 25 cases without molecular events in primary tumor DNA was found to be positive in their plasma samples. The presence of hypermethylation of p16 gene, but not E-cadherin gene in primary tumor DNA, was statistically associated with clinical staging ($p = 0.028$), tumor size ($p = 0.017$) and status of nodal metastasis ($p = 0.002$), while its molecular event in plasma DNA demonstrated significant correlation with status of nodal metastasis ($p = 0.012$). The presence of hypermethylated p16 gene and elevated CEA level in blood could predict disease with advanced staging, a large-sized primary tumor and extensive nodal metastasis ($P = 0.033$, 0.022 and 0.003 respectively).

Conclusion: p16 gene methylation is a promising blood marker for monitoring affected patients. p16 gene and CEA combination is promising for the prediction of prognosis of invasive ductal breast cancer in Chinese.

6.4

E-CADHERIN EXPRESSION IS SILENCED BY DNA METHYLATION IN CERVICAL CANCER CELL LINES AND TUMORS

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E-cadherin, one of the adhesion molecules, plays an important role in human cancers. Loss of its function is thought to contribute to cancer progression and invasion. Previous data showed that E-cadherin expression was lost in some of the cervical cancer cell lines. Here we present that loss of E-cadherin protein expression in 3 cervical cancer cell lines (SiHa, Hela, C33A) was due to hypermethylation in the CpG islands. DNA sequencing demonstrated that all the 10 CpG islands were completely methylated. The mRNA level in these cell lines was also much lower when comparing with other two cell lines (Caski and C41). Using methylation inhibitors, 5-azacytidine and 5-azadeoxycytidine, E-cadherin protein expression can be reactivated in SiHa cell line. The mRNA level was obviously increased in all 3 cell lines during demethylation treatment. At the same time, DNA methyltransferse-1 (DNMT1) and Cadherin-11, a type II cadherin molecule, were also studied. High DNMT1 mRNA was shown in the cell lines which lack E-cadherin expression. Cadherin-11 was expressed in 2 of the 3 cell lines lacking E-cadherin expression. After demethylation the E-cadherin reexpression in Siha cell line was in accordance with a lower level of DNMT1. We then studied 20 cervical cancer tissues and 10 normal cervical samples. We found E-cadherin methylation was associated with low E-cadherin expression and high level of DNMT1 expression. Our study suggests that loss of E-cadherin function through hypermethylation is important in cervical cancer development; it may be as a result of high level of DNMT1 and is associated with cadherin-11 expression.

6.5

PROFILING DIFFERENTIAL GENE EXPRESSIONS IN RADIOSENSITIVE AND RADIORESISTANT CERVICAL CANCER CELL LINES

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Radiotherapy is a standard treatment for cervical carcinoma. The success of the therapy mainly depends on the intrinsic radiosensitivity of cancer cells. Presence of altered expressions of a subset of genes in cancer cells may confer to radioresistance in response to radiation treatment. In the present study, we attempted to compare the gene expression patterns in radiosensitive and radioresistant cervical cancer cell lines by means of cDNA expression array. Cervical cancer cell lines of SiHa and c33-A are shown previously being relatively radioresistant and radiosensitive. CLONTECH's Atlas™ human apoptosis array constructed with 205 known genes was selected for gene profiling. ^{32}P-labeled cDNA probes were synthezised from polyA$^+$ RNA extracted from two cell lines, then hybridized to cDNA blotted membranes. Parallel analysis of the hybridization signals enable us to compare genes that were expressed differentially on radiosensitive and radioresistant cell lines. In each experiment, the extent of the hybridization signal of each gene was normalized by comparing with poly$^+$ RNA of a set of housekeeping genes. Seventeen genes showed more than two-fold different expressions between two cell lines. These include genes of the cell cycle regulators (CDC2, CDK5, CCNB1, CCND1, CDC34, CDC37 homolog), p53 pathway (p53 induced protein, PIG7, PIG12), bcl-2 family (bclw), caspases and their regulator (caspase-4 precursor, CRAF1), ligand and receptor (IGFBP6) and other regulators (PDCD2, CD27BP, CD27LG, GADD153). The differential gene expressions are going to be confirmed by RT-PCR or Northern blot. The relationship between the different gene expressions and radiosensitivity of cancer cells will be further investigated

6.6

Recurrent Chromosome Changes in 31 Primary Ovarian Carcinomas Detected by Comparative Genomic Hybridization

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Ovarian cancer is one of the most frequent gynecological malignancies worldwide with poor prognosis. The development of new diagnostic, preventive, and treatment approaches requires good understanding of the mechanisms of the complex multi-steps process of tumor pathogenesis in the ovarian cancer. Comparative genomic hybridization (CGH) has been applied to detect recurrent chromosome alterations in 31 primary ovarian carcinomas. Several nonrandom chromosomal changes including gains of 3q (17 cases, 55%) with a minimum gain region at 3q25-q26, 8q (16 cases, 52%), 19q (12 cases, 39%), Xq (11 cases, 3 5%), 1 q (10 cases, 3 2%), 17q (10 cases, 3 2%), 12q (9 cases, 29%) with a minimum gain region at 12q12, and 20q (9 cases, 29%). High copy number gain (DNA sequence amplification) was detected in 10 cases. Amplification of 3q25-q26 and 12pl 1.2-q12 were detected in 4 and 3 cases, respectively. The regions most frequently lost included: 16q (9 cases, 29%), lp (7 cases, 23%), 18q (7 cases, 23%), and 22 (7 cases, 23%). The recurrent gain and loss of chromosomal regions identified in this study provide candidate regions that may contain oncogenes or tumor suppressor genes respectively involved in the development and progression of ovarian cancer.

6.7

Screening ovarian cancer related genes by Differential Displayed PCR method

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Objective: To screening ovarian carcinomas expressed ovarian related genes.

Method: Using mRNA Differential Display PCR method, the different expression gene fragments between ovarian carcinoma tissue and control normal ovarian tissue were identified cloned and confirmed by reverse dot blot and northern blot, then sequenced and analyzed. In situ hybridization method was used to examine gene expression in ovarian carcinoma and normal tissue.

Results: Three different displayed cDNA gene fragment were cloned and identified by dot blot and reverse dot blot, two of them were confirmed by northern blot to be different displayed gene fragments: ovc-1 and ove-2. Results of sequence and homology analysis showed that ovc-1 was a novel gene and ovc-2 was 86% identical with HSMHCC47 gene. In stiu hybridization results showed that ovc-1 and ovc-2 genes were differently expressed in 36 samples of ovarian carcinoma tissues and 16 samples of normal tissues ovc-1 was expressed in more ovarian cancer(25/36) than normal ovarian tissue (6/16), although ovc-2 was expressed in more normal ovarian tissue(10/16) than ovarian cancer tissue(12/36).

Conclusion: ovc-1 and ovc-2 genes may be the ovarian related gene. Further study of these genes was helpful to clarify the mechanisms of ovarian carcinoma.

Key Word: Ovarian Cancer, DD-PCR

6.8

UPREGULATION OF ID-1, TRPM-2 AND MMP-7 DURING SEX HORMONE-INDUCED PROSTATE CARCINOGENESIS IN THE NOBLE RAT

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Prostate cancer is the most frequently diagnosed malignancy in the Western world and the changes in the ratio of testosterone and estrogens with advancing age is one of the potential risk factors in the development of this disease. However, the molecular mechanisms associated with hormone imbalance in prostate carcinogenesis are poorly understood. In this study, using the combination of testosterone and estradiol-17β, we induced a high incidence of prostate hyperplasia, dysplasia and adenocarcinoma in the Noble rat. Using this animal model, we studied the gene expression profile during the sex hormone-induced prostate carcinogenesis process using a cDNA array technique and the results were further confirmed by RT-PCR, Western blotting and immunohistochemistry analysis. We found the upregulation of TRPM-2 (testosterone-repressed prostatic message-2), MMP-7 (matrix metalloproteinase-7) and Id-1 (inhibitor of differentiation or DNA binding) during the development of sex hormone-induced prostate cancer. Increased expression of TRPM-2 and MMP-7 was observed both in premalignant and malignant tissues after sex hormone treatment, indicating their role in the early stage of hormone response and their initiating effect in the prostate cancer development. In contrast, Id-1 was expressed at relatively low level in all premalignant samples but increased in malignant cells. Using immunohistochemistry and Western blotting we also found two molecular weight forms of the TRPM-2 protein that were present in both cell nucleus and cytoplasm after sex hormone treatment. Our results provide first evidence on the upregulation of TRPM-2, MMP-7 and Id-1 during the sex hormone-induced prostate carcinogenesis process and strongly suggest their association with the development of prostate cancer.

6.9

Biopanning and Identification of the Binding-peptide of MUC1/Y Protein

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MUC1/Y,an isoform of MUC1, is highly expressed in breast and ovarian cancer tissues but not in those adjacent tissues. It is a potential ideal target molecule for tumor-targeting therapy.

By RT-PCR, the full-length cDNA of MUC1/Y was cloned from Hela cell. Then the extracellular domain of MUC1/Y(MUC1/Yex) was expressed in E.coli fusion expression system. Using MUC1/Yex protein, phage displayed 12-peptide library were biopanned and the specificity of selected phage clones were tested by ELISA and immunohistochemistry. The results showed that the fusion protein GST-Yex induced by IPTG consisted of about 25-30% of the total bacteria proteins. And the induction temperature affects the solubility of GST-Yex. The purity of the purified protein is ≥90% with a production of 70-80mg/L. After 4 rounds biopanning ,60 phage clones were picked out randomly for ELISA with GST and normal MUC1 as controls. 16 were selected for further ssDNA sequencing. Three binding peptide sequence were got including 14 HHWHSRSQLSWF, 1 HLKHKNYLPPTP and 1 GNWYRPHYLQP. Immunohistochemistry analysis showed that the selected phage clones could bind MCF7, OVCA3 cell and breast cancer tissue in vitro while no binding to normal PBLs and colon cancer tissue were observed. The results indicated preliminarily that the selected phage clones could bind specifically to MUC1/Y and MUC1/Y-expressing tumor cells and tissues.

7.1

EFFECT OF FLUTAMIDE AND TAMOXIFEN ON SEX-HORMONE INDUCED MAMMARY CARCINOGENESIS IN NOBLE RATS

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Breast cancer is the most common cancer in women in the Western world. This experiment aimed at investigating the efficiency of tamoxifen and flutamide as a tumour-blocking agent to the sex-hormone induced mammary carcinogenesis in Noble rats. Sexually matured female Noble rats at 3 months old were randomly separated into 4 different groups. Group 1 was surgically implanted subcutaneously with silastic tubings filled with testosterone propionate and 17-estradiol in the ratio 8:1. Group 2 was implanted with extra tubings filled with flutamide in addition to the same amount of sex hormones while in Group 3 the extra tubing was tamoxifen. Group 4 was controls implanted with empty tubules. Re-implantation was done at three months intervals. All groups of rats were allowed to have food and water ad libitum. Their weights were recorded monthly and they were palpated regularly for mammary tumours starting from two months after treatment. Palpable mammary tumour masses first appeared at 5 months post implantation in Group 1 and at 9 months in Group 2. No palpable tumour mass was noted in Group 3 and Group 4 up to 12 months period. Rats were sacrificed when the tumour masses exceeded 2 cm in diameter, or when they were moribund. All remaining rats would be sacrificed at 12 months post hormone treatment. Histology of these tumour masses showed that all of them were adenocarcinomas. Cumulative index of mammary carcinoma development in the four groups were 82%, 55%, 0% and 0% respectively at 12 months post implantation. Pituitary adenoma were also noted in group 1 and 2 rats but not in Group 3 and control rats. Circulating prolactin levels were high in the pituitary adenoma bearing rats. Result suggested that flutamide could slow down tumour development and reduce the incidence while tamoxifen was efficient in the blocking of sex-hormone induced mammary carcinogenesis and could be used for the prevention of mammary cancer.

7.2

To screen or not to screen: mammography for Chinese women

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Objectives: Following European and North American randomised controlled trials (RCTs) supporting mammographic screening for early breast cancer detection, it has become routine practice in most Western countries. There are no data from Asia and, the efficacy and effectiveness of screening mammography in Chinese women have yet to be rigorously considered. We systematically reviewed the evidence for population-based screening for breast cancer, and examined the applicability of these results to Chinese populations.

Methods: Primary reports were identified by a search of the Cochrane Library and MEDLINE. Information on breast cancer incidence and mortality was collected from the International Agency for Research on Cancer and the Hong Kong Cancer Registry. Main outcome measures included breast cancer-related mortality and the number needed to screen to prevent one such death.

Results: We identified 8 RCTs and calculated the pooled relative risk for breast cancer-related death in the screened group to be 0.80 (95% confidence interval = 0.70, 0.92). In Hong Kong, there were 868 new cases of breast cancer, and 270 breast cancer-related deaths, for women aged 50 and over in 1996, giving an incidence of 123.3, and a mortality rate of 38.4, per 100,000. Therefore, 17,601 healthy women need to be screened for ten years to prevent one case of breast cancer-related death. In addition, we estimated the positive predictive value of screening mammography to be between 1.5% and 11.5%, assuming regular annual screening for women aged 50 and over. A positive screen inevitably leads to further tests, with considerable associated anxiety and trauma. Further, it has been estimated that for every $100 spent on screening, an additional $33 was spent on evaluation of the false-positive results.

Conclusions: There is insufficient evidence to justify population-based breast cancer screening by mammography for Chinese women. For those at high risk for the disease, careful individual clinical assessment should guide the need for and frequency of mammographic screening.

7.3

Management of Non-palpable Breast Cancer

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Abstract: With increasing focus on the early diagnosis and intervention of breast cancer, more screening programs are now being conducted for asymptomatic women. Screening mammography has adopted a major role in such screening programs. As a result, there will be an increasing number of mammographically detected non-palpable breast lesions that will require further management by the attending physicians. Advanced Breast Biopsy Instrumentation (ABBI) is a recent addition to the traditional list of breast biopsy techniques for the management of such lesions. It's sensitivity and specificity are comparable to the traditional gold standard - wire localization biopsy. The complication rate is similar, and yet is a more cost-effective technique that has gained much patient's satisfaction. The technique provides an adequate and accurate excision of the non-palpable lesion with minimal architectural disturbance. Further management will depend on the biopsy results. This paper will review the early experience in the use of the Advanced Breast Biopsy Instrumentation (ABBI) in our hospital. Among the 15 biopsies done, 2 patients were diagnosed as having carcinoma of the breast. Re-excision was done for one of them in the day-centre due to close margin. The use of a larger cannula may have eliminated the subequent excision. However, the technique is currently only approved for diagnostic purpose. Further trials will be needed to evaluate its potential therapeutic use.

7.4

Results of treating patients with advanced metastatic breast cancer by capecitabine as a single agent

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Practically, all patients who die from breast cancer are the result of metastasis. Surgery plus chemotherapy offer the best chance of cure or disease control. For advanced metastatic breast cancer, chemotherapy could modestly prolong survival, but at a price of compromising the general well-being of the patient. In other words, extension of survival is often offset by a deduction in the useful lifetime as a result of aggressive treatments. Chemotherapy is usually being administered in a hospital setting. Capecitabine (Xeloda), an oral fluoropyrimidine carbamate mimicks continuous 5-FU infusion, can be administered at home. As a prodrug, preferentially activated at the tumour site, potentially has higher efficacy and lower toxicity. This series included 21 patients with advanced metastatic breast cancer, previously heavily treated with anthracycline or taxane based regimens. They received capecitabine as a single agent in 3-week cycles (2 weeks of treatment with 1 week rest). 50% of patients had a fall in CEA and CA 15.3 levels. Though 40% of patients experienced adverse effects, majority were those of grade I toxicities. For patients with advanced metastatic breast cancer, this agent may be legitimate though survival benefits could only be demonstrated by comparative studies.

7.5

ATTENUATION OF EPIDERMAL GROWTH FACTOR (EGF)-STIMULATED LNCaP PROSTATE CANCER CELL PROLIFERATION BY MELATONIN

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Melatonin, a pineal gland neurohormone, has been shown to exert oncostatic effects. Previous studies by our group have demonstrated direct anti-proliferative action of melatonin, possibly via the membrane mt_1 receptor subtype, on androgen-sensitive human prostate cancer LNCaP cells [1]. In light of the accumulated evidence that deregulated autocrine and paracrine stimulation of cell proliferation by peptide growth factors is important for the pathogenesis of uncontrolled prostate cancer cell growth, it would be of interest to study whether or not melatonin and peptide growth factors interact in the regulation of prostate cancer cell proliferation. Given that the proliferation of human prostate cancer LNCaP cell line was stimulated by epidermal growth factor (EGF) [2], the effects of melatonin and 2-iodomelatonin, a high-affinity melatonin membrane receptor agonist, on EGF-stimulated LNCaP cell proliferation were investigated in the present study. Intriguingly, the EGF (10^{-8} M)-stimulated proliferation was attenuated, concentration-dependently, by melatonin (5×10^{-11} M to 5×10^{-5} M). Similarly, 2-iodomelatonin (5×10^{-11} M to 5×10^{-5} M) reduced the EGF-induced increase in ^{3}H-thymidine incorporation into LNCaP cells in a concentration-dependent fashion. To explore the possible mechanism of the observed interaction between melatonin and EGF, the cellular effects of melatonin and 2-iodomelatonin on the expression of cyclin D1, a protein known to be important in G1/S cell cycle progression and was induced by EGF in LNCaP cells [3], was also examined. Melatonin or 2-iodomelatonin (5×10^{-7} M) inhibited the steady-state cyclin D1 levels in LNCaP cells. Our findings indicate that in LNCaP cells, significant cross-talk between mt_1 melatonin receptor- and EGF-mediated signaling in the modulation of cell proliferation probably exists. Part of this interaction may be mediated via opposite changes in cyclin D1 levels induced by melatonin and EGF.

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7.6

POSSIBLE ASSOCIATION BETWEEN CARCINOMA OF BREAST, CARCINOMA OF FALLOPIAN TUBE AND TAMOXIFEN USE

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The first patient has carcinoma of right breast (T2N0M0) and mastectomy in 1990 followed by carcinoma of left breast (T2N1M0) in 1992. Adjuvant chemotherapy and radiotherapy were given after mastectomy followed by tamoxifen for 4 years. She presented in 1999 because of postmenopausal bleeding. Hysteroscopy and D&C were normal. Bleeding recurred later and ultrasound scan showed an adnexal mass. Laparotomy showed a primary left fallopian tube carcinoma 5x3x2 cm. There was no evidence of metastasis and clinically it was stage Ia. The histology showed serous carcinoma.

The second patient has carcinoma of right breast (invasive ductal carcinoma, T2N0M0) and mastectomy in 1997. Tamoxifen was given after the operation. She has postmenopausal bleeding in 1999 and endometrioid adenocarcinoma was found on D&C. On laparotomy, a right fallopian tumour was found around 1 cm. TAHBSO and peritoneal washing were performed. A small focus of invasive endometrioid carcinoma was found in the fallopian tube with surrounding in situ changes (likely double primary). The final diagnosis was carcinoma of corpus stage IbG1 and carcinoma of fallopian tube stage Ia. From literature, the association between carcinoma of breast and carcinoma of fallopian tube was rare. The association between endometrial carcinoma/hyperplasia and tamoxifen was well reported but the association between carcinoma of the fallopian tube and tamoxifen is rarely reported. Further genetic/molecular studies is warranted.

7.7

RESULTS OF TREATMENT (Rx) OF PRIMARY OVARIAN GERM CELL TUMORS (OGCT) — LOCAL EXPERIENCE IN 17 YEARS

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From 1983 to March 2000, 40 consecutive patients (pts) with primary OGCT were treated (dysgerminoma=13, malignant teratoma=MT=27). Follow up ranged from 2.8 to 204.2 months (median=57.4 months). No dysgerminoma (dysG) pt died. Two pts with malignant transformation (undifferentiated carcinoma) of teratoma died despite resection, chemotherapy(C/T) or radiotherapy(RT). The other 25 MT pts survived with no evidence of tumor. Primary operations included laparotomy, total hysterectomy and bilateral (or unilateral) salpingo-oophorectomy. For the dysG group (mean age=24), most were early stage (I=7, II=1, III=4, paraaortic node relapse in preceding stage I=1). Postoperative(postop) C/T with PVB (cisplatinum, Vinblastin, Bleomycin) was used till 1989. Then Etoposide has replaced Vinblastin (i.e.BEP). Post-C/T resection for residual mass was performed in 2 pts with initial advanced or relapsed disease (all had necrosis only). Two Ia pts (no postop Rx=1, postop whole abdomen RT=1) have remained well. All dysG pts survived with no disease. For the MT group excluding the 2 pts with malignant transformation (Immature=21, mixed GCT=3, Yolk sac=1), mean age is 23. In the immature teratoma (ImT) group (stage I=12, III=8, IV=1., grade I=12, II=6, III=3), no correlation between stage and grade was found. Nineteen pts had postop BEP (or carboplatin to replace cisplatinum, ie, JEB). Two (Ic, grade I) had no postop Rx. One stage IV pt (liver metastases, grade I) had 6 cycles of BEP and resection of residual masses (histology →mature teratoma) in pelvis and liver. She developed restrictive bleomycin lung (total Bleomycin dose=345mg) which has slowly recovered. She remained relapse-free. Four ImT pts relapsed (2 at the contralateral ovary, 2 in the pelvis). They were salvaged by resection and C/T. All ImT pts survived. Three pts with mixed GCT and one with yolk sac had stage I treated with postop BEP/JEB. All survived with no relapse. In conclusion, all pts (except the two with malignant transformation) survived with no disease. Primary OGCT are therefore highly curable, even at relapse, with platinum based C/T + resection. Survival is almost 100% in this series. C/T toxicities were manageable if Bleomycin tolerance dose was not exceeded. There was menstrual interruption during C/T but irreversible amenorrhoea was not seen. A successful pregnancy was seen in a 26 year-old pt three years after Rx.

7.8

RECURRENT BRCA2 MUTATION IS FOUND IN CHINESE OVARIAN CANCER PATIENTS

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Epidemiological studies have shown 5 to 10% of cases of sporadic breast and ovarian cancer can be attributed to mutations in the breast cancer susceptibility genes, BRCA1 and BRCA2. Recurrent mutations due to founder effect have been reported specific to certain populations. Information regarding BRCA mutations in the Chinese population is scant. It would be helpful for pre-symptomatic screening if specific mutations of high prevalence could be identified in the Chinese population. Single stranded conformation polymorphism (SSCP) was used to screen for the possible recurrence of four BRCA1 and BRCA2 mutations previously found to be unique to our Chinese population. Consecutive cases of primary breast carcinoma, under 45 years age and primary ovarian carcinoma diagnosed in Chinese women unselected for age, were retrieved from the files of the Departments of Pathology, Queen Mary Hospital and Pamela Youde Nethersole Eastern Hospital. All cases were unselected for family history. DNA was extracted from formalin-fixed paraffin embedded tumor blocks. These included 65 cases of breast cancer and 106 cases of ovarian cancer. Three fragments covering all four mutations of interest were amplified by PCR. Two ovarian cancer samples (2/106) (1.88%) were found to habor the BRCA2 mutation C3337T. The BRCA1 mutations C633T, 589delCT and IVS 22+7 were not detected in any of the samples. Our study has thus identified a recurrent BRCA2 gene mutation C3337T, present in 3 unrelated patients with ovarian carcinoma of southern Chinese origin. Further haplotype analysis and the finding of this mutation in breast/ovarian cancer families would be necessary to establish the possibility of founder effect which would make it a potential candidate for genetic testing in Chinese women.

7.9

DIFFERENTIAL EXPRESSION AND ALLELIC LOSS OF BRCA1 AND BRCA2 GENES IN SPORADIC OVARIAN CANCER

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Somatic mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 are uncommon and the role of these genes in sporadic ovarian cancers (OC) is unclear. Alterations other than coding region mutations may contribute to its pathogenesis. We investigated the expression levels of BRCA1 and BRCA2 in sporadic OC comparing it with that of non-tumor tissue. Thirty three cases of OC were evaluated for BRCA1 and BRCA2 mRNA levels by quantitative RT-PCR. Microsatellite analysis was further performed to detect possible allelic loss. Four microsatellite markers each, for BRCA1 and BRCA2 respectively, were used to analyze for loss of heterozygosity (LOH). Results showed statistically significant reduction of BRCA1 expression in 23 tumor samples ($p=0.001$). For BRCA2 in contrast, 19 cases showed statistically significant overexpression ($p=0.012$) with only 4 cases showing reduced expression. Allelic loss for BRCA1 was found in 10 of the 23 cases showing reduced BRCA1 expression. On the other hand, there was no correlation between altered expression levels and allelic loss for BRCA2. Our findings of reduced BRCA1 expression and BRCA2 overexpression suggest the involvement of both these genes in sporadic OC. The reduced expression of BRCA1 with or without LOH implies that multiple mechanisms may be involved in down-regulation in these tumors. Possible preferential allelic expression or other aberrant regulatory mechanisms causing decreased levels of BRCA1 expression and elevated levels of BRCA2 expression in sporadic ovarian cancers are being further investigated.

7.10

Telomerase Activity in Ovarian Epithelial Carcinomas and their Clinical Significance

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To determine telomerase activity in epithelial ovarian carcinomas (EOC) and their relationship to ovarian carcinomas and progression, and to evaluate it as a tumor marker for EOC diagnosis and prognosis indicator, telomerase activity was analyzed in 43 samples of EOC, 11 of each of benign ovarian tumors and normal ovarian tissues, as well as 4 borderline ovarian tissues with the use of telomeric repeat amplification protocol (TRAP). Telomerase activity positive rate in EOC was 76.7%(33/43 cases), 9%(1/11) in benign tumors .It was undetectable in normal ovarian tissues and benign ovarian tumors. There were significant differences among EOC and normal ovarian tissues and benign ovarian tissues ($p=0.0001$ and 0.0004 respectivily), But the differences in some patient's prognostic factors, such as tumor types, histological classification, clinical stage, and tumor metastasis were not significant. The results demonstrate that telomease activity is a common event in ovarian carcinogenesis. It occurs in the early period of EOC and lasts for the whole course of tumor progression. It could be used as a tumor marker for early diagnosis of EOC, but for the patient's prognostic value reminds to be further studied.

8.1

N-(4-HYDRXOYPHENYL)RETINAMIDE INDUCES UP-REGULATION OF GADD153 IN A NASOPHARYNGEAL CARCINOMA CELL LINE

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N-(4-hydrxoyphenyl)retinamide (4HPR), a synthetic derivative of retinoic acid, can inhibit cell proliferation and induce apoptosis in a variety of tumor cell lines, and appears to be a promising chemopreventive agent. To investigate the molecular mechanism of the induction of apoptosis by 4HPR, a cell line CNE3, which was originally established from a poorly differentiated nasopharyngeal carcinoma, was treated with 4HPR. The cells were observed to undergo apoptotic cell death in a time- and dose-dependent manner, as evident by their morphological changes examined by fluorescence microscopy; the formation of 'DNA ladder' on agarose gel; and the presence of sub-G_1 DNA content in flow-cytometric histograms. To identify genes whose expression was altered due to the effect of 4HPR, the cellular RNA was extracted and hybridized with a cDNA array with DNA probes corresponding to genes involved in apoptosis. Among a series of altered gene expressions, only GADD153 was up-regulated. Its expression was further corroborated with RT-PCR and Western blotting analysis. The gene expression of GADD153 was noticeably induced by 12 hours after the addition of 4HPR, which was about 36 hours ahead of the emergence of sub-G_1 peak. Our findings suggest that 4HPR stimulated a stress response as the initial event, and apoptotic death as a secondary event. Whether or not apoptosis will occur is determined by the coupling between the initial and secondary events.

8.2

INVERSE PLANNING BY CONVENTIONAL BEAM OPTIMISATION IN 3-DIMENSIONAL RADIOTHERAPY OF NASOPHARYNGEAL CARCINOMA

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Purpose: This study is to evaluate the efficiency of inverse planning by conventional beam optimization in 3-dimensional conformal radiotherapy (3DCRT) of nasopharyngeal carcinoma (NPC).

Methods and Materials: CT images of 10 NPC patients with T2 and T3 primary tumour were collected. 3DCRT plans were computed by the traditional forward planning and the newly developed inverse planning methods using the FOCUS treatment planning system. The forward plans were produced according to the routine planning criteria, whereas the inverse plans were generated by prescribing the dose requirements of the target volume (PTV) and organs at risk (OARs). The doses to the PTV and OARs were compared between the two planning methods by the dose volume histograms and normal tissue complication probability (NTCP).

Results: The inverse plans generated contained 6-8 coplanar beams, which were different from the 4 non-coplanar fields in the forward plans. There were no difference in the doses to PTV, spinal cord, brain stem and lens. The doses to the pituitary, temporal lobe and optic nerve were significantly higher in the forward plans. The NTCP of all OARs did not show significant difference.

Conclusion: The inverse planning programme provided an alternative method to produce effective conventional 3DCRT plans in the treatment of NPC.

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8.3

Comparative Genomic Hybridization Analysis Of Nasopharygeal Carcinoma – Consistent Patterns Of Genetic Aberrations And Clinicopathological Correlations

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To define the patterns of genetic imbalances in nasopharyngeal carcinoma (NPC), we studied thirty primary NPC tumors with comparative genomic hybridization (CGH). The common sites of chromosomal gains were found in descending order of frequency in 12p11.2-12 (36%), 12q14-q21 (33%), 2q24-q31 (23%), 1q31-qter (20%), 3q13 (20%), 1q13.3 (20%), 5q21 (17%), 6q14-q22 (13%), 7q21 (13%), 8q11.2-q23 (13%) and 18q12-qter (13%). The common sites of chromosomal loss were at chromosome band 3p14-p21 (20%), 11q23-qter (20%), 16q21-qter (17%) and 14q24-qter (13%). Correlation with clinicopathologic features showed that 3p loss was associated with a significantly higher risk of death related to recurrence as compared with patients without 3p loss (50 % *vs* 9 %, p = 0.029). The presence of 16q loss was associated with more advanced stage tumors (stages I & II : 6% *vs* stages III & IV: 33%, p = 0.046).

We conclude that consistent patterns of genetic imbalances can be observed in NPC. Deletion of 3p and 16q were associated with higher risk of tumor recurrence and advanced stage cancer.

8.4

MANAGEMENT OF EXTENSIVE CERVICAL NODAL METASTASIS IN NASOPHARYNGEAL CARCINOMA AFTER RADIOTHERAPY – A CLINICOPATHOLOGIC STUDY

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Aim

The efficacy of after loading brachytherapy following radical neck dissection (RND) in the management of extensive cervical lymph nodal (CLN) disease in nasopharyngeal carcinoma after radiotherapy is evaluated. The prognostic factors and the pathologic nature of the neck disease were examined prospectively.

Patients and method

27 nasopharyngeal carcinoma patients with extensive CLN metastasis following external radiotherapy were treated with RND. 13 of them had in addition, after loading brachytherapy with Iridium wire (Ir^{192}). The RND specimens of the 27 patients were examined with step serial whole organ sectioning.

Results

All patients survived and their wounds healed primarily. Pathological examination revealed 183 tumor-bearing lymph nodes, 5 times more than clinical finding. Extracapsular tumour extension was seen in 84%. Multivariate anaylsis identified the number of tumor-bearing lymph nodes to be the significant factor that affected control of disease. The 3-year actuarial tumor control for the groups with and without brachytherapy were 60% and 61% respectively.

Conclusion

Recurrent cervical lymph nodes after radiotherapy in nasopharyngeal carcinoma are extensive and RND is mandatory for a successful salvage. When the nodes infiltrate or adhere to surrounding tissue, after loading brachytherapy with iridium wire could provide satisfactory local tumor control.

8.5

IMMUNE ESCAPE MECHANISMS OF NASAL T/NK-CELL LYMPHOMA

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Several mechanisms of immune escape might be in operation in Epstein-Barr virus associated nasal T/NK-cell lymphoma (NL). We have previously shown the downregulation of the immunogenic EBNAs by alternative promoter usage and the preferential selection of deletion LMP1 genotype in nasal lymphoma. To further examine the strategies used for immune escape by this tumour, we analyzed HLA class I expression on frozen sections of 15 cases along with β_2-microglobulin (β_2m) and transporter associated with antigen processing 1 (TAP1) expression on paraffin sections of 39 cases by immunohistochemistry. The majority of nasal lymphomas showed positive staining for HLA class I, β_2m and TAP1 on most of the tumour cells, except for two cases (5%) that completely lacked β_2m staining. We next immunostained for interleukin-10 (IL-10) on frozen sections of 13 cases, all of which showed strong expression by the majority of the tumor cells. Transcription of human IL-10 but not viral BCRF1 (vIL-10) was identified by RT-PCR. The data in this study demonstrated that the antigen presentation system seems to be intact in nasal lymphomas suggesting that EBV peptide epitopes could potentially be presented by the tumour cells to the virus-specific cytotoxic T lymphocytes. IL-10 might have a direct immunosuppressive effect on the cytotoxic lymphocytes (paracrine effect) or might enhance the growth or survival of the NL tumour cells themselves (autocrine effect).

8.6

EXPRESSION AND CLINICAL SIGNIFICANCE OF DRUG-RESISTANCE GENES ASSOCIATED MARKER IN CARCINOMA

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The gene expression and clinical significance of drug-resistance marker (include GST-π, MDR1, MRP and LRP) in cilinical carcinoama (include breast carcinoma, lung carcinoma, esophageal carcinoma and ovarian carcinoma and it's relation with the curative effect was studied. In additional, the possibility using the trends of plasma level of GST-π in ovarian carcinoma for dynamic curative effect judgment was discussed too. Methods: The gene expression of GST-π, MDR1, MRP and LRP were determined with RT-PCR, the plasma level of GST-π was determined with radio-immunoassay. Results: the expression of ratio of GST-π, MDR1, MRP and LRP are more than 30% in detectable carcinoma. The highest expression ratio is found in different carcinoma, GST-π in esophageal carcinoma (80%), MDR1 in breast carcinoma (94.7%), and LRP in ovarian carcinoma (87.8%). The co-expression ratio of drug-resistance associated maker showed higher than that expression separately ($p<0.05$). The non-responder to platium based combination chemotherapy exhibited higher ratio of GST-π and (or) MDR1, LRP co-expressionn than responder ($p<0.01$). The plasma level of GST-π, after chemotherapy is significance higher than before chemotherapy. Concludes: GST-π, MDR1, MRP and LRP are major factors associated with drug-resistance. Co-expression is one of major character of drug-resistance associated marker expression. Combination of several drug-resistance associated markers may help clinic to judge the respondent of chemotherapy. In additional, using the trends of plasma level of GST-π in ovarian carcinoma for dynamic curative effect judgment is one of potential method too.

8.8

REGULATION OF ATM INDUCTION

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ATM, the tumour suppressor protein mutated in ataxia-telangiectasia, is of pivotal importance in controlling the cells primary response to DNA damage. Mutations in ATM give rise to radiosensitivity and defective cell cycle checkpoint control. In response to DNA damage ATM kinase is rapidly activated and studies to date have failed to observe a change in the level of ATM protein post-irradiation. Contrary to previous results we report here both rapid and delayed forms of induction of ATM levels within the cell. Factors effecting growth in cultured cells initiate delayed induction of ATM that reaches a maximum over a period of days. However, in fresh tissues radiation induces ATM levels rapidly in a radiation dose dependent fashion, most likely via a post translational mechanism. Some normal fresh cells with negligible levels of ATM and some cell lines with very high / preinduced levels of ATM were relatively resistant to radiation induction. Radiation induction of ATM protein appears to be associated with radio-protection.

8.10

LOCAL EXPERIENCE WITH HIGH GRADE ASTROCYTOMA

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From 1990 to 1998, 164 patients with histological proven high grade glioma were referred to our department for assessment. The data was analysed retrospectively. The median age of the population was 54 (range from 5.0 to 85.5). 112 patients had glioblastoma multiforme and 52 had grade III astrocytoma. 79% of the patients received post-op radiotherapy. The BED range from 7.2 to 72 $Gy_{\alpha/\beta}$, the median was 63.7. The median follow up period was 5.3 months (range from 0.3 to 101.6).

Median survival for patients with GBM and grade III astrocytoma was 7.0 and 11.5 months respectively. Multivariate analysis revealed that the mental function, working ability, age and the delivery of radiotherapy were significant independent prognostic factors.

9.1

Beyond Boundaries- an attempt of using Adventure-based Therapy to help long–term cancer survivors

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Once people having cancer, they will be labelled as "patient" by others in the rest of their lives. Under the influences of this "sick-role", some of the cancer survivors have a strong sense of inadequate. Some of them could not adjust to the changed relations & responses of family members and colleagues which frustrated them a lots.

The CancerLink attempted to use the Adventure-based Therapy to develop their self-confidence, expand their problem-solving capacities and get some reflections on their "sick role". Adventure-based therapy is based on the philosophy of experiential education which direct personal change at a meta-process level.

The program was held in 1999. Thirty-four cancer survivors had participated in this training. Feedback from participants was positive & encouraging.

The presenter will outline how they use this approach in this prevention.

9.2

The health care needs of the families with cancer children.

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This study aimed to investigate the health service needs of families with cancer children, and to identify the service gap from the parents' perspective. Twenty-two parents were recruited in semi-structured interviews. The transcripts were analyzed.

The findings revealed that they concerned much on special diet care and recreational needs for the cancer children. They faced the time competition between caring for the cancer children and the families. They feared about social stigma. The children's problem had affected the family life, mostly on carer's emotional needs, family relationship, social / recreational needs. Mothers were the most affected one in the family. Some parents did feel supported by getting the instrumental help from friends and relatives. On contrary, some parents were reluctant to mention her problems and seek help from others. They appreciated the psychological support and information sharing from other patients' parents. From the descriptive dialogues, majority of the parents expressed the emotional exhaustion and mental distress. Most of them agreed that the communication between different health care professionals, and information giving about the illness were enough. Some of them expected to learn throughout the care after acquiring the basic or initial care. Majority of parents responded positively on the sense of involvement in decision-making regarding children's health care. However, some parents felt dissatisfied, which was mainly concerned on the frequent change of staff.

The unique caring experiences of parents reflected the need and concern for cancer children and their families. Some parents were aware of their active involvement regarding their children's health care. The parents seldom identified support from communities. Families' voices and their implications to the health care service should always be considered.

9.3

Sexual Rehabilitation Program for Cancer Patient

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In regarding to the needs of cancer patients on sexual rehabilitation, Queen Elizabeth Hospital Department of Clinical Oncology and Cancer Patient Resource Centre had cooperated to organize a sexuality talk for cancer patients and their relatives. The objectives of program were to explore the needs of them and to see their attitude on the above issue.

An anonymous questionnaire for after treatment cancer patients was organized to collect some basic information for the talk. 19 completed questionnaires were finally collected. Patient types were included Nasopharyngeal Carcinoma, Ca Breast and Ca Gynae.

In reviewing the result of questionnaire and the program, we found that most of patients have misconceptions towards their sexual life after treatments. Besides, the shadow of cancer treatments were affected their sexual life and the intimacy with their partner. During the talk, most of their concerns were focused on the issue of fertility, how cancer treatments affected the sexuality and the relationship between cancer relapse and sexual intercourse. However, they have not raised any issue about their sexual life. Cultural taboo could be the obstacle for Chinese patients to share this issue.

Some of the suggestions are stated, first, to develop sexual education materials for ocal cancer patients. Second,to organize related training to enhance the knowledge of front line staff. Third, sexual rehabilitation program could incorporate into other rehilitation for cancer patients. Embarrassment could be lessen than to organize in a single program. Finally, to study the needs and difficulties that local patients envisaged.

*We would like to take this opportunity to thank for Dr. V. Tse to deliver the talk and Dr. W.L. Leung to lead the discussion group.

9.4

Cross-cultural validation of McGill Quality of Life Scale in palliative care for Hong Kong Chinese-final analysis

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Introduction
The value of QOL assessment in palliative care is increasingly recognised. McGill Quality of Life scale (MQOL) is designed specifically for palliative care, but its cross-cultural validity needs to be determined, before it can be applied in different cultures.
Method
All consecutive new admissions of advanced incurable cancer patients within a period of 18 months were recruited in a multi-centre study. Their QOL were assessed using a translated and slightly modified version of MQOL for the Hong Kong Chinese (MQOL-HK). The QOL of recruited subjects were evaluated within 72 hours of admission. Validity and reliability were assessed.
Results
A total of 462 patients were recruited. Mean age was 61.5 years (s.d. 14.5, range 16-89). 53 % were male. The top diagnoses were lung, colorectal, liver, breast and nasopharyngeal cancers. The average time for completing a questionnaire is 30 minutes. Principal components analysis demonstrates that there are 5 domains in MQOL-HK: physical, psychological, existential, support, and sex, accounting a total of 59% variance. Internal consistency of the MQOL-HK is good with Cronbach alpha of 0.8. There is good construct validity with overall score ($p=0.001$) and concurrent validity with Spitzer index ($p=0.004$). Intra-class correlation for inter-rater and test-retest reliability is high ($p<0.001$). Multiple regression analysis shows that existential domain is the most important domain ($p=0.000$), and sex the least important. Significance of eating and "face" for HK Chinese is also confirmed. The mean QOL score was 6.85 out of 10. The item on most severe physical symptom had the lowest score (4.59 out of 10). The item on face had the highest score (8.87 out of 10).
Conclusion
Our study demonstrates that QOL in palliative care does have cross-culturally robust constructs. Cross-cultural validity of MQOL is confirmed. The MQOL-HK is acceptable, valid and reliable. Existential domain is proven to be important domain for HK Chinese. "Face", eating, and sex are also relevant. Physical symptom is the worst QOL score on admission and needs adequate attention. An international cross-culturally validated instrument is a valuable asset for comparison of interventions and outcomes across the world.

9.5

The process of empowerment among Chinese cancer patients in Hong Kong

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The paper presents the process of empowerment for cancer patients based on empirical evidence of a phenomenological study of 12 cancer patients. In-depth interviews were conducted to describe the process of empowerment as it pertains to cancer patients from the patients' perspective.

Empowerment is an intrapersonal and interpersonal process through which the patient obtains strength and mobilizes both internal and external resources to develop self-reliance, partnership and perceived control over issues of individual concern. The first stage of empowerment is described as a motivational process which the informants identify meaning of life and illness which motivated and sustained the process of empowerment. It is then followed by obtaining resources and changing their perspectives of thinking. Empowerment is motivational, relational and interpretative. As a result of being empowered, the individual attains a set of insights and abilities, which are the outcomes of the empowering process, including acceptance of illness, gaining confidence, knowledge and skills and flexible optimism. Empowerment of Chinese cancer patients in Hong Kong does not only imply that the patient is in control of environment, but also include secondary control of accommodating to the environment. It emphasizes both acceptance and activism as core values of empowerment. Nurses need to assist people challenged to live with cancer to identify, develop and mobilize the internal and external power resources available in their immediate environment.

9.6

A Practical Model of Collaboration Between Hospice Bereavement Team and Community Bereavement Centre in Provision of Bereavement Care – Experience in Hospice Unit of Caritas Medical Centre

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Bereavement care is an important component of the care for the dying and their families and the role of community bereavement care providers is beyond doubt in its provision. Successful referral of families to the community bereavement workers relies on good collaboration with the referrers.

A practical model of collaboration between the bereavement team of the Hospice Unit in Caritas Medical Centre, which consists of designated medical social workers and hospice nurses, and the Jessie and Thomas Tam Centre, a community bereavement centre, was implemented. The objective is to improve the bridging so as to facilitate families to receive bereavement service from the community centre.

In this practical model:

a) Support sessions were carried out in the referring centre i.e. Hospice Unit of Caritas medical Centre before the death of the terminal cancer patients
b) Support sessions were jointly operated by workers from both parties
c) Terminal cancer patients and their families were recruited from the inpatient and outpatient pool of the Hospice Unit
d) Support sessions were operated using photography and body massage as the tools.
e) Patients' information was shared between workers before the sessions
f) Practical skills were shared between workers during and after the sessions

24 support sessions were carried out on a trial basis from the period of September 1999 to March 2000 with 96 patients and 99 relatives participated. The sessions were well received by patients and families. A total of 22 families were successfully recruited to the Jessie and Thomas Tam Centre after the death of the patients so that bereavement care could be continued. The experience of interaction between the workers from both parties was highly valued by the staff.

Our experience with this model of collaboration has illustrated that it is feasible and effective in bridging the bereavement service between hospital team and that in the community.

10.1

High-density allelotyping on chromosome 8p in hepatocellular carcinoma – allelic losses associated with tumor progression.

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Frequent deletions on chromosome 8p have been reported in hepatocellular carcinoma (HCC) and the presence of one or more tumor suppressor genes (TSG) have been implicated. To localize regions of possible TSG and to evaluate the clinicopathological significance of chromosome 8p deletions, we performed high-density allelotyping on 8p in HCC from 60 Chinese patients with HCC resected and examined clinicopathological and prognostic correlation. Microsatellite analysis for loss of heterozygosity (LOH) was performed using 24 polymorphic markers. Allelic loss at one or more loci was observed in 46 (77%) HCCs. Twelve (20%) HCCs showed frequent interstitial deletions and 19 (32%) exhibited 8p hemizygosity. Three regions with high frequencies of LOH were identified (8p23.1-23.2, 8p22 and 8p21.1-21.3). Detailed deletion mapping delineated two distinct minimal deleted regions, one within a 4.4-cM interval at 8p23.1, and the other within a 10.1-cM interval at 8p21.3. Tumors with frequent interstitial losses or hemizygosity were significantly associated with larger tumor size (>5 cm) ($p = 0.033$). LOH on locus D8S1721 (within the 4.4-cM minimal deleted region) was more frequently seen in tumors with venous permeation ($p = 0.037$) and in tumors without tumor encapsulation ($p = 0.001$), both features of more aggressive tumour behavior. LOH on locus D8S1771 (within the 10.1 cM minimal deleted region) was more frequently found in tumors with poorer cellular differentiation ($p = 0.038$). Moreover, allelic losses on the distal part of 8p23 were significantly associated with shorter overall survival rates ($p = 0.012$). To conclude, specific regions of frequent allelic deletions and minimal deletion regions were identified, suggesting the presence of TSG(s). The close association of allelic losses in specific regions on 8p with a more aggressive tumour behavior and poorer prognosis suggests that loss or inactivation of TSG(s) located within these regions confers a tumor growth advantage and contributes to the progression of HCC.

10.2

Mutation and Expression of β-Catenin Gene in Hepatocellular Carcinoma - Clinicopathological and Prognostic Significance

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Recently, Wnt signaling pathway has been identified as a major molecular mechanism leading to cancers. Activation of the Wnt signaling pathway results in the formation of stabilized free cytoplasmic β-catenin, which then enters the nucleus and forms a complex with members of the Tcf/LEF transcription factors to up-regulate expression of target genes. In this study, we performed mutation analysis on the exon 3 of β-catenin gene, investigated the subcellular expression of β-catenin protein in 60 primary HCCs from Chinese patients and performed clinicopathological correlation. Somatic mutations in exon 3 of β-catenin gene and nuclear accumulation of β-catenin protein were observed in 12% and 17% in our HCCs respectively. All the mutations were present at sites responsible for GSK-3β mediated phosphorylation and ubiquitination leading to stabilization of free cytoplasmic β-catenin. Nuclear accumulation of β-catenin protein was observed in all 7 cases with β-catenin mutation and in 3 additional cases without mutation. Nuclear accumulation was closely associated with mutation ($P<0.001$). No nuclear accumulation could be observed in non-tumorous hepatocytes in adjacent livers. In the remaining cases, over-expression of β-catenin without nuclear accumulation was observed in 31 (62%) of 50 cases. This suggests that the mechanisms leading to over-expression of β-catenin may be heterogeneous and independent of Wnt signaling pathway. Over-expression of β-catenin in these 31 cases was more frequent in tumors greater than 5 cm in diameter ($P=0.022$) and in tumors with poor cellular differentiation ($P=0.037$). Patients with over-expression of β-catenin protein had significantly shorter disease free survival (DFS) than those with normal expression ($P=0.039$). To conclude, β-catenin mutation and deregulation play an important role in the hepatocarcinogenesis in patients from Hong Kong and over-expression of β-catenin via mechanism(s) independent of Wnt signaling pathway appeared to have pathological and prognostic significance.

10.3

COMPARISON OF MODIFIED COLORIMETRIC MTT ASSAY AND SULFORHODAMINE B ASSAY FOR TUMOR CHEMOSENSITIVITY TESTING

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Objectives: Modified MTT assay using balancing-cell equation (BCEq-MTT assay) for in vitro tumor chemosensitivity testing was applied and compared with Sulforhodamine B (SRB) assay.

Methods: Traditional MTT (Tra-MTT) and SRB assays were carried out to measure tumour chemosensitivity of four tumour cell lines (Hep-G2, etc). Each cell line was exposed to 6 grade dilutions from 1% to 500% of standard test drug concentrations (STDC) of Adriamycin and Mitomycin C for 3 days with different culture duration. For BCEq-MTT assay, the equation to calculate the percentage of tumour growth inhibition (%TGI) is:

$$\%TGI = 1 - \{[\ln A_{max} - \ln(A_{max} - A_t)]/[\ln A_{max} - \ln(A_{max} - A_c)]\}^{1/b} \times 100\%.$$

(notes: A_{max} = a constant number, A_t = absorbance of tested group, A_c = absorbance of control group, b = allometric power)

Results: Comparison of the results of %TGI and IC_{50} in MTT assay showed that %TGI predicted by Tra-MTT assay was lower than that by BCEq-MTT assay or SRB assay, and IC_{50} predicted by Tra-MTT assay was in average 3 fold of that by BCEq-MTT assay or SRB assay. %TGI and IC_{50} predicted by BCEq-MTT assay were approximately the same value as predicted by SRB assay in 6-day culture duration.

Conclusion: BCEq-MTT assay is applicable for in vitro tumor chemosensitivity testing. It's a successful solution to the underestimation of chemosensitivity of traditional MTT assay compared with SRB assay.

10.4

Correlation of p53 Status and Pathologic Complete Response in Locally Advanced Rectal Cancer Patients Treated by Pre-operative Chemo-radiation

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The relation of p53 status and pathologic complete response (pCR) to pre-operative chemo-radiation has been controversial. Whether the use of continuous 5-FU infusion concurrently with pelvic radiation results in any difference in pCR in tumors with different p53 status has not been studied. The study group comprised 26 patients with T3/4 adenocarcinoma of rectum treated between March 1994 to July 2000 with pre-operative pelvic radiation of 39.6 – 59.4 Gy. Most patients (23/26) received concurrent 5-FU under different regimens (11 had continuous infusion and 12 had bolus). All patients underwent surgical resection. p53 immunohistochemical staining was performed on pre-treatment biopsy specimens. The staining pattern and the chemotherapy regimen used were correlated with pCR rate and survival by Fisher's exact test. Concurrent continuous 5-FU infusion with pelvic radiation is associated with a higher pathologic complete response rate (45.5% vs 6.7%, $p = 0.054$) and a trend towards longer survival ($p = 0.091$) compared to 5-FU bolus /no chemotherapy. p53 status is not related to pathologic complete response ($p = 0.630$) nor survival ($p = 0.439$). Other prognostic factors are still being analyzed. With our limited experience, we did not find p53 status in rectal CA has any prognostic values. However, the use of continuous 5-FU infusion is associated with a higher complete pathologic response and a trend towards increased overall survival. Further study with larger patient population and longer follow-up is warranted.

10.5

OVEREXPRESSION OF PROTEIN KINASE C-β1 ISOENZYME SUPPRESSES SC-236-INDUCED APOPTOSIS IN GASTRIC EPITHELIAL CELLS

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Background & Aims: Specific COX-2 inhibitor suppressed tumor growth in nude mice bearing gastric cancer xenografts.(1) This study investigated the role of protein kinase C isoforms in COX-2 induced apoptosis. Methods: Gastric cancer cell line AGS was studied. The protein levels of 12 PKC isoforms and apoptosis-related genes including p53, $p21^{waf1/cip1}$, bcl-2, bax, bad and c-myc were detected by Western blotting. The effect of PKC-β1 overexpression by transfection with its complementary DNA (cDNA) on SC-236-induced apoptosis and apoptosis-related genes was further investigated. Results: SC-236 induced apoptosis in AGS cells. Treatment with SC-236 decreased the protein expression of PKC-β1, increased the expression of PKCδ and PKCη, but did not alter the expression of the other PKC isoforms in AGS cells. Overexpression of PKC--β1 attenuated the apoptotic response of AGS cells to SC-236, associated with overexpression of $P21^{waf1/cip1.}$ Conclusions: SC-236-induced apoptosis in gastric cancer cells is partly mediated by differential regulation of PKC isoform expression. Enhanced expression of exogenous PKC-β1 protects against SC-236-induced apoptosis through upregulation of $p21^{waf1/cip1}$.

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10.6

BCL10 SOMATIC MUTATIONS RARELY OCCUR IN B-CELL NON-HODGKIN'S LYMPHOMAS OF GASTRIC ORIGIN-DETECTION OF HIGH FREQUENCY OF POLYMORPHISMS IN *BCL10* CODING REGION

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The *BCL10* gene has recently been cloned from the chromosomal translocation t(1;14)(p22;q32) found in a low grade mucosa-associated lymphoid tissue (MALT-type) lymphoma, and has been implicated in the pathogenesis of this and several other tumor types(1). *BCL10* is a cellular homolog of the equine herpesvirus-2 E10 gene, which contains an amino-terminal caspase recruitment domain (CARD) and plays a role in apoptosis. BCL10 was shown to have frequent somatic mutations and short deletions within the coding region in MALT lymphomas and a variety of other lymphomas and solid tumors. High-grade MALT lymphomas, showing the histology of diffuse large B cell lymphomas (DLBCL), were reported to show a slightly higher mutation frequency than low-grade MALT tumors. These observations have been recently questioned. In this study, we examined *BCL10* gene mutations by direct sequencing of the entire coding region of the *BCL10* gene, amplified from paired normal and tumor genomic DNAs, as well as tumor cDNAs, in 23 cases of primary gastric B-cell lymphomas (GL), comprised of 3 MALT, 17 diffuse large B cell lymphomas (DLBCL) and 3 MALT/DLBCL cases. Heterozygosity due to three types of known polymorphisms in codon 5 (17.3%), codon 8 (21.7%), and codon 213 (8.6%) were observed in both normal germline DNA and tumor DNAs and tumor cDNAs in individual cases. In one case (4.3%) G/C heterozygosity in codon 8 in normal germline DNA was reduced to homozygosity (LOH) in tumor DNA and cDNA. Mutations inactivating *BCL10* gene product function and the post-transcriptional alterations indicated by abnormalities in *BCL10* mRNA sequence in tumor cDNAs were not found in any of these cases. Since RT-PCR analysis showed that all the cases of GL expressed exons 1 to 3 of *BCL10* mRNA, it excluded the possibility of *BCL10* being a deleted tumor suppressor gene in GL. Overall, our results show that somatic mutations in the *BCL10* gene rarely occur in GL and indicate that this gene is unlikely to be of pathogenetic significance in this disease.

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10.7

Intensive chemotherapy with peripheral blood stem cell support for leukemia and lymphoma relapse after allogeneic bone marrow transplantation: clinical results and chimerism findings.

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Background Disease relapse is the commonest cause of treatment failure after allogeneic bone marrow transplantation (BMT) for leukemia and lymphoma. The prognosis is poor, and salvage therapy is associated with high morbidity and low efficacy.

Material and methods: Initial chemotherapy was ICE (idarubicin 6mg/m^2 dailyx5, cytosine arabinoside (Ara-C) 600mg/m^2 daily x5, etoposide 150mg/m^2 daily x3) for leukemia, and BEAM (BCNU 60mg/m^2 x1, etoposide 75mg/m^2 x4, Ara-C 100mg/m^2 x4, melphalan 30mg/m^2 x1) for lymphoma. PBSC was harvested from the previous donor after 5 days G-CSF (10mg/kg) mobilization.

Results A median of $5.6x10^8$/kg lymphocytes and $2.6x10^6$/kg CD34 +ve cells were infused. There were two therapy-related deaths (2 CML-BT) and two deaths due to leukemia (2 AML). The median time for white cell recovery was 14 days (range 10 to 29). Complete remission was obtained in 13 cases (5AML, 6ALL, 1HD, 1NHL) (65%) and partial remission in 1 case (NHL). Patients with clinically isolated extramedullary relapse all showed complete donor chimerism in the marrow and responded completely. Patients with complete lost of graft were refractory. In 8 case of mixed chimerism, 19-40% donor DNA was detectable at relapse, and 6/8 cases (75%) achieved CR. Complete donor chimerism was demonstrated in 5 cases in persistent remission, but chimerism remained mixed in 1 case that relapsed at 2 mo. The median follow up was 6 mo. (range 1-16). Two patients died in remission. One patient (AML) died of relapse, and 2 cases (ALL/CML) suffered isolated pelvic relapse. Significant chronic GVHD was present in seven cases.

Conclusions ICE and PBSC is effective as first line salvage. Predictors for an unfavourable outcome include CML-BT, complex cytogenetics, short disease free interval. Isolated EMD and ALL show the best response. Therapy should be commenced before donor chimerism is lost. However, minimal residual disease was still detectable in two thirds of survivors, and may need further donor lymphocyte infusion.

10.8

CT-Pathologic Correlation of Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) in Non-Small Cell Lung Cancer: A Pilot Experience

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Purpose: To correlate tumor sizes on computerized tomography (CT) with tumor sizes measured microscopically (i.e. GTV-CTV margin) in non-small cell lung cancers.

Methods and Materials: Patients with operable non-small cell lung cancer are identified pre-operatively. Once the surgical specimen is available, it is oriented with the surgeon and the pathologist. Seven whole-mount, cross sectional histologic glass slides were made from five tumors using formalin fixation and H&E staining. The pathologist then outlines the cancer-containing area (Micro-GTV) and the area of surrounding inflammatory response (Micro-GTV + inflammation). Pre-operative CT scan is used for outlining tumor on the corresponding slice (CT-GTV). Correlation of the areas of Micro-GTV, Micro-GTV + inflammation and CT-GTV was performed.

Results: There is an obvious trend that the CT-GTV is bigger than the Micro-GTV except for specimen #1 where the two areas are about equal. However, if we compare the CT-GTV and the Micro-GTV + inflammation, the difference between the two areas become smaller.

Conclusions: Modern CT scan might over-estimate the GTV in non-small cell lung cancer. The GTV to CTV margin could actually be zero or even a negative value. The findings in this small study are interesting and provoking. Further study with larger number of patients and more rigid quality control is warranted to confirm our findings.

10.9

DIFFERENTIAL GENE EXPRESSION IN GESTATIONAL TROPHOBLASTIC DISEASE USING cDNA ARRAY

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Gestational trophoblastic disease (GTD) is a disease derived from the placental trophoblasts and includes hydatidiform mole (HM), invasive mole, choriocarcinoma (CCA) and placental site trophoblastic tumour. Most HM spontaneously regressed after suction evacuation while a portion may persist requiring chemotherapy. The profiling of differentially expressed genes in the human CCA cell line JAR as compared with normal placenta was performed using cDNA expression array. The relationship between the apoptosis related genes and progress of HM was further investigated using human apoptosis array. Poly(A)-RNA (QuickPrep^{R} Micro mRNA Purification Kit, Pharmacia Biotech) from a normal human first trimester placenta and the JAR cell line were reversely transcribed into cDNA. The cDNA probes were hybridized to membranes which contain 588 known genes involved in important biological processes (CLONTECH's ATLAS^{TM} Human cDNA Expression Array). Similarly, mRNA from metastastic and regressive HM moles were studied with membranes including 205 genes related to apoptosis (CLONTECH's ATLAS^{TM} Human Apoptosis Array). Several mRNAs, such as the tyrosine kinase EGF receptor Her4 (ERBB4), Natural killer cell enhancing factor, apoptosis associated proteins: CD70 antigen & c-myc transcription factor, glutathione S-transferases M1 & T1 and transcription factor TF11B were strongly expressed in JAR. Cell cycle control proteins such as p120 antigen, cyclin G2 and DNA binding protein DB1 showed decreased expression in JAR when compared with normal placenta. On the other hand, regressive and metastatic HM show similar expression pattern in the apoptosis array. Only a few genes show increased expression in metastatic mole including p53-induced protein, mcl-1 and transforming protein rhoA H12. Differential expression of these genes in trophoblastic tissue will be further studied.

11.1

The Use of Intraductal Ultrasound in the Management of Biliary Stricture

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Background : The underlying pathology of biliary stricture is an important information to direct subsequent intervention. Current diagnostic methods, including percutaneous ultrasound, computed tomography, magnetic resonance & brush cytology, are not adequately sensitive to differentiate benign and malignant pathologies.
Aim : To define the use of intraductal ultrasound (IDUS), in addition to other pre-operative tests, in the management of biliary stricture.
Patient and Methods : Retrospective data of patients with biliary stricture from 1994 - 1999 was collected. The use of brush cytology and other imaging studies, in the diagnosis of biliary stricture, was reviewed. From end of 1999 onwards, consecutive patients with biliary stricture were selected to undergo IDUS. The high resolution (20 MHz) and the small size of the miniature ultrasound probe (6 F) allow better delineation of the anatomy and provide valuable information about the biliary stricture. Finally, the IDUS image was compared with the final histology and see whether we can obtain any relevant correlation.
Results : During the period 1994 – 1999, brush cytology, either in antegrade or retrograde approach, was performed in 98 patients with biliary stricture. The sensitivity and accuracy were only 47% (31/66) and 84.3% (27/32) respectively. Despite of the improved and standardized technique in obtaining brush cytology and use of conventional imagings like computed tomography (CT) and percutaneous ultrasound (US), the underlying nature of the stricture was still not certain in significant number of patient. From end of 1999 onwards, we had recruited 20 consecutive patients with biliary stricture for IDUS. It was shown that IDUS could further characterize the nature of biliary stricture. It provided additional informations such as : (1) the origin of pathology, (2) the relationship of the stricutre with the hepatic bifurcation, (3) lymph node status along the porta hepatis, (4) any vascular encasement and (5) other concomitant pathology like small common bile duct stone and chonorchiasis. To further improve the diagnostic accuracy, IDUS was also performed in the resected specimen and the image was compared with the final histology. Patients with potentially resectable tumour would further undergo diagnostic laparoscopy (DL) and laparoscopic ultrasound (LUS) to rule out carcinomatosis peritonei and to search for vascular invasion in the mesenteric axis before planned resection. The combination of both diagnostic tests could provide important information about staging of the tumour before planned dissection.
Conclusion : IDUS is a promising diagnostic imaging in biliary stricture. It allows better definition of the biliary stricture. The combined use of IDUS and other investigations like brush cytology and laparoscopic staging should be able to offer accurate information to guide subsequent intervention.

11.2

Genome-wide expression profiling of hepatocellular carcinoma by cDNA microarray technology

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Liver cancer is the second most common cause of cancer deaths in Hong Kong, of which hepatocellular carcinoma (HCC) constitutes the major group of all liver cancers. Life expectancy after the diagnosis of HCC is extremely short, usually within 3 months. Prognosis of HCC patients after hepatectomy, the only form of curative treatment other than liver transplantation, is not promising and 5-year survival rate remains at a low level. Nevertheless, majority of patients benefit from the operation and a proportion of them remain well for several years after the surgery. Patients' outcomes are heterogeneous and the existing clinical parameters cannot predict the results or their responses to a particular treatment in an individual. These can be due to the molecular heterogeneity of the tumor. Detail molecular characterization of the tumor will certainly provide more information with clinical implication.

We have examined 40 specimens, with 20 pairs of HCC tumor and their corresponding non-tumorous adjacent liver tissues, using the high density cDNA microarray slides that have printed with 23,000 expression genes. Distinct expression profiles were observed in the tumor and the non-tumor liver tissues. This is an important finding as this indicates expression study which provides information whether the liver tissues reveal malignant properties. Gene clustering analysis revealed some remarkable gene clusters with different expression levels in tumor and the non-tumor liver tissues. Four major gene clusters were observed: 1. The HCC cluster. Genes in this cluster included alpha fetoprotein, some oncogenes and a number of ESTs. The tumors showed a high expression level but low level in the non-tumor tissues, and these genes were proposed to be HCC specific. 2. The liver function cluster. Many of the genes involved were responsible for the normal liver function, like the albumin and alcohol dehydrogenase gene. High expression level was observed in the non-tumor but low level in the tumor tissues. 3. The extracellular matrix cluster. Majority of them were extracellular matrix protein, like collagen and connective tissue growth factor. In general, low expression level was observed in non-tumor tissues but variable level in tumor. 4. The immunoglobulin cluster. Most of them were related to the immunoglobulin. Expression level in the non-tumor was high, possibly because of lymphocyte infiltration as most of the tissues were with chronic hepatitis. Genes in this cluster showed variable expression level in the tumor, possibly reflecting different degree of lymphocyte infiltration.

The expression data will be further correlated with the clinical details of the patients. Global surveys of the differential gene expression profile in the tumor tissues, their non-tumor counterpart and completely normal livers will be targeted to identify marker genes that will help understand the pathogenesis of the disease, facilitate early diagnosis, better prognosis and disease management.

11.3

HEPATOCELLULAR CARCINOMA: MN-DPDP ENHANCED MRI VERUS CONTRAST ENHANCED HELICAL CT; PRELIMINARY RESULTS

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Objective: A phase IV study is conducted to compare the efficacy of Mn-DPDP enhanced MRI and CECT in the detection and characterization of HCC.
Methods: Starting from December 1999, consecutive patients with suspected HCC referred to the Department of Surgery are invited to participate in the trial. All patients had at least one liver lesion detected by prior imaging studies. MR scans of the liver were obtained before and 15-30 minutes after infusion of Mn-DPDP at the dose of 5 μmol/kg body weight and injection rate of 2-3 ml per minute. Twenty-four-hour delayed MR scans were also obtained. Pre-contrast MRI protocol includes T1W and T2W sequences, while post-contrast MRI protocol comprises T1W and fast-STIR sequences. All adverse reactions related to the Mn-DPDP infusion were recorded. Helical contrast-enhanced CT scans were taken in the arterial and portal venous phase with delayed scans obtained at 8 minutes. The CT and MR images were evaluated by the investigators to determine the number of lesions detected as well as the lesion characteristics. The correct diagnosis (as correlated with the gold standard of histopathological findings) detected in the pre-Mn-DPDP MR images, CECT images and post-Mn-DPDP MR images were compared. For patients who did not undergo surgery/biopsy, the clinical and imaging findings up to one year after study will be used to determine the final diagnosis.
Results: Up to August 2000, twenty patients have been studied, including 15 males and 5 females, with a mean age of 53.8 (range 19-74). Only one patient developed minor reaction of urticaria and pruritis after Mn-DPDP infusion, suggesting that the MR contrast has a high safety profile. For the 20 patients studied, there are 10 HCCs, 1 regeneration nodule, 1 cyst, 1 metastasis, 1 extrahepatic tumour, 1 focal fatty infiltration and 2 haemangiomas. Four patients have indeterminate lesions, pending imaging and clinical follow-up to give the final diagnosis. All HCCs were detected by both techniques. HCC lesions show variable enhancement with Mn-DPDP, including portal vein tumour thrombus. Regeneration nodule demonstrates homogeneous enhancement. Delayed peripheral enhancement is seen in hepatic metastasis from colonic carcinoma. Non-hepatic lesions (cyst, haemangioma) do not demonstrate enhancement with Mn-DPDP. The MR contrast is unable to determinate the vascularity of the lesion, a useful feature in the characterization of HCC which is well assessed by CECT. Mn-DPDP enhanced MRI determines the hepatocellular nature of a hepatic lesion, finding of which is not possible with CECT.
Conclusion: Our preliminary result shows that contrast-enhanced helical CT better characterizes vascular hepatic tumours including hepatocellular carcinoma. Mn-DPDP enhanced MRI is useful in differentiating hepatocellular tumour from lesion of non-hepatocellular origin. Both techniques have a high sensitivity in detecting focal hepatic lesions.

11.4

Study On Relative Risk of Anti-HBe and Hyaluronic Acid in HCC Patients

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The Anti-HBe and serum hyaluronic acid (HA) of 177 cases of primary hepatocellular carcinoma (HCC) patients and 120 cases of non-HCC patients (including chronic hepatitis, hepatocirrhosis) were analyzed. The Anti-HBe positive rates were significantly higher in HCC group (HCC group: 67.8%, non-HCC group: 45%, u=30971,p <0.01). The relative risk of Anti-HBe to HCC was 2.75 with 95% reliability ranges from 1.68 to 3.92. In Anti-HBe positive patients associate with serum HA >200ng/ml, the relative risk to HCC was 7.14. The correlation index was 0.138 between content of HA and HCC (T=2.021,0.05>P>0.01).

The study shows that the HBV virus is still actively reproduced in patients whose HBe-Ag have been conversed to Anti-HBe. The variance often happens in Pre-C-Region of this virus. This variance may interfere with the apoptosis of liver cancer cell and promote the onset of HCC. HA is supposed to be cleaned out by endotheliocyte in hepatic sinus. This kind of immunity damage may cause the dysfunction of phagocytosis and imbalance of metabolism leading to apoptosis.

11.5

The Antitumor Effect of A Traditional Chinese Herbal Medicine Injection Produced by Membrane Filtration

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It is well known that the synthetic antitumor medicines are still low in the effectiveness of therapeutic treatment, while chemotherapy and radiotherapy have various side effects such as alopecia and emesis. Traditional Chinese Medicine (TCM), with comprehensive ingredients extracted from natural plants, has exhibited effective results in treating cancers without significant side effects. In this study, the antitumor effect of an anticancer TCM, Tai-ji (T-J) injection, which is extracted from ginseng, musk and scullcap etc, was evaluated through both laboratory experiments and clinical examinations. Two steps of membrane filtration are used for the production of T-J injection. Ultrafiltration with MWCO 20000 is used to purify the herb decoction solution in stead of the alcohol precipitation, which leads to loss of some components. Ultrafiltration with MWCO 5000 is applied to remove pyrogen and other impurities to ensure the quality of the injection. It has been demonstrated by the exosomatic screening tests that T-J injection is approximately 10% more effective than taxol and homoharringtonine, two commonly used antitumor medicines, for treating buccalcarcinoma, hepatocarcinoma and colocarcinoma. Based on clinical trials, the T-J injection is approximately 12% more effective than the previous form of capsule, when both are used to treat hepatocarcinoma. The analysis of high-pressure liquid chromatograph (HPLC) shows the composition of T-J injection, suggesting that the comprehensive TCM ingredients may have higher antitumor effect than an antitumor medicine of single component. This study indicates that the modern membrane separation can be used in TCM production for the improvement of the quality and effcetiveness, and that the comprehensive TCM ingredients can be better than a single medicinal component.

Key words: T. C. M.; T-J injection; Antitumor effect; Antitumor medicine; Membrane filtration; Ultrafiltration; HPLC

11.6

Result of pulmonary metastectomy in Grantham Hospital from 1984-2000

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From February 1984 to June 2000, 88 patients with pulmonary metastasis were operated in Grantham hospital. There were 33 women and 55 men. Their age ranged from 15 to 80 years with a mean of 50 years. One hundred and fourteen thoracotomies were performed. Twenty, 4 and 1 patients underwent second, third and fourth resections respectively. Fifty patients (57%) died at the time of analysis. Thirty-one patients (35%) are still alive without residual disease. Two (2.3%) patients are still alive with residual disease. Five (5.7%) patients lost follow-up. The mean survival period was 37 months with a range of 0 to177 months. Nineteen specimens were found to have tumour size greater than 5 cm. This may reflect the late detection of metastatic tumour and probably accounts for the higher percentage of our patients receiving more major lung resection (50%) than just wedge or segmental resection (50%). The actuarial survival rate was 66%, 33%, 21% at 2 year, 5 year and 10 year respectively.

11.7

DUAL EFFECTS OF CIGARETTE SMOKE EXTRACTS ON CELL PROLIFERATION IN CANCER CELLS

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Various studies have been shown that cigarette smoking is closely associated with gastrointestinal disorders, in particular, peptic ulcers, inflammatory bowel diseases and cancers. However, the underlying mechanism still remains unclear. In order to maintain the integrity in the gastrointestinal tract, it is important to have a good control of cell number, in which cell proliferation plays a significant role within the system. Failure in regulating this process would lead to the development of cancers. Hence, the aim of the study is to examine the effects of cigarette smoke extracts on cell proliferation in gastric epithelial cells (AGS) and colon epithelial cells (HT-29). Cigarette smoke extracts were extracted by respective solutions of ethanol and chloroform. Cell proliferation was assessed using [^{3}H]-thymidine incorporation assay. Apoptosis was measured by means of a cell death detection ELISA^{PLUS}. Both cigarette smoke extracts stimulated cell proliferation in a dose dependent manner in the AGS cells, which was accompanied by an increase in c-myc expression. On contrary, cigarette smoke extracts inhibited cell proliferation in the HT-29 cells in the same concentrations (10-100 μg/ml). The highest concentration of both extracts enhanced AGS cells to proliferate up to 50% of the control group, while in the HT-29 cells, it caused a 50% reduction in cell proliferation. The concentration used in both extracts did not exhibit significant apoptotic effect on these two cell lines. Cigarette smoke extracts shown to have no significant effect on lactate dehydrogenase activity (LDH) and cell viability. The present results indicated that cigarette smoke extracts had differential effects on cell proliferation in the AGS and HT-29 cells. Since both cell lines are derived from human carcinomas, these results would only explain the epidemiological findings with a prevalence of gastric carcinoma but not the colon cancer for cigarette smokers.

11.8

Repeated pulmonary metastectomy
- Grantham Hospital Experience from 1984-2000

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From February 1984 to June 2000, 88 patients with pulmonary metastasis were operated in Grantham hospital. Of these patients, 20 patients had repeated pulmonary metastectomies (3rd operation in 4 patients and 4th operation in 1 patient). There were 14 men and 6 women with a mean age of 40 years (range from 15 to 71). Majority of the patients (65%) had a latent period longer than 12 months. Six patients are still alive and 13 patients died at the time of analysis. One patient was lost to follow-up. The mean survival period was 47 months with a range from 6 to 177 months. The 2, 5 and 10 year survival rates after first resection were 73%, 35% and 18% respectively. It is comparable to the survival rates with the whole group (88 patients) whose survival rates were 66%, 33% and 21% at the 2, 5 and 10 year respectively. Repeated pulmonary metastectomies are likely to have a beneficial effect on survival in selected patients.

11.9

Video-Assisted Thoracic Surgery (VATS) Lobectomy for Lung Cancer

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Backgrounds: Video-assist thoracic surgery (VATS) has been shown to be safe and effective in the management of a variety of thoracic condition. Its application in major lung resection remains controversial. We would like to show our results of VATS lobectomy for highly selected lung cancer patients.

Methods: This is a retrospective study of 20 VATS lobectomy procedures. All patients were good risk patients with clinical stage I non-small cell lung cancer. Surgical access was through a short 4 to 5 cm submammary incision and through three ports incision in lateral chest wall. All surgery was performed using an endoscopic hilar dissection technique. Survival calculation was using Kaplan-Meier.

Results: Twenty VATS Lobectomies were performed from1995 to 1999. Follow up period ranged 16 months to 60 months with a mean of 51 months. The size of tumour ranged 1.5 to 3 cm (mean 2.3 cm). The staging of tumour was T1 N0 M0 in seventeen patients, T2 N0 M0 in one patient. T1 N2 M0 in one patient, T3 N1 M0 in one patient. The cell type included 16 adenocarcinoma, 3 squamous cell carcinoma, 1 lymphoepithelioma-like carcinoma. There was no conversion to open thoracotomy. Operation time averaged 160 minutes. Mean blood loss 200 ml. Complications included air leakage (>4 days) in 4 patients, atrial fibrillation in 1 and sputum retention in 1. Mean hospital stay was 10 days (ranged 8-45 days). Follow-up of 20 patients, 5 patients died of systemic recurrence, 1 recurrence within thorax and patient still survives after second operation of excision. No port site or pleural recurrence occurred. 3-year free of tumour was 82%. 4-year free of tumour was 68%.

Conclusion: Video-assisted lobectomy may be a suitable operative technique in selected early lung cancer (Stage I non-small cell). Our study showed that VATS lobectomy can be performed with low morbidity and shorten length of stay. The result of long term survival is comparable with conventional thoracotomy method.

11.10

Positron Emission Tomography in Non-small Cell Lung Cancer

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Background: The role of Positron Emission Tomograhpy (PET) in imaging non-small cell lung cancer can be divided into three general areas: (1) Characterizing solitary pulmonary nodules as malignant or benign (2) Staging lung cancer both locoregionally and systematically and (3) assessing response to treatment.

Methods: This is a retrospective study of 26 patients with whole body PET in our department from 1999 to 2000. Standardized uptake value SUV more than 2.5 was considered positive for malignancy.

Results: 6 Patients out of 26 patients were referred for PET imaging for diagnosis of pulmonary nodules. 1 Patient had positive standardized uptake value (SUV) 5.5 with lymph node secondary. Second and third patient had benign nodule SUV 1.5 and 1.7 respectively. Forth patient SUV 1.1 with pathology of tuberculosis. Fifth patient SUV 3.9 interpreted as sarcoidosis or lymphoma but pathology was lymphoepitheloma-like carcinoma with mediastinal lymph node secondaries. Sixth patient SUV 3.3 but pathology was sclerosing haemangioma.

PET imaging was used for staging in 18 patients. One patient had negative lymph node confirmed with right lower lobectomy. 2 patients had local chest wall involvement which was not detected by all investigation. 2 patients had N2 disease diagnosed by PET. After neo-adjuvant chemotherapy, no lymph node metastasis were found during surgery in these two patients. 3 patients had detected bone secondaries by PET. One patient had detected adrenal secondary by PET. 3 patients had parietal pleural secondaries not detected by PET. The other 6 patients were referred for other treatment with N2 disease detected by PET.

2 patients had PET imaging to assess response to treatment: 1 patient had RT treatment for Pancoast's tumor with residual lesion of SUV 2.4. No tumor found on resected specimen. Second patients after chemotherapy, PET was unable to show up brain secondaries which was detected by CT scan and MRI.

Conclusion: Data in our study to support of PET's role in characterizing solitary pulmonary nodules and in locoregional and systemic staging of non-small cell lung cancer and assess the response to therapy are quite promising.

11.11

NON-SMALL CELL LUNG CANCERS FROM SMOKERS AND NON-SMOKERS SHOW DIFFERENT GENETIC ABERRATIONS IN CHROMOSOME 3p

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Lung cancers show frequent chromosome 3p deletions, implicating the presence of potential tumor suppressor genes (TSG). The patterns of 3p deletion between non-small cell lung carcinomas (NSCLC) from 27 smokers and 33 non-smokers were compared. Loss of heterozygosity (LOH) of microsatellite markers was analyzed using DNA from matched normal and tumor tissues by PCR using a panel of 13 markers covering 3 regions, including D3S1259, D3S1351, D3S1560, D3S1597, D3S2432 at 3p26-24; D3S1029, D3S1295 at 3p22-21 and D3S1234, D3S1274, D3S1300, D3S1312, D3S1766, D3S4103 at 3p14-12. The results showed that NSCLC from smokers harbored high frequencies of LOH in all regions studied (38.1-69.6% in 3p26-24, 54.5-57.9% in 3p22-21 and 37.5-62.5% in 3p14-12). In NSCLC from non-smokers, frequencies of LOH at 3p26-24 (22.2-39.1%) and 3p22-21 (13.6-27.3%) were lower than those from smokers. For the 3p14-12 region, most markers showed significantly lower LOH frequency (14.3-20.0%) except D3S1234, D3S1300 and D3S4103 within the FHIT gene, a candidate TSG spanning the FRA3B common fragile site at 3p14.2, with LOH frequencies of 52.2%, 48.9% and 50.0% respectively. To further study the role of FHIT in lung cancers from smokers and non-smokers, Fhit protein expression levels were determined by immunohistochemistry (IHC). The results showed that 64.3% of NSCLC from smokers had markedly reduced or no expression of Fhit, while only 8.3% of cancers from non-smokers showed reduction or lack of Fhit expression. Comparison of results from 22 smokers and 29 non-smokers for whom LOH data were available showed that a high percentage of smokers had LOH and reduced expression of FHIT (40.9%), supporting that FHIT is a potential TSG and a target for cigarette smoke carcinogenesis. For non-smokers, although LOH of the FHIT locus was common, the infrequent loss of Fhit expression does not support its direct involvement in these tumors. The overall data suggest that different carcinogenic pathways be involved in smokers and non-smokers who develop lung cancers.

11.12

THE CLINICAL OBSERVATION FOR TREATING ADVANCED LUNG CANCER BYINHALING GASFICATIC PREPARATION OF IMMUNO-THERAPY

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To inquire new method for treating advanced lung cancer, the technique of inhaling gasficatic preparation with immunochemo-therapy in vaporizatic form produced by ultrasonic atomizer was used. It was primary observation by using the method to control tumor grow, alleviate patient s suffering. 8 patients (pts) with lung cancer, primary/second (5/3), were accepted to the study. The pts were prescribed by inhaling in gasficatic with 5-FU 0.25 to 0.5 qd*10-20 day followed IL-2 20*10 unit qd*10 day. The results show that the pathologic PR (pPR) was one of eight (12.5%), objective response rate (oRR) 37.5 %(3/8), in which chest pain was eliminated (1 pt), thorax stuffy and breathe hard alleviated from 2 pts. The side effect were presented in those that hematologic toxicity consisted of 14.3% grade 1 leukopenia in two of whole fourteen therapeutic-time in 8 pts, and mouth ulcer in one time (7.1%). The therapy is convenient and available in treating advanced lung cancer. It is necessary that the contents on reducing rate of tumor metastatic to lung and prolonging survival period should be further studied.

11.13

A clinical audit on the management of cancer dyspnoea in the setting of an acute clinical oncology center

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Aims: Monitor our current standard in symptom control and further improve our palliative service for cancer dyspnoeic patient. **Methods:** Setting standards based on the well-documented literatures and local experiences. A Phase I cross sectional survey was performed to compare our current practice to the standard. Then the results were discussed in our departmental meeting to formulate a "revised protocol" as guideline to our first line medical staffs. Three months later, similar Phase II survey was repeat to compare our practice to the "revised protocol". Finally the effectiveness of this audit cycle and the resultant clinical benefits were assessed and analyzed. **Results:** The cross sectional surveys (Phase I/II) recruited all the in-patients registered in our hospital on the date of 1-5-00 and 20-8-00 respectively (102/88 pts). All the records of those patients with dyspnoea as their major complaint were analyzed retrospectively (26/16 pts). In the Phase I and II surveys, the incidence of dyspnoea were similar (25/18%) and majority of patients were suffered from lung and breast cancer. Causes included pleural effusion (8/7 pts), lung infiltrates (9/2 pts), SVCO (2/4pts), infection (3/1 pts). Actually most patients were multi-factorial. The incidence of giving reversible measures (e.g. tapping, RT, chemotherapy) was increased in the Phase II survey from 19% to 75%. For the other symptomatic measures like the use of opioid, steroid, physiotherapy and selective prescription of O2 were increased in Phase II survey (38 to 50%; 28 to 62.5%; 12 to 31% and 70 to 87.5% respectively). However the practice of underused benzodiazepine (< 5%) and the empirical use of O2 and bronchodilator were still common in Phase II survey. Lastly the incidence of patient reported symptoms improvement on discharge/ transferal was increased from 50 to 65%. **Discussion:** This audit cycle is an effective exercise to improve our clinical practice. Since the improvement is stepwise, by repeating this cycle and remodeling our practice accordingly could formulate the most optimal standard in our setting with the available resources.

12.1

HYPERMETHYLATION OF THE E-CADHERIN PROMOTOR REGION IN ESOPHAGEAL CARCINOMA

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E-cadherin(E-cad) is a 120kD transmembrane glycoprotein which is involved in mediating cell-cell adhesion(1) . Diminshed E-cad expression has been related to the development and behavior of epithelial cancer including esophageal cancer(2-4). However, downregulation of E-cad expression is heterogeneous and may involve genetic or epigenetic mechanisms. Recent reports have indicated that hypermethylation of the E-cad promotor region CpG island may play an important role in the loss of its expression(5-7). To study the mechanisms underlying the downregulation of E-cad in esophageal carcinoma, six esophageal cancer cell lines and 33 esophageal cancer samples were used in this study. Firstly, we examined the methylation status of the 5' CpG island promotor region of the E-cad gene by methylation-specific PCR (MSP). Alterations in E-cad expression were examined by Western-Blotting. Then the methylation status of E-cad promotor region in clinical samples was examined by MSP. Our results suggest that CpG island methylation is common in esophageal carcinoma and may be involved in the downregulation of E-cad.

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12.2

Molecular markers and prognosis in colorectal cancer

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In the attempt to identify molecular markers of reliable prognostic value in colorectal cancer, we investigated p53, $p21^{waf1}$ and $p27^{kip1}$ expression in neoplastic tissues of patients at different stages of tumor progression. In the first phase of the study surgical specimens from 288 consecutive patients with stage I-IV colorectal cancer were analyzed for p53 protein expression by IHC and for gene mutations by PCR-SSCP, followed by DNA sequencing. p53 protein accumulation and gene mutations were detected in 146/288 (50.7%) and 105/288 (36.5%) tumor samples, respectively. The abnormal p53 expression pattern and gene mutations were not correlated with gender, age, or tumor grade; on the other hand, a significant association between p53 alterations and more advanced tumor stages emerged ($p=0.0094$ for IHC, and $p=0.0021$ for SSCP). Moreover, tumors in the rectum compared to proximally located lesions showed a significantly higher frequency of p53 protein accumulation (56 vs 36.7%; $p=0.0038$) and mutations (41 vs 24%; $p=0.0089$). A second study on the cyclin-dependent kinase inhibitors $p27^{kip1}$ and $p21^{waf1}$ was carried out on a group of 124 patients with stage I-III colorectal cancer. IHC revealed detectable levels of $p27^{kip1}$ and $p21^{waf1}$ in 86% and 26% of tumors, respectively, and a positive correlation between absence of $p27^{kip1}$ and higher tumor stage and grade. Kaplan-Meier curves showed that the 5-year DFS and OS were 77.8 and 85.6%, respectively, in patients with tumors expressing $p27^{kip1}$ protein compared to 35.3 and 41.2% in those without $p27^{kip1}$ expression ($p<0.001$). No statistically significant differences were found between the 5-year DFS and OS of patients scoring negative and positive for $p21^{waf1}$ expression.

12.3

Prospective randomized study of post-operative chemotherapy with levamisole and UFT for head and neck carcinoma.

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Objective : To evaluate the benefit of adjuvant levamisole/UFT (futraful and uracil) chemotherapy in head and neck squamous cell carcinoma.

Design : prospective randomized study.

Patients and method : Sixty-seven patients with stage III and IV squamous cell carcinomas of oral cavity, oropharynx, hypopharynx and larynx with no distant metastasis were randomized for the chemotherapy study. 37 patients were randomized for chemotherapy and 8 of them were subsequently excluded. In this study, a total of 29 patients on levamisole/UFT therapy and 38 patients on the control group were analyzed.

Results : The rates of distant metastasis were 10% for chemotherapy group and 29% for control group (p=0.06). The 5-year disease-free actuarial survival rates for patients with and without adjuvant chemotherapy were 57% and 39% respectively (p=0.207).

Conclusion : The combination of levamisole with UFT has beneficial effect for the reduction of distant failures in head and neck cancer patients. The reduction of distant metastasis did not significantly improve the overall long term survival because of the predominant sites of treatment failure at local and regional sites.

12.4

RADIOTHERAPY FOR MAJOR SALIVARY GLAND CARCINOMA: A SINGLE INSTITUTION EXPERIENCE

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Purpose : To evaluate the outcome and natural history of patients with major salivary gland carcinoma treated in our institution from 1982 to 1998

Materials and Methods : Between 1982 to 1998, 110 patients with major salivary gland carcinoma were referred to our department for radiotherapy. Records were reviewed retrospectively. 84 out of 110 patients were treated by surgery followed by post-operative irradiation. The male to female ratio is 1:1 (39 : 45). Median age for the whole group is 55(Range 21-85). Patients were staged according to the tumor-node-metastasis (TNM) staging system of the American Joint Committee on Cancer. 50 patients had stage I, 8 had stage II, 5 had stage III and 21 had stage IV disease. Forty-five (54%) patients had involved or closed resection margins. 17 (20.2%) patients had adenocystic carcinoma, 29 (34.5%) patients had mucoepidermoid carcinoma, 9 (10.7%) had adenocarcinoma, 8 (9.5%) patients had acinic cell carcinoma and 21(25%) patients had other histological types. Radiotherapy was delivered by megavoltage photons or electrons or a combination of both. Median dose (in TDF) is 64 Gy. The median follow up was 47.5 months.

Results : The 5 and 10 year overall survival were 82% and 78% respectively. The 5 and 10 year local failure free survival were 89.5% and 86% respectively. The 5 and 10 year regional free survival were 97.2% and 91.8% respectively. Twenty patients experienced disease recurrence.

Conclusions : Surgical resection and post-operative radiotherapy is well-tolerated and effective with high local control rates. This paper presents our single center experience.

12.5

Pharyngolaryngo-oesophagectomy with Pharyngogastric Anastomosis – A Meta Analysis

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Background. One of the management options for tumors arising from the hypopharynx and is to carry out the surgical procedure, pharyngolaryngo-oesophagectomy and pharyngogastric anastomosis (PLO & PGA). This operation although is effective in relieving the distressing dysphagia, it is associated with definite morbidities as the surgical field transgresses three compartments of the body. Identifying the mortality risk factors contributes to establish the present status of this surgical procedure.

Methods. All publications in the literature reporting the results of PLO & PGA from 1960 to 1998 were reviewed and a Meta analysis was carried out on the grouped data. The indications of the operation, mortality and morbidity were evaluated and the factors affecting hospital mortality were examined.

Results. A total of 28 publications were included for analysis with a total of 1,118 patients. The male to female ratio was 2.3 to 1; the age ranged from 20 to 80 yrs, median 56 yrs. The overall hospital mortality was 13% (145/1118) and complication rate 48% (542/1118), many were minor events. The most frequent complications were related to the cardiopulmonary system (241/542). Logistic regression has identified the location of primary tumor and leakage at the phayrngogastric anastomosis to be the two significant factors contributing to hospital mortality.

Summary. PLO & PGA when employed for the appropriate patient achieves good outcome. The associated mortality and morbidity can be reduced with improved surgical techniques together with prevention and prompt management of complications.

12.6

Clinicopathological significance of bcl-2 expression in patients with surgery for laryngeal carcinoma

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Abnormality of apoptosis are commonly found in cancer. The bcl-2 genes are important in the control of apoptosis. This study aims to evaluate the prognostic significance of bcl-2 expression in patients treated with surgery for laryngeal carcinoma.

Operative specimens of patients with laryngeal carcinoma treated with surgery were retrieved for study. Immunohistochemical staining was performed to assess the degree of cytoplasmic staining for bcl-2 by a four-point semi-quantitative scale. The significance of bcl-2 staining was evaluated against staging, recurrence pattern and survival data.

Positive bcl-2 expression was found in 11% of the 176 laryngeal cancer specimens studied. Bcl-2 expression was found to correlate with tumor grading and nodal metastasis. Risk of nodal metastasis was found to increase with a positive bcl-2 expression, moderate or poor differentiation and supraglottic involvement of the tumor.

In conclusion, bcl-2 over-expression was present in a proportion of laryngeal cancer studied and carried a significant prognostic value for nodal metastasis.

12.7

Assessment of chromosomal gains and losses in oral squamous cell carcinoma by comparative genomic hybridization

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We analysed the genetic changes of 33 oral squamous cell carcinomas by comparative genomic hybridisation (CGH). The CGH technique provides information on chromosomal gains and losses of the whole tumour genome in a single experiment and can therefore identify regions that harbour putative tumour suppressor genes (in the case of loss of chromosomal material) or oncogenes (in the case of gain or amplification of chromosomal material). Gains in DNA sequence copy number were detected frequently for chromosome arms 3q(12/33), 8q,11q,20q(11/33 each),5p,7p(8/33 each) and 1q(5/33), and losses in chromosome arms3p(8/33),18q(6/33),5q,6q(5/33each).The patterns of DNA copy number aberrations proved to be rather peculiar in oral SCCs, gains of genetic material dominating compared with losses.These results suggest that gains of 3q,8q,1q,20q and loss of 3p play important roles in the development and/or progression in OSCC.

12.8

E-CADHERIN AND CATENINS (α, β, γ) IN ORAL TONGUE CARCINOMA

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Purpose: E-cadherin and catenins are important epithelial adhesion molecules in normal epithelium. Loss of E-cadherin-catenin adhesion contributes to progression of many epithelial cancers. E-cadherin and catenins statement in CA tongue were reviewed in relation to their clinicopathological features and prognostic values.

Method: Immunohistochemical staining were carried out with E-cadherin and (α, β, γ)-catenin monoclonal antibodies for 85 surgical specimens of CA tongue, 9 metastatic lymph nodes and 7 recurrent tumours.
Results: Nodal metastasis was found in 68% patients with weak statement of γ-catenin compared with 9% with strong statement in primary tumours (chi-square, $p=0.02$). Patients with weak E-cadherin statement had 53% 5-year survival compared with 85% with strong statement (Wilcoxon, $p=0.0159$)

Conclusion: both E-cadherin and catenins were highly under-expressed in CA tongue, metastatic lymph nodes and recurrent tumour. γ-catenin had predictive value for nodal metastasis. E-cadherin was more important prognostic factor for recurrence and survival.

12.9

Malignant Tumours in the Head and Neck Region in Childhood: Good Outcome with Current Therapeutic Approach

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Objectives: Types of malignant tumours found in the head and neck region in childhood and their therapeutic approaches differ significantly from that of adult, but there are very few data about these aspects locally.
Methods: We reviewed our patients' records from July 1990 to June 2000. Children (<18 yrs) with malignant diseases [including Langerhan's Cell Histiocytosis (LCH)] primarily arose from the head and neck regions were studied. Children with brain tumours were excluded. Comparison of survival of different diseases was by Logrank test.
Results: Within this 10 years period, 392 children with malignant disease attended our service. There were 26 (6.7%) children with disease primarily arose from the head and neck region. The M: F ratio was 14:12 and the median age was 4.5 years (0-16 yrs). The disease types were namely: non-Hodgkin's lymphoma (NHL) n=7, LCH n=6, retinoblastoma (RB) n=4, rhabdomyosarcoma (RMS) n=4, Ewing's sarcoma (EWS) n=2, peripheral primitive neuroectodermal tumour (pPNET) n=1, neuroblastoma n=1, thyroid carcinoma (ThyCA) n=1. The overall 4 years event free survival (EFS) was 83% and the median follow up period was 4 years. Children with LCH, NHL & RB (all with 100% EFS) had significantly better outcome than those with EWS/pPNET (EFS 50% at 4 yrs) or RMS (EFS 50% at 2 yrs) (p=0.002). Surgery or radiation therapy (RT) alone was the treatment of choice for children with RB (all with localized disease). Surgery with RT was used in a child with papillary ThyCA. All other children received chemotherapy according to disease specified protocol. Children with NHL & 5/6 LCH were treated with chemotherapy alone. NB, RMS, EWS and pPNET required multi-modality approach and despite good initial response with chemotherapy in all patients, late relapse remains a problem.
Conclusions: Despite the difficulty in completely resecting the tumour in the head and neck region, the overall outcome of childhood head and neck malignancies is satisfactory. Children with NHL and multi-focal LCH responded well to chemotherapy and this should be the primary form of treatment. Even with current chemotherapy regimen, most sarcoma in the head and neck region requires combined modalities of treatment for better chance of cure.

12.10

Is Deltopectoral Flap Reliable for Head and Neck Reconstruction?

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Deltopectoral flap (DPF) is a fasciocutaneous flap that was frequently used for head and neck reconstruction in the 60's. However, it is associated with high failure rate and complications. Its usage has been superseded recently by the myocutaneous and free flaps. We report our experience on the use of this flap.

One hundred and thirty eight DPFs were performed on 133 patients between January 1976 and June 2000 by our division. One hundred and thirty three flaps (96.4%) were used for external skin coverage after resection of head and neck malignancy. Five flaps (3.6%) were used for pharyngeal and oral mucosal lining. Nineteen flaps were used to protect the brachytherapy tubes that were inserted for after-loading brachytherapy. One hundred and fourteen patients (82.6%) had previous irradiation to the operative site.

The overall complication rate was 8.6% (12 DPFs). There were 1 total flap loss and 6 distal flap necrosis, which required surgical debridement. There were 3 wound abscesses, 1 wound collection and 1 haematoma formation. There was no procedure-related mortality. The complication rate was higher in those patients who had salivary and sputum contamination and all of the complications occurred in patients with previous irradiation, but they were statistically not significant.

In conclusion, DPF provides an alternative and reliable method for Head and Neck reconstruction. It is easy to raise. Although the donor site needs skin graft to cover, the morbidity is acceptable.

12.11

SPECIAL ALLOMETRIC KINETICS IN MTT ASSAY FOR QUANTITATIVE ASSESSMENT OF CELL VIABILITY

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Objectives: To resolve the discrepancies on colorimetric MTT assay.

Methods: Traditional MTT assay was used for the observation of MTT reduction of four cell lines (Hep-G2, etc). Samples were incubated with different MTT concentration for different incubation time for investigation of kinetics and evaluation of MTT cytotoxicity. Logistic model and allometric formula ($Y = KX^b$) was adopted to analyse the relationship between cell density and its capacity of reducing MTT.

Results: The absorbances of MTT formazan produced by viable cells were time and MTT concentration related that confirmed kinetics exists in MTT assay, but it doesn't follow typical first class kinetics. During MTT incubation the appearance of formazan crystals indicates cell death due to MTT cytotoxicity. Observed progressive cell death with time was an S-shaped logistic response curve. The relationship between cell density and its capacity of reducing MTT showed allometry ($Y = KX^b$) phenomena. By combining first class kinetics, logistic model and allometric equations together, balancing-cell equation (BCEq) for allometric kinetic analysis of MTT assay was advanced. Accordingly, the equation to calculate the percentage of tumour growth inhibition (%TGI) is:

$$\%TGI = 1 - \{[\ln A_{\max} - \ln(A_{\max} - A_t)]/[\ln A_{\max} - \ln(A_{\max} - A_c)]\}^{1/b} \times 100\%.$$

Conclusion: The relationship between cell function of reducing MTT and cell number is not linear but follows a special allometric kinetics.

13

Genetic susceptibility to environmental cancer

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Recent data from the human and the environmental genome programs indicate that inheritance of certain polymorphic genes may affect metabolism of carcinogenic agents and may cause some individuals to be particularly susceptible to the development of environmental cancer. For example, certain genes in the cytochrome p450, N-acetyl transferase and glutathione S transferase gene families are associated with the development of lung cancer among cigarette smokers. We have data to support the mechanism of the association: susceptible individuals have increased chromosome aberrations compared with those having the resistant version of the same genes. However, genetic susceptibility to environmental cancer can be modified by multi-factorial mechanisms in a multi-stage carcinogenic process. First, the susceptible versions of the metabolizing genes have different ethnic-dependent prevalence around the world. Second, some metabolizing enzymes have multiple activating and detoxifying functions that are dependent upon the availability of different substrates. Third, the life-style experience of the individuals may influence the susceptibility. The latter phenomenon has been loosely identified as acquired susceptibility. Such life-style experience includes aging, poor nutrition, and history of infection and exposure to mutagenic agents. Understanding genetic susceptibility and the role of modifying factors in environmental cancer will be crucial to our effort in disease prevention and management.

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Environmental Contamination and Cancer

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Cancer is a major worldwide scourge. The marked increase in cancer incidence in developed countries through the 20th Century is being reproduced in developing countries as we enter the 21st Century. Control of infectious diseases and of other causes of death in the young inevitably produces a transition toward an increase in importance of cancer and of other chronic diseases. That infectious disease has far less mortality now than in the past reflects primarily the value of preventive actions based upon understanding of causation and only secondarily on our impressive array of antibiotic therapies. For cancer, unfortunately, we have far more understanding of treatment modalities than we do of how to prevent this collection of dreaded diseases.

There is no question that the overwhelming majority of human cancers are due to environmental factors, in the broadest sense of that term. This includes lifestyle, such as tobacco and alcohol use, food intake and a variety of toxic pollutants. Studies of immigrants to other cultures demonstrate that the predominant basis for cancer incidence is societal rather than genetic. Yet genetics undoubtedly plays a major role in the susceptibility of individuals to specific cancer-causing environmental factors. The explosion in understanding of the human genome will soon provide us with an understanding of the genetic basis that is necessary, but not sufficient, for the development of cancer in an individual. Sufficiency will depend upon environmental factors. And many of these environmental factors will be locally generated, and locally preventable.

We already know certain of these environmental factors, such as benzene, polycyclic aromatic hydrocarbons, ionizing radiation and another two dozen or so known causes of human cancer. These are known epidemiologically because humans have suffered and died. Knowledge provides us with the ability to act preventively so as to avoid these causes of cancer. Our goal for the future is to have the requisite understanding to drastically decrease the impact of cancer by preventive activities.

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Smoke kills in Hong Kong: Environmental priorities in cancer prevention

Hedley AJ
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Air pollution from traffic, industry and power generation has increasingly been a feature of human settlements since the 19th Century. Between 1930 and 1952, several major pollution episodes in Belgium, Pennsylvania and London killed thousands.

Today time series studies show the effect of key pollutants (PM_{10}, NO_2, SO_2 and O_3) on morbidity, hospital admissions and premature death from cardiorespiratory disease. Recently new evidence in the US from long term cohort studies has demonstrated a much increased risk for lung cancer in non-smoking females and males associated with PM_{10} and SO_2, and with high levels of O_3 (>100ppb) in males.

Residential exposure to radon has long been considered an environmental risk for lung cancer, possibly responsible for up to 10-15% of all cases. There is considerable uncertainty about the estimates but also a strong association between smoking, radon exposure and cancer risk.

The most important avoidable indoor air pollutant in Hong Kong is environmental tobacco smoke (ETS). Studies in primary school children, workers and the general adult population indicate that exposure to ETS is common and leads to injury to the respiratory system giving rise to chronic bronchitic symptoms. More than 30 studies worldwide, including Hong Kong, demonstrate an association between long term ETS exposure and lung cancer.

The preventive health priorities are clear from epidemiological evidence; the obstacles to prevention are lack of political will and strong vested interests.

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ADVOCACY AND POLICY

Christine Loh

It is becoming better understood that the state of the environment has serious impact on human health. The cummulative impact of air, water and noise pollution alone can cause many health problems, which are compounded for vulnerable groups, such as children and the elderly. The main cause of environmental degradation is economic development. It is fashionable among policy makers to claim that they are striking the right balance between the need for economic development and protecting the environment when in truth, the balance has been and still is heavily tilted in favour of development.

It is insufficent for society to regard environmental policy as essentially improving pollution control. Protecting the environment is not just a technical issue that can be solved by improved technology alone. It does require a new look at the way we have constructed our economic system that takes natural resources as assets which are there to serve human economic advancement. With this neo-liberal view, there is unlikely to be sufficient resources for mankind to significantly repair the earth in our life times. As much as think about how to have better policies to regulate industry, reduce wastes, make polluters pay, trade emissions credits, etc, which will buy time, we urgently need to revisit basic economic concepts about what "development" truly means to us as human beings.

17.2

Risk Factors for Colorectal Cancer

Dr. JWC Ho, Ms. SHS Lam
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Colorectal cancer (CRC) is one of the most common cancers in the developed world including Hong Kong. Various personal, familial and environmental risk factors are related to CRC development. On the whole, CRC is thought to be the result of an intimate and poorly understood interplay between environmental and genetic factors. Dietary and lifestyle factors are among the most important environmental factors implicated. However, the precise nature of the relationship of CRC with each nutrient or lifestyle factor and the actual magnitude of the relationship are not clear. So far, studies have suggested that overall diet and lifestyle, rather than individual factors, play the more important role. Result of studies on various important dietary and lifestyle factors, including fiber, energy intake, fat consumption and physical activities will be reviewed. Result of a local case-control study on environmental factors will be discussed.

17.3

Colorectal Cancer Screening

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The evidence that the mortality from colorectal cancer can be significantly reduced by FOB screening will be reviewed. Data from the three informative randomised trials will be presented to demonstrate the benefits and adverse affects of screening.
The limitations of FOB screening will be discussed together with the possibility of developing more sensitive and specific faecal tests based on the detection of tumour products in the stool.

The place of endoscopic screening of the population will be evaluated and the results of recent trials presented.

The role of screening the preventing of colorectal cancer will be reviewed and follow up data from the Minnesota, Funen and Nottingham trials presented.

18.1

Plasma DNA in health and disease: a new tool for molecular diagnosis

Y.M. Dennis Lo
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Recently, there is much interest in the use of circulating DNA in the plasma and serum for molecular diagnosis. In particular, tumour-derived DNA has been found in the plasma and serum of patients with a wide variety of cancers. We have studied the use of circulating DNA in the detection of nasopharyngeal carcinoma (NPC) and hepatocellular carcinoma (HCC). Thus, for NPC, we have used Epstein-Barr virus (EBV) DNA as a plasma and serum marker. We have demonstrated that the concentration of such plasma/serum EBV DNA correlates with clinical stage and allows us to monitor for tumour recurrence following radiotherapy. In addition, we have elucidated the kinetics of circulating EBV DNA concentration during the course of radiotherapy. We believe that such monitoring may indicate the radiosensitivity of a particular tumour and may be useful for the evaluation of novel therapeutic modalities. For HCC, we have shown the usefulness of employing tumour-associated aberrant DNA methylation of tumour suppressor genes for HCC detection. We have also recently achieved the quantitation of circulating HCC tumour DNA by quantitative methylation analysis. In conclusion, we believe that plasma DNA analysis is a powerful tool for the detection and monitoring of many tumour types.

18.2

RECENT ADVANCES IN THE USE OF TUMOUR MARKERS IN CLINICAL PRACTICE

Dr. Chan Yuk Tat Eric, Department of Pathology, Queen Mary Hospital

The clinical applications of tumour markers in malignant diseases include screening, diagnosis, predicting prognosis and monitoring. Among the tumour markers currently available in clinical practice, very few are useful for screening, some are for diagnosis and most are for monitoring therapy and detection of recurrence.

In Hong Kong, one of the most important markers in screening for malignancy is alpha-foetal protein (AFP) for hepatocellular carcinoma (HCC) in asymptomatic hepatitis virus carriers. AFP is an oncofoetal glycoprotein of 70 kDa molecular weight and is produced in foetus by the yolk sac and liver. In adult, mildly elevated level is found in infancy and during pregnancy; moderately elevated level in hepatitis, cirrhosis, biliary tract obstruction and alcoholic liver disease. Marked elevation of AFP is found in malignant diseases including HCC (60-80%), non-seminomatous germ cell tumours (50-70%) and hepatoblastoma. Since AFP is not elevated in all patients with HCC and moderately raised level may be found in non-malignant conditions, other markers have been investigated to replace or supplement AFP in the diagnosis of HCC.

Diagnosis of cancers in symptomatic patients is frequently aided by the use of tumour markers. Serum prostatic specific antigen (PSA) level is a single-chain kallikren-like, serine protease glycoprotein of 34-kDa molecular weight. It is produced by epithelial cells lining the acini and ducts of the prostate. Serum level is increased in malignant and benign (including inflammatory) prostatic conditions. In cases of borderline total PSA level, the percentage of free/total PSA is useful. In serum, PSA is either free or bound to α1-antichymotrypsin. The proportion of free PSA is lower in malignant than in benign prostatic diseases.

Most tumour markers are useful in monitoring treatment and detection of recurrence. Carcino-embryonic antigen (CEA) is not recommended for the diagnosis of colorectal cancers because neither the diagnostic sensitivity nor specificity is satisfactory. In patients known to have colorectal cancers and elevated CEA before surgery, the use of CEA in monitoring recurrence is found to be valuable.

19.1

Psychosocial clinical guidelines for breast cancer

Professor Sally Redman, National Breast Cancer Centre, Australia

The National Breast Cancer Centre was established in 1995 with a remit of improving breast cancer outcomes nationally, including the well being of women diagnosed with the disease. A systematic approach to improving supportive care has been taken based on an iterative process of establishing need, reviewing evidence, developing guidelines, encouraging their implementation.

The Centre has taken a systematic approach to improving supportive care including: reviewing research, developing and implementing guidelines and monitoring the impact of these initiatives.

There is a growing body of level I and II evidence demonstrating the effectiveness of a number of psychosocial interventions in improving in the well being of women with breast cancer. Based on detailed reviews of this research, evidence based guidelines for the provision of psychosocial care for women with breast cancer have been developed. The guidelines represent agreement among women, clinicians and experts in psychosocial care about best practice in this area and have been endorsed by the National Health and Medical Research Council.

Guidelines alone are insufficient to change practice. Strategies to encourage the full uptake of the guidelines are being implemented with a particular focus on modifying health systems including policy, clinician training and health service delivery. These strategies include a national clearinghouse for training in communication skills and approaches to encouraging the appointment of specialist breast nurses. This paper will outline progress to date in encouraging an evidence based approach to care.

19.2

A case presentation - how psychosocial guidelines would have influenced the care of Angie

Ms Vivian Chan Ward Manager Department of Clinical Oncology/ Chairperson Hospice Nurses Association

Body image is the persons' psychological experience of her or his body. It may influence attitudes and feelings towards the body including the appearance, function and values associated. These self concepts are influenced by physical development and is affected by discrepancy between the real and the ideal self, alongside the responses of significant others.

Different individuals may respond differently to altered body image, while mental adaptation is slower than the actual physical changes. All these will affect the physical, social and psychosocial well being of the individual.

As a caring professional it is essential to identify concerns, open true and honest discussion of feelings and emotions accepting then with unconditional positive regards. This extends to maintaining the patient's autonomy by encouraging participation in decision making and in the care of the affected body part. It is also important to help them focus on the abilities instead of the limitations resulting from physical changes.

How psychosocial guidelines would have affected care our young woman who was facing all these difficulties we can reflect alongside the possibilities and recommendations for future care of people living with needs such as " Angie's".

20.1

Hormone replacement therapy and breast cancer

Chiun-sheng Huang, M.D., Ph.D.
Department of Surgery, National Taiwan University Hospital

Many epidemiologic and cell biology studies have documented that estrogen can cause breast cancer. A recent analysis of more than 90% of the world's epidemiologic data shows that breast cancer risk increases in women who are current or recent, but not past, users of postmenopausal hormone. The risk increases with increasing duration of use, but this excess risk has largely disappeared after 5 years. For each year a women uses postmenopausal hormones, her risk of breast cancer increases by 2.3%. As regards the content of hormones, addition of progestin to estrogen may lower the risk of endometrium cancer caused by estrogen, but increase the risk of breast cancer. One study shows breast cancer risk is increased by 8% for each year of progestin-estrogen combined use and by 1% for each year of estrogen only use. The increased risk was greater for women of low than those of high relative weight. The breast cancers diagnosed in women who had used postmenopausal hormones were less advanced clinically than those diagnosed in never-users, which can be explained by that women are more likely to be examined for breast cancer before starting hormone replacement therapy and have more frequent mammographic or other examinations while they are taking postmenopausal hormones. Several factors would lead to an underestimate of the adverse effects of postmenopausal hormones, e.g., women who take postmenopausal hormones are at lower risk of breast cancer at the time of menopause than women who do not take postmenopausal hormones. That the association between postmenopausal hormone and breast cancer risk is observed only in lean women suggests there seems to be a maximally effective dosage of estrogen in regard to breast carcinogenesis above which higher dosages had no effect. Therefore, hormone replacement may increase greater risk of breast cancer among Asian women originally with lower risk or estrogen level than Western women with higher risk or estrogen level.

20.3

Oral Contraceptives and Ovarian Cancer

Dr. T.Y.Ng
Department of Obstetrics and Gynaecology, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China

Epithelial ovarian cancer accounts for 90% of ovarian cancers. Nonepithelial ovarian cancer including malignancies of germ cell origin, sex cord-stromal cell origin, metastatic carcinomas to the ovary and a variety of extremely rare ovarian cancers accounts for the other 10%.

Epithelial ovarian cancer has been strongly correlated with prior reproductive history and duration of the reproductive career. Early menarche and late menopause increases the risk. These factors and the relationship of infertility and parity have led to the hypothesis that suppression of ovulation may be an important factor.

There are now several case-control and cohort studies showing that OC reduces the risk of epithelial ovarian cancer. The relative risk of ovarian cancer is reduced to 0.5 to 0.3 depending on the duration of use and previous reproductive history. This protection for OC users is thought to persist for 10 to 15 years. In women who are at risk of epithelial ovarian cancer (BRCA1 and BRCA2 mutation), a case-controlled study has also shown a reduction in risk of OC users to 0.4 to 0.5. The protective effect of OC has also been seen in borderline malignancy ovarian neoplasms and probably benign ovarian cysts. There is some suggestion of protection for nonepithelial ovarian cancers such as sex cord-stromal tumours but not for germ cell tumours.

The oral contraceptive pill is the only documented method of chemoprevention for ovarian cancer, and it should be recommended to women for this purpose. When counseling women on birth control methods, the noncontraceptive benefits of OC including chemoprevention of ovarian cancer should be emphasized. This is also important for women with a strong Family history of ovarian cancer.

21.1

Imaging of Skull Base

FL Chan
Department of Radiology, Queen Mary Hospital, Hong Kong.

The skull base bears close proximity to many special structures that can derive a multitude of pathology. Demand for its full evaluation has grown in light of more aggressive surgical approach and endoscopic surgery. Skull base imaging delineates the anatomy and pathology in this complex but critical region. It characterizes the neoplasm and precisely maps out the lesion extent to assist in the diagnosis, evaluate the prognosis, triage unresectable from operable lesions, and direct surgical or radiation planning. The radiologist must know why the imaging is performed and what to scan. Computed tomography (CT) and magnetic resonance imaging (MRI) are the mainstay modalities, and they are often complementary. With a firm knowledge of the anatomy and tumour behaviour, meticulous application of thin sections to the region of interest permits proper radiological management of the clinical problem. Anatomical localization of the center of the neoplasm as the site of origin predicts the pathology, and imaging characterization will refine the differential diagnosis. While the axial sections assess the cross-sectional scope of the neoplasm, coronal imaging is essential to demonstrate its intracranial and extracranial extent. CT evaluates the bony cortex of the base, and the calcific matrix of the neoplasm. MRI provides multiplanar imaging and is the choice for assessment of marrow infiltration, transcranial extension of the pathology and perineural neoplastic infiltration. The latter two issues are facilitated by fat-saturated contrast-enhanced T1-weighted imaging, which is also preferred for detecting tumour outcome and local recurrence. MRI also serves better to direct management, and has the potential to monitor the interventional procedure and the intraoperative status of the neoplasm during operation.

21.3

Surgical Approaches to the Inferior Skull Base: Their Indications and Limitations

Seiji Kishimoto M.D.
Department of Head and Neck Surgery, Tokyo Medical and Dental University, Tokyo, JAPAN

The inferior skull base including paranasal sinuses, nasopharynx, clivus, parapharyngeal spaces and infratemporal fossa, is located deep in the central part of the skull and is comprised of many critical and complex structures. Surgical access to those areas is therefore often difficult.

Although numerous approaches for the treatment of the tumors involving the inferior skull base have been advocated, little attention has been focused on comparing and contrasting these. Furthermore, the indication for and limitation of each procedure remain to be clarified.

The majority of approaches involve two procedures: an incision of the soft tissue (skin and/or mucous membrane) and osteotomy of the facial skeleton. In order to determine the indication for and efficacy of these surgical interventions, the author proposes the adoption of a novel and simplified classification system for the numerous complicated approaches according to the aforementioned two main approaches. The indication for and limitations of each procedure should be analyzed in terms of minimal morbidity and optimal visualization.

21.4

Skull Base Surgery – Hong Kong Experience

William I. WEI, L.Y. WONG, L.K. LAM, W.M.NG
Division of Head and Neck Surgery, Dept of Surgery, University Medical Centre, Queen Mary Hospital.

From January 1993 to June 2000, we have performed resection of skull base tumour in 47 patients. Among them the tumour was located in the central skull base in 17 patients and this was removed with the maxillary swing approach. The remaining 34 patients underwent combined craniofacial resection. The latter group was reviewed.

The location of tumours was in the anterior skull base in 24 patients and lateral skull base in 10. Their age ranged from 12 to 84 yrs, mean 46 yrs while 23 of them were male and 11 female. Seven patients have in addition orbital exenteration and in 4 patients part of the brain was removed with the tumour. Among the resected tumours, 26 were malignant tumours and 8 were benign. The commonest malignant tumour was olfactory neuroblastoma that occurred in eight patients followed by undifferentiated carcinoma and adenocarcinoma.

Complications included leakage of cerebrospinal fluid that occurred in 3 patients and meningitis in one patient. All patients were discharged and they were followed up from 2 months to 6 years, median 32 months. The overall 3-year disease free survival was 65%. For those with malignant tumour, the 3-year disease survival was 59% and benign tumour 85%. Removal of brain or orbital exenteration does not seem to affect the survival.

22.1

Psychosocial guidelines in Hong Kong: How can we make it work?

Peter W.H. Lee, Lina Y.F. Wu, Amy S.M. Fung, Damaris S.M. Hung, Clinical Psychology Unit, Queen Mary Hospital

Clinical guidelines in cancer care are regarded by clinicians involved in cancer patient care as being highly useful. When carried out systematically in an enabling and mutually supportive context of understanding and team work, such guidelines are undoubtedly of great clinical value. However, while clinical guidelines can be objectively and clearly stated, their effective implementation often involves much ambiguities and practical difficulties inherent in the context in which they are being implemented. The speakers' experiences in developing and implementing psychosocial guidelines in palliative care, and in the management of patients with breast and gynaecological cancers are presented. Major obstacles include: the dubious nature of the so called "team" approach; the realistic limitations in time and commitment of personnels involved; the lack of a critical mass of clinicians and care workers; the lack of a mutually agreed understanding of the guidelines in practice; and the often unspoken but dissenting personal and professional values of the workers involved. The effective implementation of psychosocial guidelines requires a concerted and committed effort from the most senior to the novice worker within the oncology team. Much time and effort should be reserved particularly during the initial start-up phase for consolidating the skills and commitment of all the team members involved. The benefits of having an energetic, influential, and inspiring team leader are enormous. Heightened awareness of positive feedback together with pride in service delivery and team membership against a background emphasis on evidenced based practice are advocated.

23.1

THE WHO CLASSIFICATION FOR LYMPHOMAS

John K.C. Chan, Department of Pathology, Queen Elizabeth Hospital, Hong Kong.

The REAL Classification of lymphomas, proposed in 1994, represents a new paradigm in lymphoma classification, consisting of a list of biologic entities defined by clinicopathologic and immunogenetic features. The non-Hodgkin lymphomas comprise precursor lymphoblastic and mature cell neoplasms of B, T or putative natural killer cell lineage. An individual entity can exhibit a range of morphologic appearances and a range of clinical behavior. The categories in Hodgkin lymphomas are identical to the widely used Rye classification except for the additional of a new category termed "lymphocyte-rich classical Hodgkin lymphoma". The REAL classification has been validated by a major multi-institutional study involving 1,378 cases (The Non-Hodgkin Lymphoma Classification Project), showing that it is both reproducible and clinically relevant. The new World Health Organization classification of hematopoietic and lymphoid tumors, to be published in 2001, is a joint project of the Society for Hematopathology and European Association of Hematopathologists, under the auspices of the World Health Organization. This classification includes not only lymphoid neoplasms, but also myeloid, histiocytic and mast cell neoplasms. The lymphoma component of the classification is merely an update of the REAL classification, with Minor changes in terminology and regrouping of entities necessitated by new information that has become available since its proposal. There continues to be an emphasis on biologic entities and on the site of disease in the definition of disease entities. The main changes from the REAL classification are as follow: (1) "Follicular lymphoma" to replace "follicular center lymphoma", "lymphoplasmacytic lymphoma" to replace "lymphoplasmacytoid lymphoma", "T-cell prolymphocytic leukemia" to replace "T-cell chronic lymphocytic leukemia", "extranodal NK/T cell lymphoma" to replace "angiocentric lymphoma"; (2) The entities considered provisional in the REAL classification are accepted as definitive entity, with the exception of "anaplastic large cell lymphoma, Hodgkin-like", which is deleted; (3) Anaplastic large cell lymphoma is split into the primary systemic type and primary cutaneous type, while Burkitt-like lymphoma is largely submerged into the category of Burkitt lymphoma. The next major impetus influencing the approach to lymphoma classification will no doubt be molecular genetics, in particular DNA microarrays, which will yield an enormous amount of new data that will aid in the understanding of lymphomas.

23.2

Distinguishing Between Phenotype and Genotype in Non-Hodgkin's Lymphoma (NHL)

Randy D. Gascoyne, Hematopathologist, British Columbia Cancer Agency, Vancouver, BC, Canada

NHLs are characterized in the majority of cases by unique cytogenetic/molecular genetic abnormalities, including the t(14;18)/*bcl-2* oncogene rearrangement found in most cases of follicular lymphoma (FL) and rearrangements involving band 3q27/*bcl-6* oncogene characteristic of diffuse large B-cell lymphoma (DLBC). These changes may represent primary disease initiation events or occur during clonal evolution of the neoplasm. The specific molecular characteristics of these changes underlie the pathogenesis of the NHL, but do not directly correlate with phenotype. The specific phenotype of lymphoma cells has a significant effect on the behavior of the lymphoma cells and thus is usually predictive of clinical features and survival characteristics.

Most FLs harbor a t(14;18) leading to over-expression of Bcl-2 protein. However, 10-12% of FL cases demonstrate a clonal karyotype with no evidence of a *bcl-2* gene rearrangement. Some of these cases express Bcl-2 protein, presumably by a mechanism other than translocation. The role of gene duplication, cryptic rearrangements and gene insertion will be discussed. Similarly, most cases of FL express Bcl-6 protein, but do not show evidence of *bcl-6* oncogene translocations. DLBC lymphomas show similar discordance between molecular genetic alterations and protein expression, highlighting the diversity of mechanisms utilized by the malignant cells to promote both survival and enhanced growth. This talk will focus on understanding the differences between molecular genetic events and the phenotypic expression of a functional protein.

23.3

ACUTE PROMYELOCYTIC LEUKEMIA – A UNIQUE SUBTYPE OF ACUTE LEUKEMIA

Dr. Robert J. Mayer
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Acute promyelocytic leukemia differs from other subtypes of acute myeloid leukemia because of its associated coagulopathy, unique chromosomal aberrance (t(1517)), and unique response to such non-cytotoxic therapeutic agents such as all-trans retinoic acid (ATRA) and arsenic. Treatment with ATRA appears to lead to differentiation of the malignant hematopoietic clone, thereby providing a remarkable model of the molecular biology of leukemogenesis and the apparent differentiating effect when a missing ligand is provided. The results of recent randomized trials have clearly shown that the combination of ATRA (and potentially arsenic) with cytotoxic chemotherpay can lead to the cure of the majority of patients with acute promyelocytic leukemia.

24.1

Alterations at early Stage of Human Lung Carcinogenesis

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. Carcinogenesis of lung is a multi-step process preceded by premalignant lesions. At the present time, it is not very clear that how normal bronchial epithelial cells become premalignant and then malignant cells, and what phenotypic and genotypic alterations could be during the very early stages of lung carcinogenesis. By transfection with plasmid DNA containing the early region of SV40, we established 4 immortalized human bronchial epithelial cell lines. During continuous cultivation, those cells presented sequentially the properties such as enhanced proliferation, EGF- and anchorage-independent growth, increased resistance to serum-induced differentiation and cis-platin-induced apoptosis, and chromosome aberrations. All these alterations indicated that the immortalized cells were approaching malignancy. However, the cells were not tumorigenic, when they were inoculated subcutaneously into nude mice. The phenomena suggest that those immortalized cells were probably still at the premalignant stage. Our model of xenotransplantion with rat trachea containing the immortalized human bronchial epithelial cells (into nude mice), demonstrated that the cells in later passages developed different histological lesions, including metaplasia, dysplasia, which are considered as premalignant lesions of human lung cancer. The results, together with our previous reported data of human primary non-small cell lung cancer demonstrated that a series of molecular and cytogenetic alterations, including chromosome deletion and aneuploid, altered expression of oncogenes and tumor suppressor genes could be found not only in invasive lung cancer but also in early stages of lung carcinogenesis. Our studies have indicated that, the premalignant lesion, a concept of histopathology, could be characterized by genetic alterations. However, it still keeps unclear that why some premalignant lesions progress to invasive cancer, while others remain for a long period or even reverse to normal cellular phenotype, and that what the additional genetic changes required for the development of invasive cancer are. More studies are needed before we can answer the questions.

24.2

Use of biomarkers for understanding cancer risk

William W. Au, Ph.D., Department of Preventive Medicine and Community Health, The University of Texas Medical Branch, Galveston, TX 77555-1110, USA

We have been using chromosome aberrations (CA) as an effective biomarker to test the hypothesis that susceptible individuals have significant increase of CA from exposure to carcinogens and have increased risk for cancer. Lung cancer patients with the GSTM1 null, NAT1*10 and/or GSTT1 null alleles have significantly more CA than comparison controls. To improve the exposure dosimetry conditions, we have exposed human lymphocytes to a cigarette smoke carcinogen in vitro, NNK (0, 0.24, 0.72 and 1.44 mM). NNK induced a significant dose-dependent increase of CA. Lymphocytes with the GSTM1 null genotype have significantly more CA than cells with GSTM1 WT at every NNK concentration but not with GSTT1 null. In another experiment, treatment of human lymphocytes with benzopyrene (0, 10, 50 ug/ml) induced a significant dose-dependent increase of CA. The frequencies are significantly higher in cells with the susceptibility GSTM1 and EH variant alleles than the resistant alleles. We have developed a CA-based challenge assay as a biomarker to indicate abnormal DNA repair response and as an indication of acquiring susceptibility to environmental cancer. Our data show that exposure to high concentrations of environmental mutagens (cigarette smoke, butadiene, uranium and pesticides) induced abnormal response but not at low concentrations (butadiene and benzene). The biomarker information can be used to enhance the interpretation of susceptibility and health risk.

24.3

New molecular cytogenetic techniques in leukaemia

Dr Edmond S K Ma
Division of Haematology, Department of Pathology, The University of Hong Kong

Analysis of genetic changes has extended beyond conventional cytogenetics into the new molecular cytogenetic techniques including fluorescence *in situ* hybridization (FISH), comparative genomic hybridization (CGH), spectral karyotyping (SKY) and multicolour FISH (M-FISH). In the study of leukaemia, these techniques may be applied in resolution of complex cytogenetic changes, characterization of marker chromosomes, and detection of cryptic rearrangements. A case of acute promyelocytic leukaemia with cryptic *PML-RARα* fusion on 17q and add(15p) as a secondary abnormality. SKY showed that chromosome 11 material was added to 15p, forming a der(15)t(11;15), which was refined to der(15)t(11;15)(q13.2;p13) by CGH. Interstitial insertion of chromosome 15 material into chromosome 17q was detected using whole chromosome painting (WCP) probes by FISH. The reasons why WCP probes are more sensitive than SKY probes in this case may be related to different labelling methods of respective probes and the choice of filters for signal detection. We next investigated 12 cases of childhood ALL with *TEL AML1* gene fusion by FISH and CGH in order to document secondary genetic changes. Three patients (25%) showed amplification of *AML1* gene with (n = 2) or without (n = 1) trisomy 21. Gene expression study in two of these patients showed an increase in *AML1* transcripts that paralleled the increase in gene copy number. There was loss of chromosome 12 and hence the normal *TEL* allele together with duplication of the der(12)t(12;21) in one case. Finally, one patient showed a +21 clone distinct from the one harboring *TEL AML1* fusion, while another showed duplication of the fusion signal. The frequency of *AML1* amplification and its occurrence not in association with +21 as illustrated by one of our cases suggest that this is an important secondary abnormality in this group of patients.

25.1

"Voices of caregiver" –the experience of CancerLink

CHOW Sau-fong, Centre Director, CancerLink-Support & Resource Centre, HKCF

The "voices of caregivers" is a vital part of hospice & palliative care that seldom be addressed.

The CancerLink has run the CancerLink Hotline for four years. Statistics consistently showed that over half of the calls ere made by caregivers. Most of them reflected that they feel powerless & helpless in the caring process.

The presenter will illustrate what are the fears & concerns of caregivers. Besides, what is it culturally or environmentally within Hong Kong that makes home based caring difficult. The difficulties that caregiver encountered during the caring process. Also, the most important, how can we work together to support patients and their caregivers.

25.2

The Interface of palliative care in acute care setting

Dr Rico Liu, Consultative Palliative Care Team and Clinical Oncology, Queen Mary Hospital

Palliative care concerns the care of patients with advanced malignancy to enhance their quality of life. Looking after the dying has been the main theme in the early hospice movement. Often, this would involve transferring patients to a hospice where medical, nursing and psychological cares were offered. However, there is an increasing emphasis to provide palliative care well in advance of the terminal phase. WHO definition of palliative care stated that " Many aspect of palliative care are also applicable earlier in the course of the illness in conjunction with anti-cancer treatment". Providing palliative care in acute care setting is precisely the effects of this idea. It is already seen in the UK and Australia that palliative care teams in acute hospitals have become an integral part of palliative care service. Perhaps a similar development will be seen in Hong Kong.

In this presentation, the experience in providing palliative care by the Palliative Care Consultative Service (PCCS), to cancer patients in Queen Mary Hospital (QMH) is shared. The team was set up by the Department of Clinical Oncology, QMH in 1999. It comprises doctors, nurse specialist, registered nurse, clinical psychologist and medical social workers. Mutildiscipinary approach was adopted to provide comprehensive physical and psychosocial care to patient and their families. 24-hr hotline was setup to provide telephone support for patients discharged home. Domiciliary visit helped to keep some weak but well supported patients at home. Relatively well patients were followed up in palliative care clinic. The team facilitated hospice referral for some terminally ill patients. Besides service provision, the team was actively involved in education. Workshops related to palliative care issues were conducted for hospital staff. Palliative care teaching module was developed for medical students of University of Hong Kong. The team was also involved in organising a Certificate Course in Palliative Nursing for this year.

In conclusion, establishing a palliative care service in acute hospital is an effective way of helping cancer patients who are still being managed in acute hospital setting and through education, to disseminate the ideal of palliative care to hospital staff. Our service, being a consultative service, does not take up any hospital bed which has greatly reduced the cost of running. The service should not be seen as the substitute for hospice care. A truly comprehensive care for the whole disease course of these patients relies on close collaboration of hospital consultative team, home care team and hospice.

25.3

WORKING MODEL OF COMMUNITY PSYCHOSOCIAL CARE

Florence Chu
Family Service Centre, Children's Cancer Foundation

Since its inauguration in 1989 under the name of the Children's Cancer Fund for the Chinese University of Hong Kong, the Children's Cancer Foundation has expanded its range of services for children with cancer and their families from one hospital to a territory-wide level.

Seeing the impact of the illness is on the whole family, emotionally and psychologically, a community-based Family Service Centre was established in 1993. Through a team of professionals including clinical psychologist and social workers, a variety of services including family counselling, play services, psychotherapy, bereavement care, social and recreational activities, half-way-homes, etc. are provided hoping that the difficulties brought about by childhood cancer towards a family would be alleviated. In delivery services, the principles of "continuity of care" and "family as a unit" are closely adhered to. Working side by side with the medical teams in hospitals has greatly enhanced early intervention in providing psychosocial care to families.

In 1999, a home palliative care team was formed to deliver home care services to children with advance and incurable cancer. Through the service by two nurses and the professional team, the Foundation hopes to provide other alternatives to families when their children are facing impending death.

In the years to come, with the support from public donation, the Foundation would continue to commit all efforts to improve the quality of life of children with cancer and their families in caring their physical, psychological and social well-being.

Tissue microarray technology for translating molecular discoveries to clinical applications

Olli Kallioniemi. Cancer Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, U.S.A.

Completion of the human genome sequence provides unique resources for investigators in all fields of biomedical research. This is particularly evident in the rapid expansion of the field of functional genomics. cDNA microarrays make it possible to determine expression levels of up to 50,000 genes in a single experiment. Similar high-throughput screening methods are becoming available for proteomic studies. With such rapid expansion of genomic and proteomic screening, it has become an increasing challenge to translate all this information to improved understanding of biology and disease processes. Particularly important task is the prioritization of individual gene and protein targets for the development of novel diagnostic and therapeutic approaches.

We developed a novel technology, tissue microarrays (TMAs) or "tissue chips" to facilitate translational genomics research (Kononen et al., 1998). This "genome-scale" research tool enables high-throughput, massively parallel molecular analyses of very large numbers of tissue specimens or cells. TMAs are constructed by acquiring cylindrical cores from 500-1000 individual tissue specimens into a tissue microarray block, which is then sliced to 300 identical sections for probing targets in cells either at the DNA, RNA or protein level. A single immunostaining or in situ hybridization reaction provides information on all of the specimens on the slide, while subsequent identical TMA sections can be analyzed with other probes or antibodies. Construction of multiple replicate TMA blocks may allow up to 100 000 sections to be generated from a given set of tissue specimens. This new technology expands the scope of microarray technologies to the rapid molecular analysis of thousands of tissue specimens with thousands of probes at the DNA, RNA or protein level. This facilitates linking gene expression information directly with the biological data on the cells and tissues as well as with associated demographic and clinical information on thousands of patients. Applications of the TMA technology in translational genomic research of cancer are presented.

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COLORECTAL CANCER: FROM MOLECULAR PATHOGENESIS TO MULTIMODALITY MANAGEMENT

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Remarkable progress has occurred during the last fifteen years in both understanding the molecular etiology and also providing more effective means of treatment for patients with colorectal cancer, the second leading cause of cancer-related death in the United States. The process through which normal mucosa transforms into a benign polyp and into a potentially life threatening malignancy has been related to a sequence of molecular changes in DNA including specific mutations in both proto-oncogenes and tumor suppressor genes. The prophylactic use of cyclo-oxygenase inhibitors (i.e. aspirin, nonsteroidal anti-inflammatory drugs, etc.) as a form of chemoprevention appears to inhibit this process. Screening for colorectal cancer, while remaining a controversial issue, has progressed from the use of examination of the stool for occult blood to fiberoptic sigmoidoscopy and – more recently – fiberoptic colonoscopy in even virtual colonoscopy. For more than 40 years, 5-fluorouracil (5-FU) therapy represented the cornerstone of management of patients with metastatic disease. 5-FU acts primarily by inhibiting the enzyme, thymidylate synthase, thereby impeding DNA synthesis. Increasing the intracellular pool of reduced folates through pretreatment with leucovorin (i.e. folinic acid) enhances binding or 5-FU to thymidylate synthase, thereby making it a more effective anti-cancer compound. During the last three years, emerging data have suggested that irinotecan (i.e. CPT-11), an inhibitor of the enzyme topoisomerase 1, prolonged survival in patients with advanced disease who had previously been treated with 5-FU also improves the outcome when it is added to 5-FU and leucovorin as initial therapy for metastatic disease. Oxaliplatin, a platinum compound which acts synergistically with 5-FU in vitro against human colon cancer cells, has also been shown to add to the efficacy of 5-FU and leucovorin. The results of multiple recent randomized trials have also clearly shown that use of 5-FU-based chemotherapy can enhance the likelihood of cure for patients with Stage III (but not, apparently, Stage II) colon cancer and that the combination of radiation therapy and 5-FU-based chemotherapy can improve the likelihood of cure for patients with Stages II and III rectal cancer. Both irinotecan and oxaliplatin are now also being examined in the adjuvant setting. As the new millennium begins, the progress that has occurred in understanding the molecular causes, developing strategies to prevent and detect, and enhancing the means of treating colorectal cancer have at long last shown a decrease in the mortality rate of this common malignant condition.

Gastric Cancer

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Gastric cancer continues to be a leading causes of cancer related deaths worldwide. Disparities in survival following an R0 resection between medical centers in East and West have in part been explained by the large percentage of western patients presenting with more advanced stages of disease and a general reluctance to remove and analyze regional lymph nodes. As a consequence we still do not have a standard definition for an R0 resection. This was demonstrated in the recent intergroup trail reported at ASCO in May 2000. The trial (n=556) compared the survival between a surgery only arm and an experimental arm of surgery and postoperative chemotherapy and radiation. A D2 lymphadenectomy was recommended but not mandated. A subsequent review of the surgery revealed that 54% of the resected cases actually had a D0 lymphadenectomy. No mention was made of the number of resected nodes. Staging by the current UICC/AJCC definition of N stage requires that 15 or more nodes be examined. This definition of N stage if uniformly applied should help to bring about more uniform survival results around the world by reducing the influence of stage migration. The intergroup trial demonstrated a significant benefit for the experimental arm at three years but survival overall was inferior to that reported from other US centers where a more complete R0 resection is performed.

The traditional paradigm of radiographic staging followed by immediate surgical resection has had little impact on improving survival. Stage for stage western treatment outcomes remain inferior to those in the East. Greater attention is now being placed on improving pretreatment staging which is changing the management paradigm for gastric cancer, placing more emphasis on stage directed treatment. Video assisted laparoscopy has had a pivotal role in this transition. Laparoscopy can identify low volume distant disease in viscera or more commonly, in the peritoneum, without laparotomy allowing for systemic directed therapies, which can be delivered earlier in the patients treatment course. In the absence of M1 disease patients with advanced stages of gastric cancer can be selected before resection for alternative neoadjuvant treatment directed at increasing the R0 resection rate and reducing recurrence. A number of Phase II trials of neoadjuvant therapy have to date show this approach to be safe. It appears that responding patients do enjoy a survival benefit but this has not yet been proven in proper prospective randomized trails. With responses running in the 40% range it would be advantageous to identify responders early. Data from Memorial hospital and other centers suggest that molecular markers of chemosensitivity, such as TS, TP, DPD, and ERCC1 measured by immunohistochemistry, RT-PCR or by other techniques may predict outcome. This would clearly be a substantial improvement in directing therapy.

Neoadjuvant and other novel treatments targeted at systemic recurrence are desperately needed if improvement in gastric cancer survival is to be achieved. Surgical therapy must be standardized in order to properly evaluate any new therapies.

Consumers as advocates in cancer care

Professor Sally Redman, National Breast Cancer Centre, Australia

Women with breast cancer or consumers have been powerful advocates for improving care in Australia and internationally. In Australia, the Breast Cancer Network of Australia (BCNA) is an umbrella organisation for approximately 50 breast cancer consumer groups. The National Breast Cancer Centre has worked closely with the BCNA to support consumer advocacy.

Consumers have contributed by: raising public awareness about breast cancer, raising funds for research, advocating for changes to health service delivery and highlighting issues of concern to consumers. Women with breast cancer have worked at the local, state and national level. In Australia, they have provided unique input into the development of clinical practice guidelines and assisted in their implementation.

Consumers have also focused attention on the need for accurate and detailed information and involvement in treatment decisions. Most women want full information about their cancer and their treatment options; they also want to participate in decisions about their care.

However, little is known about how best to involve consumers in contributing to health care decisions and as advocates. The Centre has developed a consumer science and advocacy training program for consumers based on Project Lead in the US; results of an evaluation of this training program will be presented. A new project, *A seat at the table,* initiated by the BCNA to ensure high quality consumer input will be described.

30

Is Stress Carcinogenic?

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The quest to identify the cause or causes of cancer has long been a major aspiration in the field of medical oncology. It has been reported that as many as 40% of the cancer patients regard their cancer as being caused by a stressful life event prior to its onset. Psychosocial conceptualisations of cancer aetiology have however, always generated scepticism in scientifically minded medical researchers. The looseness in terminology, reliance on anecdotal "evidence", conflicting findings, limitations of subjects' retrospective recall, subjectivity of stress interpretations, lack of a clear dose-effect relationship, lack of a sound theoretical model, as well as the near practical impossibility in gathering convincing evidence are major stumbling blocks towards answering the question "is stress carcinogenic?" Cancer progression involves agents which initiate, agents which promote, and multiple stages of synergistic relationships amongst different aetiological factors. Determining causal relationships in cancer is complex as the cancer process is time-dependent and multicausal. Research into cancer onset is difficult as until more obvious signs and symptoms become evident, much of the initial process of cancer progression remains obscure. This presentation will review evidence (and counter-evidence) and theoretical models implicating the role of psychosocial stress in cancer aetiology and progression. While much can be said about the palliative and distress reducing role of stress management and alleviation, evidence for a direct casual relationship between stress and cancer remains tenuous. Future research strategies in clarifying the stress-cancer link are proposed.

31

DURATION OF CANCER SURVIVAL RELATES TO QOL

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Background: This cohort study describes the relation between QoL and 2 year survival in Chinese cancer patients after adjustment for clinical factors, treatment, mood, social support, and satisfaction.
Methods: 1,243 patients newly referred to five regional clinical oncology units in Hong Kong, diagnosed with breast (BrC), nasopharynx (NpC), lung (LuC) or liver (LiC) cancer had QoL (FACT-G (Ch)) measured on referral and were followed for up to two years. Data on disease stage at baseline, treatment received, symptoms, psychosocial and demographic factors were collected. Outcome after two years was confirmed using the central Register of Deaths, emigration records, and case note tracing. Proportional hazards analysed survival with median-dichotomized baseline QoL, and gender, age, diagnosis, stage, treatment, reported pain and symptoms, physical condition, social support, mood, and satisfaction with care and communications as predictors.
Results: 1,050 /1,127 cases, were eligible for analysis (254 BrC, 20%; 243 NpC, 19%; 377 LuC, 30%; 253 LiC, 20%). Participants with above median FACT-G (Ch) scores survived longer (mean 597, 95% CL 573-622 days) than did those with below median FACT-G (Ch) scores (mean 439, 95%CL 411-467 days), (Log Rank = 60.64, df = 1;p<0.0001). After adjustment for clinical and psychosocial factors, diagnosis of LuC (Hertzog ratio =13.68, 95% CL 7.93-23.61) or LiC (13.43, 7.57-23.85), more advanced disease (2.43, 1.86-3.17), appetite loss (1.56, 1.24-1.95), severe pain (1.42, 1.16-1.74), subsequent treatment (1.35, 1.10-1.67) and low QoL (1.29; 1.05–1.58) predicted increased risk of earlier death. Sub-scale analysis indicated that the FACT-G (Ch) Physical sub-scale accounted for the majority of variance. Sub-group analysis indicated single marital status was consistently associated with lower survival.
Conclusions: After adjustment for clinical and psychosocial factors poor self-reported QoL independently predicted reduced survival over the subsequent 2 years. Perceived social support, mood, satisfaction with care and communications, dypsnoea, malaise and weight loss did not independently predict survival in multivariate analyses. Excepting marital status, psychosocial dimensions appeared not to predict survival.

32.1

Microarray technologies for basic, translational and clinical cancer research

Olli-P. Kallioniemi. Cancer Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA

Large-scale scanning of the human genome has become possible with the introduction of a number of new technologies of functional genomics, such as the cDNA microarrays. The ability to survey 5000 to 50 000 genes in a cancer specimen in a single experiment provides significant new opportunities, as well as also challenges. Particularly important will be the ability to translate genomic scale information on cancer biology to better diagnostic, prognostic and therapeutic applications in the clinical setting.

We have developed a novel technology, tissue microarrays ("tissue chips") for "genome-scale" translational and clinical cancer research *(Kononen et al., 1998)*. This technology enables high-throughput, massively parallel molecular analyses of very large numbers of tissue specimens or cells. The arrays are constructed by acquiring cylindrical biopsies from 500-1000 individual tumor tissues into a tissue microarray block, which is then sliced to over 200 sections for probing any DNA, RNA or protein targets. A single immunostaining or in situ hybridization reaction provides information on all of the specimens on the slide, while subsequent sections can be analyzed with other probes or antibodies. Tissue microarrays expand the scope of biochip technologies to the rapid molecular analysis of thousands of fixed and archival tissue specimens with multiple probes for nucleic acids or proteins.

In our research, we apply cDNA microarrays for the discovery of genes in hormone-refractory prostate cancer in the CWR22 prostate cancer xenograft model. Tissue microarrays are then applied to perform gene validation in vivo in large patient materials. We have identified a number of genes, such as those affecting calcium signaling and the PI3K pathway, whose increased or decreased expression is associated with the failure of endocrine therapy in human prostate cancer *(Bubendorf et al., 1999; Mousses et al. Submitted, 2000)*. In breast cancer, our research is focussing at the identification of gene amplifications that play a role in tumor progression. For example, amplification of the ribosomal S6 kinase gene (at 17q23) leads to gene overexpression and may contribute to the aggressive disease course and poor patient survival *(Barlund et al., 2000)*.

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32.2

Gene Expression Profiling of Chemotherapeutic Response in Lymphoma

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Microarrays are a powerful technology for large-scale gene expression analysis. This technology has been useful in studying different aspects of disease. Our laboratory studies the regulation of gene expression in normal and malignant lymphocytes. Thus, we have developed a specialized microarray called the "Lymphochip" that is enriched in genes that regulate lymphocyte function. We have recently used the Lymphochip to subtype an aggressive malignancy, diffuse large B-cell lymphoma (DLBCL), into two groups. Patients in the germinal center B-like DLBCL group had a significantly better overall survival than the activated B-like DLBCL group. To date, there is no effective treatment for ~60% of DLBCL patients. In the process of identifying potential agents that perturb specific signaling pathways of these lymphoma cells, we came upon flavopiridol, a cyclin-dependent kinase (CDK) inhibitor. Flavopiridol arrests cell cycle at many points. We sought to determine how flavopiridol affects the gene expression profile by microarray analysis. In contrast to two other CDK inhibitors (roscovitine and 9-nitropaullone), flavopiridol inhibits global gene expression identical to transcription inhibitors such as actinomycin D and DRB. We have categorized the genes by half-lives and function through statistical analysis. During this process, we discovered unknown genes with predicted protein motifs that may play important regulatory roles in cell function. These studies demonstrate that mRNA turnover can be analyzed on a genomic-scale and that microarrays can be utilized to rapidly identify drug targets.

33.1

Occupational Cancer

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Occupational cancers are a group of irreversible, self-propagating response to occupational hazards. It is estimated that between 2 to 8% of cancers are attributable to occupational exposures and the proportion would be higher among the working population.

Documentation of many human carcinogens came from occupational studies. Pott first described cancers of the scrotum among chimney-sweeps in 1775 and attributed the cause to soot. Many reports on occupational cancers followed in the following two centuries. Currently, more than half of the 78 IARC (International Agency for Research on Cancer) Group 1 agents, mixtures and exposures are primarily occupational carcinogens.

Occupational carcinogens can be grouped into chemical, physical and biological agents. Chemical agents can be further subdivided into polycyclic aromatic hydrocarbons, aromatic amines, biological alkylating agents, dusts, metals and related substances, organic solvents and others.

The most commonly affected system/organ is the respiratory tract, followed by the skin and the urinary bladder, likely because of the heavy exposures.

Occupational cancers can have relatively short latency periods and the age at presentation is relatively young. They are also usually more malignant with rapid progression. Some cancers tend to be multiple and recurrent and multiple sites can be affected by some agents. Occupational cancers tend to have characteristic cytology, which may be different from non-occupational cancers.

A number of occupational cancers are compensable in Hong Kong and doctors have the legal responsibility to notify such cases to the Labour Department.

Prevention is of utmost importance. Primary prevention is most relevant and has been found to be very successful in the past. Removing the agent is most effective. Reducing the exposure and directly protecting the workers can also help. Secondary prevention is of limited use in actual practice.

33.2

SMOKING AND CANCER MORTALITY IN HONG KONG

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Objective: To assess cancer mortality attributable to smoking in Hong Kong.

Methods: A case control study based on the four death registries in Hong Kong. Information on smoking habit of deceased persons (cases) and of surviving relatives (controls) was collected from the same informants who applied for death certificates. 27419 cases and 13018 controls aged 35 or above were included from December 1998 to January 2000. Only the results on malignant neoplasms are reported below.

Results: There were 5930 cancer deaths in men and 3793 in women. The controls were 3905 men and 9113 women. The age and education adjusted odds ratios (OR) (95% confidence interval) for cancer deaths due to ever-smoking in men aged 35-69, and 70+ were 2.22 (1.94-2.55) and 1.84 (1.63-2.08), and in women, 1.60 (1.33-1.93) and 2.00 (1.76-2.28), respectively. The corresponding ORs for lung cancer were 4.99 (4.00-6.22), 4.90 (3.93-6.10), 3.06 (2.30-4.07) and 4.10 (3.43-4.91). In men aged 35-69, significant linear trends with OR increasing with amount smoked daily were observed for all cancers, lung cancer, oesophageal cancer, stomach cancer, liver cancer, cancer of 5 minor sites combined (mouth, pharynx, larynx, pancreas and bladder). No increased OR was found for colo-rectal cancer.

Conclusions: Smoking is a major cause of cancer death. In 1998, tobacco caused 2192 cancer deaths in men and 389 in women, or 37.0% and 10.3% of all cancer deaths aged 35 or above respectively.

Acknowledgement: We are grateful to the Department of Immigration for support to this project.

33.3

Breaking Bad News – A Chinese Perspective

Dr. Chun-yan TSE
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Hong Kong.

The degree of information received by terminal cancer patients about their illness varies across different countries. In USA, the majority of doctors indicated a preference for truth telling. However, the approach differs in many other countries, and this difference is often attributed to cultural difference. Some cultures perceive the disclosure as a harmful act violating the principle of non-maleficence. Many Chinese families object to let the patient know the diagnosis or prognosis, and some experts recommended to respect the wish of the family. Reports showed that doctors in China often inform the family members instead of the patient. However, in a population study in Hong Kong in 1996, the majority of those interviewed wanted information even if the news was bad. The authors concluded that there was no support for the idea that the family should be informed instead of the patient. Thus, the existing empirical evidence for the Chinese showed contrasting attitudes among the medical profession, the family members and the individuals. This paper attempts to analyze the possible reasons for the contrasting attitudes and the relationship to the Chinese culture. Gaps in our knowledge are identified, and a pragmatic approach is recommended before better knowledge is available from future studies.

35

Approaches to research in psychosocial care

Professor Sally Redman, National Breast Cancer Centre, Australia

Psychosocial research requires both qualitative and quantitative approaches. It is most likely to succeed when a multidisciplinary approach is used involving those with psychosocial, clinical and design skills. A consumer perspective will assist in ensuring that the research is relevant.

The workshop will be interactive; several research questions generated by participants will be considered and draft protocols will be developed to illustrate the different types of research techniques involved. Questions to be considered in relation to the protocols will include:

- What is the role of qualitative methodologies? What are the key quality control issues?
- How can questionnaires best be developed and validated?
- What types of sampling issues arise in psychosocial research and how can they best be overcome?
- How can methodological rigour be balanced against real world constraints?
- How can research be designed to ensure that it has an impact on practice on when completed?

36

Families and Cancer: A Family Systems Perspective

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Chinese culture emphasizes the importance of the family over the individual and values obligation and loyalty in addition to affection or emotional ties between family members. Chinese people greatly emphasize the importance of family as the basic unit for life. Within the Chinese cultural environment, when family relations are sound and stable, it is easier for family members to deal with a crisis cooperatively. When relations are not as strong pre-existing problems can have a detrimental impact on the illness management and outcome. This has major implications for families experiencing cancer. It is therefore important that health care professionals know how to conduct comprehensive family assessments and implement appropriate intervention strategies for families experiencing cancer. This workshop will offer participants the opportunity to learn a systems approach to cancer care for families. The focus will be on family systems assessment and intervention strategies using the Calgary Family Assessment Model (CFAM) and The Calgary Family Intervention Model (CFIM).

37

Making Good Use of the Precious Moment :
Possibility of Anticipatory Grief Work in Hospitals

Amy Yin Man CHOW, Centre Director,
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Bereavement counselling is usually perceived as the task commenced after the death of the patients. Yet, a lot of bereavement problems are related to unfinished businesses of the deceased as well as the unresolved interpersonal conflicts among family members. The bereaved persons are usually regret for not making full uses of the pre-death moment. Interventions for handling the regrets at post-death phase are taxing lots of energy with slow progresses. In addition, the bereaved will recall the days of last weeks' hospitalization repeatedly for thousand times after death. Thus a good memory with the patient in hospital will be treasured by the bereaved person life-long.

The Chinese translation of Bereavement Counselling is "善別輔導" (literally means good separation). The aim of bereavement counselling is then for facilitating a good separation for both the patient and his/her family members. Thus intervention at pre-death phase is of paramount importance as both parties are available. This workshop is aimed to offered health care professionals a chance to prepare oneself as well as to experience possibility of carrying out anticipatory grief work in hospitals. The concepts and theoretical background of anticipatory grief work as well as working with families will be highlighted. Experiential exercises on self-reflections as well as demonstrations on possible means of making good uses of the precious moment will also be carried out.

38

Working with Difficult Emotions

Lucy Chung MSc, DNA, RN, RM
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Psychosocial care is an essential and integral part of cancer care, and the provision of such care involves a high level of communication skills as well as the ability of the carer in working with difficult emotions. This workshop aims at exploring anger and helplessness which are emotions commonly experienced by patients, family members and professional carers. The focus of the workshop will be on helping health care professionals to develop a better understanding and acceptance of these emotions and explore ways of handling them effectively.

39.2

Timing of infections and risk of childhood leukaemia

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Childhood leukaemia is a heterogeneous disease with respect to biological subtypes and molecular lesions. The most common type of childhood leukaemia is common acute lymphoblastic leukaemia (cALL) of the B precursor subtype which peaks between 2 and 5 years of age. This peak of cALL, present in developed countries associated with a high standard of living, is reduced or absent in poor or underdeveloped communities. Based on this observation together with other factors including the association between socio-economic class and risk of ALL, the link between leukaemic clusters and population mixing, and the time trend data of leukaemia in different countries, a 'delayed exposure' hypothesis to common childhood infections has been proposed by Greaves and Alexander. The major feature of this hypothesis is that infants who are protected from exposure to infectious agents in the first year of life are at an increased risk of cALL when exposed to common infections in later years of life. The 'delayed exposure' hypothesis model takes into account the natural history of childhood leukaemia in which there are at least 2 independent and sequential mutations in B precursor cells to produce the clinical picture of leukaemia.

We have conducted a case control study of 98 cases of childhood leukaemia (with 228 controls) diagnosed at 2 to 14 years of age in Hong Kong to test the 'delayed exposure' hypothesis. Exposure variables used as proxies for opportunity of exposure to infectious agents include history of infectious illnesses, frequency of outside contact, household type and community size. Our results show an increased risk of leukaemia including cALL for children who have been recently been exposed to infection with weaker evidence of reduced risk for children having more opportunity for infection in the first year of life. Taken together, our data provide overall support for the 'delayed exposure' hypothesis for risk of cALL in Hong Kong, a modern and developed community in which population exposure to infections is distinct from settings of previous case control studies.

39.3

Immunodeficiency and Childhood Malignancy

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Children with either primary or acquired immunodeficiency are predisposed to development of various forms of cancers. The most common of which are lymphoma and its pathogenesis has a very intimate relationship with EBV infection or reactivation. The spectrum of tumours is related to the primary form of immunodeficiency. Patients with primary immunodificiency mainly suffer from non-Hodgkin's lymphoma (NHL) or epithelial cancers and acquired immunodeficency such as HIV infection can develop various forms of NHL and sarcoma such as leiomyosarcoma. Out of our 73 patients with various forms of primary immunodeficiency (excluding neutropenia), 3 patients [Wiskott Aldrich syndrome (WAS), n=1, Ataxia Telangiectasia (AT), n=1, Common variable immunodeficiency (CVID) n=1] developed NHL and they all achieved good remission by chemotherapy with reduced dosage intensity. Two of them (WAS & CVID) subsequently underwent matched unrelated BMT and one died of chronic GVHD related complications and another survived without disease for 8 years now. 2/3 patients showed positive EBER in their tumours. For acquired immunodeficency, HIV infected children and patients who underwent stem cells or organ transplantation were at risk of developing cancer. 1/7 of our vertically transmitted HIV patient developed malignancy in the form of non-nasal NK cell NHL that was EBER positive. She died prior to commencement of chemotherapy. In allogeneic BMT setting, post transplant lymphoproliferative disease (PTLD) has been quoted to occur in 8/798 recipients. We have no PTLD yet in our 93 children after BMT (76 allogeneic, 17 autologous). We have one case of PTLD (EBER positive) after liver transplant. He did not response to withdrawal of immunosuppressive treatment and died. The pathogenesis, frequency and spectrum of childhood malignancy related to immunodeficiency will be discussed.

40.1

Surgical Management of Soft Tissue Sarcoma

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From 1986 to 1999, 263 patients affected by Soft Tissue Sarcomas (STS) were treated in our Center. Primary amputation was performed in 13 cases (5%), while limb sparing surgery in 250 (95%). Among 250 patients treated by resection, 143 were males, 107 females with an average age of 48 years (12-78). Upper limb was involved in 73 cases (29%), lower limb in 165 (66%), trunk in 12 (5%). High-grade sarcomas were represented in 190 patients (76%). An extracompartmental site or extension was observed in 200 cases (80%). Seventy-eight tumors (31%) were primary lesions, 88 (35%) recurrent tumors, while a radicalization after previous inadequate surgery was performed in 84 (34%). After radicalization, in 35 patients (41%) persistent tumoral foci were found in the scar. After limb salvage surgery, radical surgical margins were obtained in 5 cases (2%), wide in 203 (81%), marginal in 26 (10%), intralesional in 16 (7%). STS were treated by surgery alone in 61 cases (24%), by surgery plus External Beam Radiation Therapy (EBRT) in 58 cases (23%) and by surgery plus Brachitherapy associated to EBRT in 131 cases (53%). In 3 cases of locally advanced disease, we used pre-operatively Hypertermic Perfusion (with ADM).

At an average follow up of 5 years (1-14), 185 patients (74%) were Continuos Disease Free (CDF), 17 (7%) had Non Evidence of Disease (NED) after treatment of tumoral local or distant recurrence, 25 (10%) were Alive With Disease (AWD) and 23 (9%) had Died Of Disease (DOD). Local recurrences were observed in 16 (26%) of the patients treated by surgery alone, in 5 (8%) of those treated by surgery plus EBRT, in 6 (5%) of those treated by surgery plus brachitherapy and EBRT. This observation was found both in highly malignant tumors than in low-grade tumors.

On the base of our results, in order to achieve a good local control of STS, we suggest the association between surgery and radiationtherapy, even in low-grade sarcomas. Brachitherapy, giving a boost of radiation (av. 33 Gy) immediately after surgery, showed to be efficient to achieve a better local control, sterilizing the surgical bed. However, the extremely limited radiation field offered by brachitherapy, is reported to have a high risk of local relapse in the surrounding tissues. For this reason, we suggest always the association between brachitherapy and EBRT. The EBRT may be employed pre or post-operatively, with analogous results on local control. Our first choice, is post-operative EBRT, while pre-operative EBRT exposed to a higher risk of surgical complications. Pre-operative radiation is actually limited to cases in which an attempt of tumoral mass shrinking is desired, or when a Motor Unit Transplant is planned (to avoid damages caused by post-operative EBRT on flaps viability). In very selected cases of locally advanced STS requiring amputation, the use of hypertermic perfusion can be attempted, in order to expand possibilities of limb salvage.

40.2

The Role of Pathologist in the Management of Musculoskeletal Tumours

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Conventional histological sections stained with haematoxylin and eosin have proved to be a reliable method of diagnosis, and it remains the gold standard in tumour diagnosis and classification. However, the diagnostic yield of a biopsy procedure depends on the quality of the biopsy specimen. A good communication between the clinician and pathologist will improve the quality of the biopsy specimens, and hence its diagnostic yield. Frozen section diagnosis is no longer acceptable as a definitive diagnosis, and radical surgery is seldom performed based on the result of the frozen section. The judicious use of intra-operative frozen section, however, can ensure that an appropriate amount of suitable tissue has been obtained for subsequent laboratory investigations. Pathologic examination of the excised specimens enables one to assess the extent of the disease and the completeness of the excision. For osteosarcoma, the degree of chemotherapy-induced tumour necrosis can also be assessed, which has been shown to be a strong prognostic indicator. The use of synthetic implants and bone allografts contributes significantly in the reconstruction of bone defect after surgical excision of the diseased bone. Sometimes, these implants and allografts fail to function properly. Histopathological examination of these artificial implants or allografts can provide valuable information as to the cause of their failure. Immunohistochemistry and electron microscopy are instrumental for the subtyping of bone and soft tissue tumours, particularly small round cell tumours and undifferentiated spindle cell sarcomas. Molecular techniques have been extensively used in the diagnosis and classification of small round cell tumours and other soft tissue sarcomas. The classic cytogenetic abnormality of t(11;22) in Ewing's sarcoma has become the defining feature of this group of neoplasms. This characteristic chromosomal translocation can now be demonstrated by other molecular techniques, such as fluorescent in situ hybridization (FISH) and RT-PCR. Lastly, pathology department also serves as a large and reliable database of musculoskeletal tumours, which is invaluable for teaching and research.

40.3

IMAGING OF SOFT TISSUE TUMOURS

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The aims of soft tissue tumour imaging are manifold. Firstly, the detection of the tumour and differentiation from non-tumoral (e.g. cyst) or pseudotumoral conditions. Secondly, the characterization of tumour and hopefully to allow one to arrive at a definitive diagnosis. There are certain soft tissue tumours that have special imaging features allowing their diagnoses. These include lipoma, haemangioma, neurogenic tumour, subungual glomus tumour and pigmented villonodular synovitis. Other than these, imaging characteristics of the rest of the soft tissue tumours are often non-specific and require histopathological diagnoses. In these cases, imaging can be used to accurately guide the biopsy site. Lastly, staging of soft tissue tumours prior to surgery to assess the exact location of the tumour and the involvement underlying bone, neurovascular bundles and adjacent structures.

With the advent of magnetic resonance imaging (MRI) and recently of high-frequency (10MHz or more) ultrasound (HFU), the assessment of soft tissue tumours has taken a great leap forward. However, the basics of obtaining a relevant clinical history from the patient and examination of the lesion are fundamental and still apply prior to the imaging of suspected soft tissue tumour. In the clinically inconspicuous or vaguely palpable lesion, a localizer placed next to it will direct imaging to the correct area. Plain radiography, although usually non-specific, will occasionally shed light to the diagnosis and may reveal underlying bone involvement. Ultrasound and MRI findings should always be interpreted together with plain radiographs.

MRI is still the modality of choice for imaging of soft tissue tumours. It has the advantages of superior soft tissue contrast, multiplanar imaging capability and does not involve ionizing radiation. It is useful for detection, characterization and staging of soft tissue tumours. It clearly demonstrates the relationships of the lesion with vessels, nerves, tendon and surrounding structures and provides a roadmap for surgery.

High-frequency ultrasound has recently emerged as another imaging modality for the assessment of soft tissue tumours. Besides having multiplanar capability and is free of ionizing radiation, HFU has additional advantages over MRI in having a higher spatial resolution, being a dynamic study, allowing for imaging guided-biopsy (unless one has an open magnet MRI) and is much cheaper. Patients precluded from MRI and those in whom metallic prostheses interfere with MR imaging, ultrasound is the modality of choice. However, HFU suffers from a limited field-of-view, poor visualization of the underlying bone (except for its cortical surface), and being operator-dependent. It also lacks the usual systematic imaging reference lines, thus the images are more difficult to interpret by the non-operator alone. In my opinion, MRI should still remain as the modality of choice for imaging of large or deep-seated soft tissue tumours and HFU reserved for small (<5cm) or superficial lesions or when MRI is contraindicated.

40.4

The Role of Radiotherapy and Chemotherapy in the Modern Management of Soft Tissue Sarcoma

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The management of soft tissue sarcoma, once an exclusive surgical enclave, has undergone a dramatic evolution in the last two decades. Multidisciplinary management, characterised by close collaboration between the surgical, radiation and medical oncologists and other paramedical professionals, has improved not only the survival but also the functional and psychological outcome for these patients. There is now ample evidence that function-sparing wide local excision when combined with adjuvant radiotherapy produces equivalent local control rates to radical compartmental excision and amputation can be avoided in most patients. Radiotherapy may be given as external beam irradiation, brachytherapy or a combination of the two. It can also be delivered on a neoadjuvant basis or as a postoperative treatment. Factors that govern the use and timing of radiotherapy and the choice of radiotherapeutic modality, include tumour factors e.g. size, depth and grade of the primary lesion, surgical factors e.g. the status of the resection margins, anticipated functional deficit and patient factors e.g. age, performance status, other major illnesses, chance of rehabilitation, psychological profile and patients' wish. Despite this improvement in local control, the use of radiotherapy has not produced any consistent improvement in the overall survival and approximately 50% of patients with high-grade lesions ultimately will die of their disease. A recent meta-analysis on the use of adjuvant chemotherapy has suggested a small benefit but its routine use is still not well established. Nonetheless, there is a well-defined role for chemotherapy and radiotherapy in patients with advanced soft tissue sarcoma with effective palliation being produced in most patients.

P1

Establishment and Characterization of a New Xenograft-Derived Human Esophageal Squamous Cell Carcinoma Cell Line SLMT-1 of Chinese Origin

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A new human esophageal cancer cell line, named SLMT-1, was established from a nude-mouse xenograft of a well-differentiated esophageal squamous cell carcinoma (ESCC) of the lower esophagus from a male Hong Kong Chinese patient. SLMT-1, passaged over 34 times and with a doubling time of 31 hours, has the microscopic features of epithelial cells with adherent growth as a monolayer. The general biologic properties of SLMT-1 cells were characterized by (1) a positive test of tumorigenicity obtained by injecting cells subcutaneously into athymic nude mice and observing their development into well-differentiated squamous cell carcinoma; (2) immunohistochemical staining using antibodies (AE1/AE3, CAM5.2 and MAK 6) which show the presence of cytokeratin intermediate filaments; and (3) electron microscopy demonstrating the morphologic features of epithelial cells with the presence of desmosomes. The cytogenetic abnormalities found in both the primary culture and SLMT-1 included der(1;14)(q10;q10), add(1)(p1?), +1, +2, del(3)(q11), +6, +7, i(8)(q10), +8, +10, +11, -13, -15, +16, +17, -18, -19, -Y and marker chromosomes. Additional changes observed in the 34th passage included gains as well as losses of both numerical and structural abnormalities. Comparative genomic hybridization (CGH) indicated copy number gains on chromosomal regions 3q32-qter, 5p, 8p12-p11.2, 11q13-q22 and 13q22-qter, and loss of Y. The gains of 8p12-p11.2 in SLMT-1 cells are novel to ESCC. Based on its distinct and common characteristics, the SLMT-1 cell line serves as a useful tool for studying the molecular and genetic basis of the pathogenesis of ESCC.

P2

Detection of Genetic Alterations in Esophageal Squamous Cell Carcinoma Tumor Specimens and Adjacent Normal Epithelia by Comparative DNA Fingerprinting using Inter-simple Sequence Repeat PCR

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In this study, we screened 21 esophageal squamous cell carcinomas (ESCCs) for the detection of genetic alterations using inter-simple sequence repeat (ISSR)-PCR, a DNA fingerprinting approach. Three simple repetitive unanchored primers representing tri- and tetranucleotide repeats [$(GTG)_5$, $(GACA)_4$ and $(GATA)_4$] were used, and evidence of gains and losses of chromosomal sequences were detected in all tumors (21 of 21 cases) for at least one of the primers (as shown by changes in the intensities, both gains and/or losses, of profile bands of tumors compared with the corresponding normal epithelia). In 14 of these cases, apparently normal marginal epithelia adjacent to the tumors were also collected and were next examined. Nine of the 14 patients (64%) showed matching somatic mutations in the marginal epithelia adjacent to the tumors. Six of these 9 (67%) marginal epithelial samples were histologically normal, two were dysplastic and one had malignant lesion. In 3 of these 14 (21%) cases the profile bands were also seen to quantitatively increase in intensity, progressing from normal epithelia to marginal epithelia to tumors. Three profile bands showing gains (two) or loss (one) in different tumors compared to corresponding normal epithelia were cloned and their origins were determined by sequencing. One of the bands showing gain in the tumor could be matched to an EST sequence which has been mapped to the 7q22 region, a genomic amplification novel to ESCC. The other band showing gain in the tumor could be matched to a non-exonic sequence of chromosome 20, while the one showing loss in the tumor could not be matched with any known sequences. Primers designed from these sequences were used in genomic PCR amplification on the original patient sample to show that the gains and loss of ISSR-PCR bands are bona fide cases of somatic mutation. It is concluded that the ISSR-PCR strategy is adequate to the detection of somatic mutations in tumors, most of which are quantitative alterations in anonymous genomic sequences. This approach is also suitable to detect somatic mutations preceding the onset of morphologically detectable neoplasia in ESCC.

P3

INTRAOPERATIVE RADIATION THERAPY FOR BILE DUCT CANCER

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From 1980 to 1998,52 patients with proximal bile duct cancer were admitted to our hospital .All of them were histologically proved. Because the presence of severe local infiltration and metastases lymph nodes around the major blood vessels precluded resection , all patients were treated by exploratory laparotomy . Intraoperative Radiotherapy (IORT) was given after external or internal drainage. According to an additional treatment of External Beam Radiotherapy (EBRT), these cases were divided into 2 groups: IORT alone (14 cases), and IORT plus postoperative EBRT (38 cases), In IORT group , single doses of 25-35Gy were delivered to primary lessions using 12-20Mev electrons .The median survival time was 10 months . In another group, the patients reccived 15-25Gy of IORT followed by postoperative EBRT with 40-50Gy/5 weeks. The median survival time was 15 months. The results of this group appeared more favorable as compared with a historical control of 14 patients who were treated by conventional EBRT before 1980, the median survival time was 10 months. IORT is direct and exact, the effect on survival of the addition of IORT has yet to be established.

P4

Yeast One-Hybrid System Identifies the Binding Proteins for Rat Glutathione S-transferase P Enhancer I

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Rat glutathione S-transferase P (GST-P) is induced specifically at an early stage of chemical hepatocarcinogenesis as well as in the hepatocelluar carcinoma. The GST-P gene has a strong enhancer element, GPEI, which mediates very high transcription enhancing activity. By using the core sequencer of GPEI as bait in a yeast one-hybrid system, two cDNA fragments coding for the C-terminal part of the transcription factor c-jun and rat adenine nucleotide translocator (ANT) were isolated. The binding of c-jun and ANT to GPEI core sequence were confirmed by EMSA. C-jun and ANT could play an important role in the induced expression of GST-P gene.

P5

LOCAL RECURRENCE AFTER RESECTION FOR RECTAL CANCER

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Introduction: It has been emphasized that the mesorectum is the key to local recurrence after resection for rectal cancer. We studied the location of recurrence, relative to the bed of the primary tumour, the neorectum and the level of anastomoses, in patients reffered for recurrences after low anterior resection (LAR) in the "pre total mesorectal excision (TME) era".

Patients and method: The relative level above the anal verge of the primary cancer, the anstomosis and the recurrence was registered by proctoscopy in 31 patients operated on for recurrent cancer after low anterior resection. The origin of the recurrence was determined from the operative specimen.

Results: The median level of the prymari cancers was 10 cm above the anal verge, with the anastomoses 2 cm lower, the majority being within 2 cm. Most recurrences were within 1 cm of the anstomosis. No rectal cancer occurred more than 3 cm distal to the anastomosis.

Conclusion: The tumor bed is most often the origin of the recurrence: Recurrences were mostly due to inadequate radial, and in a few cases longitudinal, dissection of the mesorectum. Virtually all recurrences were within reach of the examining finger. At follow-up of rectal cancers most local recurrences can therefore be identified earlier by digital examination than by proctoscopy.

P6

Reduction of Murine Mammary Tumor Metastasis by Conjugated Linoleic Acid

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Recent studies have shown that conjugated linoleic acid (CLA) can inhibit the initiation and thus, incidence of mammary tumors in rodents. The concentration of CLA required for these effects was as low as 0.1% of the diet with no increased effects above 1%. To date, there is little evidence that CLA has any effect on growth or metastasis of mammary tumors. Here, we demonstrate that CLA, at the concentrations used in previous studies, significantly reduced metastasis, and pulmonary tumor burden of transplantable murine mammary tumors grown in mice fed 20% fat diets. Tumors of mice fed as little as 0.1% CLA and as much as 1% had significantly decreased numbers of pulmonary nodules when compared with diets containing no CLA. The volume of pulmonary tumor burden, as a result of spontaneous metastasis, decreased proportionately with increasing concentrations of dietary CLA. With 0.5 and 1% CLA, pulmonary tumor burden was significantly decreased compared to mice treated with the eicosanoid inhibitor, indomethacin and fed diets containing no CLA. These data suggest that effects of CLA on mammary tumorigenesis may go beyond the reported alterations in tumor incidence and effect later stages, especially metastasis. To investigate possible mechanisms in CLA reduction in metastasis, we evaluated transcript levels for various matrix metalloproteinases (MMP) and their inhibitors (TIMP) using quantitative RT-PCR. Dietary CLA decreased tumor transcript levels of MMP-2, MMP-15, MMP-16 and TIMP-2. Thus, alteration of MMP and TIMP may be possible means by which dietary CLA reduces mammary tumor metastasis. (Supported by grant 4CB-0157 from the California Breast Cancer Research Program)

P7

Primary Study for the Expression of Human Tissue Inhibitor of Metalloproteinase-4 in *Pichia Pastoris* Yeast System

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Matrix Metalloproteinases (MMPs) is a large family of proteinases that can lytisis the extracellular matrix and play very important role in the tumor metastasis. Tissue inhibitor of metalloproteinases (TIMPs) is the native inhibitor of MMPs. Up to date, four TIMPs (TIMP-1,2,3,4) have been descibed, TIMP-4 is the latest identified and cloned TIMP. Breast cancer cell infected TIMP-4 gene show low metastasis and angiogenesis. In this report, human TIMP-4 protein were expressed and secreted in the *Pichia Pastoris* yeast eucaryotic expression system. The TIMP 4 gene total coding regions were amplified by PCR , the DNA fragment was insert pPICZ-A vector down the a-factor signal sequence. The expression plasmid pPICZ/T4 was transformed into the KM71H yeast strain by the method of electroporation. The positive clones whose chromosome were integrated with TIMP 4 gene were identified by the direct PCR screening. After culture the yeast and induced by methanol, the recombinant protein was found with a molecular weight 23 Kd by SDS-PAGE electrophoresis. The recombinant protein's inhibition to MMP was identified by reverse gelatin zymography analysis method.

Key Words: Tissue inhibitor of matrix metalloproteinases-4, TIMP-4 yeast expression system, Reverse gelatin zymography

P8

FLUDARABINE, MITOXANTRONE AND DEXAMETHASONE (FND) IN THE TREATMENT OF INDOLENT LYMPHOID MALIGNANCIES.

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Background: Indolent lymphomas are uncommon in the Chinese people and optimal treatment is undefined. We evaluated the combination of fludarabine (25mg/m^2/day x3), mitoxantrone (10mg/m^2x1) and dexamethasone (20mg/day x5) (FND), an effective regimen in the West for low-grade lymphomas, for indolent lymphomas in Chinese.

Patients and methods: There were 44 men and 20 women, with a median age of 61 (33 -72) years. The diagnosis included follicular lymphoma (FL) (n=28), chronic B cell leukemia (B-LPD) (n=16), mantle cell lymphoma (MCL)(n=4), marginal zone B cell lymphoma (MZBL) (n=4), Maltoma with diffuse component (n=8), and T cell lymphoma (n=4). A total of 28 cases (43%) were treated at diagnosis (Dx) while 36 cases (57%) at relapse. The FND regimen comprised **Results:** Sixty cases were evaluable. The overall response rate was 70% with complete response (CR) and partial response (PR) rates of 57% and 13% respectively. Therapy was not completed in 15 cases (23%) because of infection (n=8) or rapid disease progression (n=7). A high CR rate was observed in grade 1/ 2 FL at Dx (10/10, 100%), T cell lymphoma (3/4, 75%), MZBL (3/4, 75%) and Maltoma (4/6, 66%). Intermediate response rates (CR+PR) were seen in grade 1/2 FL at relapse (6/9, 66%) and in B-LPD (5/11, 56%). The response rates in patients previously treated with purine analogues and anthracycline containing regimens were 60% and 55% respectively. Diseases with low response rates included grade 3 FL (1/3, 33%), MCL (1/4, 25%) and transformed B-LPD (0/3, 0%) Prolong marrow suppression and septicemia (n=12) occurred mainly in older patients (age>65, n=5) and heavily pretreated cases (>6 courses, n=6). Opportunistic infections included TB (n=4), cytomegalovirus gastritis (n=1) and systemic cryptococcosis (n=1). Hepatitis B carriers (n=7) were given prophylactic lamivudine and no reactivation occurred. At a median follow up time of 13.8 months, disease progression was observed in 6 responding cases (5PR, 1CR). Sixteen patients have died, 13 due to disease progression, one each from sepsis, cirrhosis and bronchogenic carcinoma.

Conclusions: FND is a safe and effective first-line and salvage treatment in indolent lymphoproliferative disease in Chinese patients. The high response rate in T-lineage disorder is encouraging. Prudent prophylaxis for opportunistic infections is required.

P9

NON-TBI CONDITIONING REGIMENS WERE ASSOCIATED WITH LESS TRANSPLANT-RELATED MORBIDITY AND MORTALITY IN PATIENTS WHO RECEIVED BMT FROM MATCHED-UNRELATED DONORS.

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Introduction. Allogeneic bone marrow transplantation (BMT) has been widely used for the treatment of haematological malignancy. In patients without a HLA-identical sibling, BMT from HLA-matched unrelated donor (MUD) become an alternate choice. Total Body Irradiation (TBI) has been included in marrow conditioning regimens but is associated with severe side effects including mucositis, nausea and vomiting and pneumonitis. The present study investigated the clinical outcomes of BMT patients using non-TBI conditioning regimens during transplantation from MUD.

Patients and Methods. From Jan 1998 to Jan 2000, 14 patients had received BMT from MUD using non-TBI marrow conditioning comprising bulsufan and cyclosphosphamide. Twenty-eight age and sex-matched patients who received BMT from MUD using TBI-conditioning were recruited as historical control. The two groups of patients were compared in terms of donor marrow engraftment and regimen- related toxicity.

Results. Patients in the non-TBI group had significantly shorter period of platelet engraftment and less requirement of total parenteral nutrition ($p<0.05$). In addition, they had less requirement of blood production transfusion and a shorter stay in hospital during transplantation, although their difference did not reach statistical significance ($p>0.05$). On the other hand, patients in the TBI group had increased risk of severe GVHD (grade ≥ 2), veno-occlusive disease and transplant-related mortality ($\leq$ 100 days). They also had a higher requirement of morphine infusion for mucositis although the objective oral assessment score and the subjective pain score during transplantation were similar in the two groups.

Conclusion. Non-TBI conditioning regimen in patients receiving BMT from MUD was associated with a lower transplant-related morbidity and mortality and a longer period of follow-up is needed to ascertain the difference in relapse rate between the two groups of patients.

P10

UNMANIPULATED BONE MARROW TRANSPLANTATION FROM ONE-HLA ANTIGEN MISMATCHED SIBLINGS CARRIES HIGH TRANSPLANT-RELATED MORTALITY COMPARED WITH THE HLA-IDENTICAL COUNTERPARTS

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Introduction. Allogeneic BMT is considered the curative treatment for many hematological malignancies but is often limited by the lack of donors. The use of sibling donors who are one-HLA antigen mismatched may increase the availability of transplants but its effects on survival and transplant-related mortality remained undefined. We compared the treatment outcomes of BMT from HLA-identical siblings (MS), one HLA-antigen mismatched siblings (MMS) and matched unrelated donors (MUD).

Patients and Methods. Medical records of patients who have received allogeneic BMT in Queen Mary Hospital from March 1990 to February 2000 were reviewed. HLA of patients and donors were defined by DNA techniques. All patients received standard anti-microbial therapies and prophylaxis against GVHD.

Results. 294 patients received BMT from MS (CML=102, AML=106, ALL=38, Others=48). 20 patients from MMS (CML=13, AML=3, ALL=1, Others=3) and 44 patients from MUD (CML=22, AML=16, ALL=3, Others=3). They had no significant difference in terms of age at presentation, neutrophil (ANC > $0.5x10^9$/L) and platelet engraftments (platelet count >$25x10^9$/L without transfusion). The median survival of patients receiving BMT from MS was 110 months whereas those from MMS and MUD were 13 and 10 months respectively ($p<0.005$). To eliminate the effects related to the difference in disease diagnoses and status at transplantation, subgroup analysis on patients with CML-CP was performed. 83 patients had received BMT from MS, 9 from MMS and 14 from MUD. BMT recipients from MUD had a significantly younger age at BMT, longer duration of disease prior to BMT and slower platelet engraftment when compared to the MS counterpart ($p<0.05$). At 100 months post BMT, the overall survival of BMT recipients from MS was 80%. The median survival of patients receiving BMT from MMS and MUD was 15 and 30 months respectively. ($p<0.001$ compared to MS). Of the 9 patients in the MMS group, 4 died of acute GVHD (Grade IV) early post BMT (1.5±0.45 months) and 1 died of disease relapse at 15.1 months.

Conclusion. The results showed that BMT from MMS and MUD carried high transplant-related mortality compared with that from MS. Modification of post-transplant immunosuppression and/or donor T-cells depletion might alleviate the severity of GVHD in that situation.

P11

CLOSTRIDIUM DIFFICILE-ASSOCIATED DIARRHOEA (CDAD) IN BONE MARROW TRANSPLANTATION

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Introduction. *Clostridium difficile*-associated diarrhoea (CDAD) had been reported to cause significant morbidity in the immunocompromised patients. A retrospective study was carried out to investigate the condition in BMT unit of Queen Mary Hospital in Hong Kong in 1999.

Patients and Methods. Medical records of 79 adult patients, who had received BMT from January 1999 to December 1999, were reviewed. CDAD was defined as presence of diarrhoea that occurred within seven days of a positive culture or toxin test (or both) and diarrhoea was defined as the passage of loose or watery stool greater than or equal to 3 times daily. Other causes of diarrhoea including graft-versus-host disease of the gut were excluded. Asymptomatic carriers were defined as patients who had positive stool culture/toxin tests but without diarrhoea. Weekly surveillance including stool culture and cell culture cytotoxin assay test were performed from admission until discharge. Patients with *Cl. Difficile* in stool were treated with a course of metronidazole (400 mg thrice daily) for ten days.

Results. A total of 31 positive stool cultures were detected in 18 patients. Only 3 out of 18 (16.6%) patients had positive toxin tests. Nine patients had diarrhea during transplantation that fulfilled the criteria of CDAD and the other nine patients were asymptomatic carriers. The mean onset time of CDAD was 15 days post-BMT (C.I. 12-18 days) and the mean duration of each diarrhea episode is 2.4 days (range 1-8), with a mean frequency of 4 times per day (range 3-10). In 15 out 16 patients who were treated with a course of metronidazole, subsequent stool cultures were cleared of *Cl. Difficile* indicating eradication. Two patients had recurrence of *Cl. Difficile* in stool after initial clearance in one of whom the bacteria could be eradicated by oral vancomycin and in the other by repeated course of metronidazole. No patient died as a result of CDAD.

Conclusion. *Cl. difficile* is a common isolate in stool specimen of BMT patients. Metronidazole achieved excellent eradication with a low relapse rate. Prospective study with a larger number of patients is needed to look into the effects of *Cl. Difficile* eradication on the occurrence of diarrhoea during transplantation.

P12

HERPES ZOSTER VIRUS INFECTION AFTER BONE MARROW TRANSPLANTATION

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Introduction. Varicella Zoster virus (VZV) reactivation is common after BMT and has been a cause of morbidity and repeated hospitalization. We looked into the risk factors of herpes zoster (HZ) in BMT patients with a view of defining the optimal prophylactic strategy in this group of patients. ***Patients and Methods.*** We retrospectively analysed 195 patients who had received BMT from Jan 1997 to July 2000 in Queen Mary Hospital. VZV serology of patients and donors were determined before transplantation by ELISA methods. Patients receiving autologous transplants or BMT from HLA-identical siblings were given acyclovir as prophylaxis against herpes simplex infection. Patients receiving BMT from matched-unrelated donors (MUD) were given high dose acyclovir until engraftment followed by ganciclovir three times a week until day 120, for prophylaxis against cytomegalovirus infection (CMV). Allogeneic BMT patients received prophylaxis against graft-versus-host disease (GVHD) comprising cyclosporine and a short course of methotrexate. Herpes zoster was diagnosed clinically based on the presence of vesicular rash that was distributed along dermatomes. The treatment included intravenous acyclovir (10 mg/kg thrice a day) for five days followed by oral valacyclovir (1 g thrice a day) or oral acyclovir (800 mg 5 times a day) for one week. ***Results.*** Thirty-three patients (17%) developed herpes zoster (HZ) in whom two had recurrent infections. The median time of infection was seven months post BMT (range: 2 to 33 months). 178 (91 %) patients were seropositive for VZV. HZ was not associated with the VZV serology of the patients prior to transplantation. On the other hand, allogeneic BMT patients who had received transplants from VZV-negative donors had increased risk of HZ ($p < 0.01$). Patients who received BMT from siblings had increased risk of HZ compared with those who received autologous transplants or BMT from matched unrelated donor (MUD). Other factors, including age, duration of transplantation, the use of total body irradiation (TBI) and the development of chronic GVHD had no significant association with the occurrence of HZ. ***Conclusion.*** HZ is a common complication after BMT. Allogeneic BMT is a significant risk factor when compared with the autologous counterparts and BMT from VZV-positive donors might confer immunity to HZ after transplantation.

P13

THE 23-VALENT POLYSACCHARIDE PNEUMOCOCCAL VACCINATION IS NOT USEFUL IN BMT PATIENTS AT RISK OF PNEUMOCOCCAL BACTEREMIC SEPSIS.

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Introduction. Long term survivors after BMT are at risk of serious infections with encapsulated bacteria, in particular, *streptococcus pneumoniae*. BMT patients in our center received a 23-valent polysaccharide pneumococcal vaccine six months after transplantation but the efficacy of vaccination remained undefined. We investigated the risk factors for pneumococcal infections post BMT and assessed the efficacy of pneumococcal vaccine in this group of patients. ***Patients and Methods.*** Medical records from 482 survivors after BMT in Queen Mary Hospital from January 1995 to December 1999 were reviewed. Nine patients had documented pneumococcal sepsis defined as the presence of *streptococcus pneumoniae* in blood cultures with clinical sepsis. Patients were analysed according to the development of chronic graft-versus-host disease (cGVHD), the use of total body irradiation (TBI) in the conditioning regimen and the source of BMT. The humoral response to pneumococcal vaccination was measured by immunoassays on paired serum before and two week after vaccination. Radio-isotope liver and spleen scans were also performed to assess the splenic function of BMT patients who had developed pneumococcal bacteremic sepsis. ***Results.*** TBI and a combination of allogeneic BMT and cGVHD significantly increased the risk of pneumococcal bacteremic sepsis ($p< 0.05$). There was no significant increase in antibody titre in BMT patients after pneumococcal vaccination in contrast to the 3 to 4-folds increase in immunocompetent controls. Nine patients have developed pneumococcal bacteremic sepsis. In four patients, infections resulted in septic shock requiring intensive care one of whom developed overwhelming sepsis leading to multi-organ failure and death within 24 hours of hospital admission. Five patients have received pneumococcal vaccination before. 99^{m}Tc Colloid liver and spleen scan were performed in six patients and revealed the absence of splenic uptake in one patient and significantly reduced uptake in three others. Two patients had normal splenic uptake. ***Conclusion.*** TBI and cGVHD were significant risk factors for pneumococcal infection after BMT and the polysaccharide pneumococcal vaccine was of no protective value. Further studies are needed to evaluate the optimal prophylactic strategy in high risk patients.

P14

A Comparative Study of Hysteroscopic Dissemination of Endometrial Carcinoma using Carbon Dioxide and Normal Saline

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BACKGROUND. The aim of the study was to compare the incidence of positive peritoneal cytology in patients with endometrial carcinoma, who underwent diagnostic hysteroscopy for staging using carbon dioxide (CO_2) and normal saline (NS) as distension media.

METHODS. A retrospective review of 163 consecutive patients with endometrial carcinoma treated at a university teaching hospital between 1994 and 1999 was undertaken. Each patient had a diagnostic hysteroscopy for determination of cervical involvement using either CO_2 or NS. Peritoneal cytology was obtained during laparotomy. Positive peritoneal cytology was considered as the primary statistical endpoint.

RESULTS. A total of 39 cases were excluded from the study because of macroscopic intraperitoneal diseases (n = 32) or histologies other than endometrioid adenocarcinoma (n = 7). Analysis was based on the data of 124 patients who had hysteroscopy for staging.

Peritoneal cytology was positive in 8 (6.5%) of 124 patients. It was significantly more common after hysteroscopy using NS than CO_2 (13.0% versus 1.4%, p = 0.021). The presence of positive peritoneal cytology was not associated with age, grade, myometrial invasion, tumor size, cervical involvement or nodal involvement. All cases with positive cytology remained alive without recurrence at 3 to 25 months follow-up.

CONCLUSIONS. Our data suggested dissemination of endometrial malignant cells is significantly more common after NS than CO_2 hysteroscopy.

P15

Detection of *p53* gene mutations in human epithelial ovarian cancer

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Background: p53 is a 53 kDa nuclear phosphoprotein which contains 393 amino acids. Functions of the wild-type p53 protein include regulation of the cell cycle and the cellular response to DNA damage, induction of apoptosis, and promotion of cell differentiation. Inactivation of the *p53* gene by mutation has been shown to be the most common genetic alteration in a variety of human cancers. This study determined mutations in the functional domain (exons 5-8) of the *p53* gene in human ovarian cancer.

Materials and Methods: Tumour samples from 52 patients undergoing surgery for primary epithelial ovarian cancer were used. Genomic DNA was isolated from tumour samples by phenol-chloroform extraction. Mutations in exons 5-8 of the *p53* gene were screened and detected by polymerase chain reaction - single strand conformation polymorphism (PCR-SSCP) analysis and direct sequencing, respectively.

Results: Seventeen of the ovarian tumours samples demonstrated a single strand conformation polymorphism band shift, including 5 in exon 5, 1 in exon 6, 7 in exon 7, and 4 in exon 8 of the *p53* gene. Further characterization by direct sequencing showed that 16 of the 52 (31%) carcinomas had mutations affecting the primary amino acid sequence, hence the function, of the p53 protein.

Conclusion: As mutations of the *p53* gene were commonly detected in ovarian tumours of different clinical stages, genetic alterations of the *p53* tumour suppresor gene could play an important role in the development of a significant portion of human epithelial ovarian carcinomas.

P16

A prospective study of the microbiological environment of the genital tract in women diagnosed to have high grade or low grade squamous intraepithelial lesions

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Introduction: Treatment of squamous intraepithelial lesions (SIL) by loop electrosurgical excision procedure (LEEP) is an excisional type of treatment. However, it is associated with a complication rate of 8-10%. Secondary haemorrhage is the commonest type of complication and when it occurs, antibiotic treatment is usually used. Whether it is related to microbiological infection or the colonization of microorganisms is unknown.

Materials & Methods: One hundred patients who had high or low grade SIL required LEEP were recruited. All were reviewed 1 week after the procedures. Vaginal and endocervical swabs were taken for microorganisms, Chlamydia and Gonococcus cultures at both examinations. Antibiotics were prescribed according to the culture results and when secondary haemorrhage occurred.

Results: There was 12% secondary haemorrhage. Of those who had secondary haemorrhage, none of them had positive culture before the treatment procedure or at the time of presentation of secondary haemorrhage and only one had positive culture 1 week after the treatment procedure. However, the overall colonization rate was 14% before and 25% after the treatment.

Conclusion: We did not find a relation between the colonization rate and the secondary haemorrhage. We postulated that the secondary haemorrhage might be caused by the inflammatory reaction rather than antibiotic treatment may not be necessary.

P17

EFFECT OF DIET ON IGF-I AND IGFBP-3 IN MIDDLE-AGED AND OLDER CHINESE IN SINGAPORE

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Insulin-like growth factor (IGF-I) and its major binding protein (IGFBP-3) have been shown to have a wide array of biologic effects and recently have been implicated in the etiology of several cancers. Nutrient intake has been associated with regulation of circulating IGF-I and IGFBP-3 levels. We characterized serum IGF-I, IGFBP-3 levels and examined the relationship with age, gender and nutrient intake among 638 Singapore Chinese (312 men and 326 postmenopausal women), aged 50-77 years, who are participants of Singapore Cohort Study on diet and health. Dietary intake was evaluated by a structured food frequency/portion size questionnaire administered in-person. IGF-I and IGFBP-3 concentrations in serum were measured by immunoradiometric assay (IRMA). The mean serum IGF-I levels (134 ng/ml vs. 108 ng/ml in men and women respectively) in our study population were lower than in Caucasian populations. Serum IGF-I levels were higher whereas serum IGFBP-3 levels were lower in men compared to women. Serum IGF-I and IGFBP-3 decreased linearly with age in both genders (P for linear trend <0.05). Serum IGF-I and IGFBP-3 did not correlate with macronutrient intake (fat, protein, carbohydrate) after adjustment for the effect of total energy intake. However, there was a weak but significantly positive correlation between serum IGF-I and soy protein intake in men, but not in women. Our observations suggest that age, gender may affect levels of IGF-I and IGFBP-3 and these potential confounders should be considered in the design, analysis and interpretation of studies of IGF-I, IGFBP-3 and disease. In addition, the possible association between soy protein intake and serum IGF-I and IGFBP-3 in this study population deserves further investigation.

P18

The Fine-scale Mapping of NIDDM Susceptibility Genes in Northern Chinese Han Population

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In our previous effort to localizing the NIDDM susceptibility genes by genome-wide scan method in 32 Northern China Han NIDDM families, we have identified some suggestive loci in chromosome 1,12,18,20, respectively, with an average resolution of 10 cM. A subsequent search for fine-scale mapping the susceptibility genes in chromosome 1 was conducted in a larger set of 60 diabetes families, by using a similar approach to genome-wide scan. A denser microsatellite markers set with an average resolution of 3.4cM was used to narrow the regions in which the disease alleles may reside.

After multiplex touch-down PCR, the products were electrophoresed in PE ABI prism™ 377 Sequencer, and the data collected were analyzed by PE Genescan and Genotyper program, then the information of each marker was exported into Excel software. Finally, the data with a certain format were run in GENEHUNTER program to calculate both the P-values and NPL values.

Altogether 12845 genotypes were analyzed in all 367 samples of 60 pedigrees. The data from 3 loci were discarded for their obvious bad results. The remaining 32 loci,which were binned into 5 regions, were analyzed carefully.

We have gained significant linkage evidence in 3 regions of all 5 regions, which means that our previous genome-wide scan results were confirmed by our subsequent fine-scale mapping studying. Interestingly, all the 5 markers in the first region, from D1S243 to D1S2663, were less than 0.05 in P value, which may suggest that more than one gene resides in this region. The results are as following:

Locus	Position(cM)	Region	P value	NPL value
D1S243	0.0	1	0.00834	1.653
D1S468	6.2	1	0.0015	2.135
D1S2845	11.1	1	0.033	1.292
D1S214	16.4	1	0.0025	2.005
D1S2663	16.9	1	0.00205	1.996
D1S2815	193.8	4	0.00126	2.17
D1S218	196.5	4	0.043	1.2
D1S2800	256.2	5	0.0128	1.579
D1S235	258.7	5	0.054725	1.36274

The evidence for the region 4 and 5 means that the disease alleles may span a range of 2.7cM and 2.5cM,respectively, which almost near the limit of microsatellite markers. A next step to conduct is finer mapping by taking advantage of SNPs.

P19

My patient die in suicide, I feel.....

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My patient committed suicide on the 1st day of Chinese New Year. We were shock and felt sad by his action. We questioned ourselves why he chooses this way to end his life? Do suffering meant unavoidable suicidal reaction ? We got sense of failure, blamed to us for not aware of his risk and caused this incident. A working group was formed with four nurses to conduct a case review study. We used literature review, case notes review, self reflection and group discussion as a way tounderstand why and how the incident happened, the signs and signals of risk, explored our strength , weakness and affirmed our view on suicide. It was a painful process to discuss about this mishap; however, we ventilated a lot on our feeling towards this patient and went through our grief. Thus, we can learn from his experience and got growth from our emotional scar.

P20

"Working Together for Better Cancer Care" – The Psycho-Social Experiences of Patients with Advanced Cancer

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"Working Together for Better Cancer Care."
Psychological distress often causes suffering in terminally ill patients and their families.

In order to help terminally cancer to cope with the disease progress, it is necessary to find out patient's Psychological distress and identify any helpful or distressing past experiences.

Method: A small study had been started to collect patients' experiences in cancer support group and hospice service.

Some questions had been used to explore patients' feelings. Good experiences and bad experiences while taking treatment and what would patient gain with disease.

The study is in progress .....

P21

ACUPUNCTURE FOR THE RELIEF OF BREATHLESSNESS IN HOSPICE PATIENTS
A PRELIMINARY REPORT OF A RANDOMISED CONTROLLED TRIAL WITH PLACEBO AND DOUBLE BLINDING

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Aim of Investigation: To investigate the immediate effect of acupuncture for the relief of breathlessness in hospice patients.
Methods: From February 2000 onwards, eligible patients with breathlessness with informed consent were recruited and randomised to a control group with placebo acupuncture and an intervention group with true acupuncture. Three special acupoints were used. Both groups of patients received five consecutive sessions of treatment. The outcome measurements were visual analogue scale and respiratory rate.
Results: At the time of reporting, 50 sets of readings from eleven patients were obtained. 26 sets from intervention group and 24 from placebo group. The mean age of the control group was 50.8; SD 20.29 while it was 66.8; SD 15.30 in the intervention group. There was statistically significant reduction ($p=0.001$) in VAS score for patients receiving acupuncture (median change=12.5%) when comparing with the control group (median change=0%). Furthermore, there was evidence to support that significant reduction of respiratory rate was found in these patients (control median 0%; intervention median 8.71%; $p=0.006$).
Conclusions: Acupuncture has been shown to have immediate effect on reduction of both breathlessness and respiratory rate. These preliminary results strengthened the drive of continuing this clinical trial in a larger scale.

P22

KINEMATIC ANALYSIS OF ROTATION PATTERN OF ACL DEFICIENT KNEE, ACL RECONSTRUCTED KNEE AND NORMAL KNEE DURING SINGLE LEG HOP AND PIVOT SHIFT TEST

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Anterior cruciate ligament (ACL) injury is a common sport injury in Hong Kong. The aim of the treatment is to regain their previous knee stability and return to their sport activity. Pivot shift test and single leg hop test are common clinical assessment to test the knee stability and its functional ability. In this study, the kinematic rotation pattern of ACL deficient knee, ACL reconstructed knee and normal knee was studied with an electro-goniomeeter to investigate whether ACL reconstruction could improve the knee stability and functional activity. There were totally 30 subjects in our study. Two females and 13 males ACL reconstructed subjects, aged from 20 to 56 years old, and one female and 14 males ACL deficient subjects, aged from 17 to 46 years old were included. The unaffected knees of subjects were the normal group for comparison. Internal and external pivot shift test were categorised in the three groups. Single leg hop tests included linear single leg hop, single leg hop and landed with internal and external rotated leg, single leg hop with pre-internal and external rotated leg tests. Antero-posterior laxity of the knee was measured by KT-1000. Activity level of subjects were measured by Tegner scale. There was significant difference ($p<0.05$) in laxity between ACL deficient group and normal group but not in their Tegner scores. There was significant difference ($p<0.05$) in internal pivot shift test performed from flexion to extension among the three groups. Otherwise, there was no significant difference in other maneuvers in demonstrating pivot shift among the three groups. There was significant difference in the single leg hop test with pre-rotated leg among the three groups ($p<0.05$). It was concluded that ACL reconstructed group had better knee stability and functional ability than ACL deficient group but yet, not as good as that in normal group.

18.3

Effective Use of Microbiological Investigations in Cancer Management

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The clinical microbiology laboratory faces enormous challenges in diagnosing infections that cause morbidity and mortality in cancer patients. In Queen Mary Hospital, over 11,000 specimens are submitted annually for cancer patients. The majority (31%) is submitted for bacterial culture and antimicrobial sensitivity. Other major categories include fungal cultures (22%), blood cultures (11%), Mycobacterium (4%) and bacterial surveillance (4%). These patients are often immunocompromised and most centers developed special laboratory protocols for processing specimens from the cancer wards. Examples from QMH will be cited and the principles involved in the formulation of these special protocols will be reviewed. The impact and effective use of automation and new molecular methods will be discussed. These new technologies will be mainly used, not so much for the usual pyogenic bacteria, but for difficult viruses, parasites, fungus and mycobacterial infections. Finally a review on the appropriate use of tests and methods to avoid abuse and overuse of microbiology testing will be presented.