CURRICULUM VITAE

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Center for Nasopharyngeal Carcinoma Research (2010-18)

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Place of Birth: Pasadena, California, U.S.A.

Education:

1970 - 1974 BA, Microbiology
Cornell University
Ithaca, New York, USA

1974 - 1978 PhD, Medical Microbiology
Cancer Biology Research Laboratory
Stanford University
Stanford, California, USA

Work Experience:

1974 - 1976 Department of Medical Microbiology
Stanford University
Stanford, California, USA
Teaching Assistant

1976- 1978 Cancer Biology Research Laboratory
Stanford University
Stanford, California, USA
Research Assistant

1978 - 1980 Center for Cancer Research
Massachusetts Institute of Technology
Cambridge, Massachusetts, USA
Postdoctoral Fellow

1980 - 1991 Department of Microbiology
University of Hong Kong

	Hong Kong Lecturer
1986-1987	Department of Medical Microbiology and Immunology University of California Davis, California, USA Visiting Assistant Professor (sabbatical)
1991-1992	Department of Anatomical and Cellular Pathology Chinese University of Hong Kong Hong Kong Honorary Lecturer
1991-2009	Department of Biology Hong Kong University of Science and Technology Hong Kong Lecturer (1991-2), Associate Professor (1992-7), Professor (1998-2005), Chair Professor (2005-2009)
2009-	Department of Clinical Oncology University of Hong Kong Chair Professor

Societies:
American Academy of Microbiology
American Society of Microbiology
International Association for Research in Epstein-Barr Virus and Associated Diseases
Society of Chinese Bioscientists in America
American Association for Cancer Research

Honors:
elected Fellow of American Academy of Microbiology, 1994
elected Fellow of Institute of Molecular Biology, University of Hong Kong, 1990
awarded the Croucher Foundation Senior Research Fellowship, 2005
appointed Academic Member of the Henan Key Laboratory for Esophageal Cancer, 2005

Major Research Interests:

My primary research interests involve molecular genetic studies to determine the importance of viral and host genetic factors in the process of tumorigenesis. My Epstein-Barr Virus (EBV) studies showed a unique and significant geographical distribution of EBV genotypes. Different parts of the viral genome are useful as molecular biomarkers to study the association of this virus with nasopharyngeal carcinoma (NPC), an important cancer of local relevance to Hong Kong. In addition to viral infection, genetic factors are also critical to NPC development. Using a functional chromosome transfer approach additional studies indicate that certain regions of multiple chromosomes are vital for NPC development. Our laboratory was the first to localize such a critical region for NPC on chromosome 3p21.3. We have subsequently shown that the 3p21.3 gene, *BLU/ZMYND10*,

plays an important role in NPC tumorigenesis. Other functional and clinical studies of NPC show that 11q13 and 11q22-23 are critical regions associated with tumor suppression in NPC. We have identified three candidate tumor suppressor genes (TSGs), *TSLC1, THY1*, and *CRYAB*, mapping to 11q22-23 that are down-regulated or lost selectively in primary and metastatic NPC. Studies are underway to understand their mechanisms of action. Other growth suppressive critical regions for NPC have been mapped to 13q12, 14q11.2-13.2, and 14q32.1. We have identified other key genes involved in NPC development, including *ADAMTS9, MMP19, MIPOL1, PTPRG*, and others for which current studies are focused on validating their functional importance. I guest-edited an important 2012 *Seminars in Cancer Biology* issue devoted to different aspects of NPC research, in which one article summarizes our progress in NPC tumor suppressor gene (TSG) discovery and study.

P53 mutation studies indicate that this important TSG plays a critical role in a number of locally important cancers. A functional *p53* yeast assay was established to analyze clinical specimens for *p53* mutations. The hot spots and the frequencies for mutation of this gene vary for different cancers in Hong Kong, highlighting the different causal factors involved in their genesis. Other cancers of interest in the laboratory include lung, colon, and esophageal cancers. Alterations of oncogenes and TSGs have been investigated and several biomarkers useful for diagnostic and prognostic purposes have been identified.

Ongoing esophageal cancer functional studies have identified critical regions for tumor suppression on chromosomes 3p14.2, 9q33-34, 13q14, and 14q32. A candidate TSG, *DEC1* mapping to 9q33-34, has been identified and studied in detail and is involved in the establishment of the tumor in nude mouse models. This discovery led us to *DNAJB6*, an important gene we have studied for its role in ESCC tumorigenesis. The 3p14.2 *ADAMTS9* and the 13q14 *THSD1* candidate TSGs were identified and shown to be down-regulated significantly in esophageal primary tumors. Thus, our studies are successfully elucidating the molecular genetic basis of cancers of importance to the Chinese in Hong Kong.

Recent approaches use whole genome next-generation sequencing (NGS) for targeted gene and genome sequencing to elucidate the genetic basis for inherited cancers, as well as to determine the molecular landscape of somatic genetic variants contributing to tumor pathogenesis. Together with global transcriptomic and methylome approaches, these integrative studies will help us identify key genes and pathways responsible for NPC and esophageal cancers.

I am currently leading two collaborative group research grants on NPC and on ESCC, which allow us to do basic, translational, and clinical studies of these Chinese cancers of strategic interest. With the NPC Area of Excellence (AoE) Research Grants Council (RGC) 8-year grant, I have officially brought together three universities (HKU, HKUST, HKBU) and five public hospitals (QMH, QEH, PYNEH, TMH, PMH) to establish a Center for NPC Research and to work in concert on NPC. I have played a major role in the establishment and current management of a Hong Kong NPC AoE Tissue Bank. Recently we were awarded a 3-year Collaborative Research Fund (CRF) grant from the RGC to study the molecular genomics of inherited ESCC. This grant brings together Hong Kong investigators in HKU, HKUST, and QEH, together with groups in Zhengzhou University in Mainland China and Griffith University in Australia. This grant is only beginning now, but we expect to identify important cancer predisposition genes involved in high risk China for esophageal cancers.

I have recently been awarded a Theme-based Research Scheme grant on translational studies of gastrointestinal cancer tumor heterogeneity and molecular

evolution. We will focus on metastasis and utilize liquid biopsies to develop non-invasive real-time monitoring of patients for earlier identification of early relapse and prognostic indicators. Using whole-genome sequencing and RNA sequencing analysis of tumor tissues and single cell circulating tumor cells, our studies will provide invaluable insight on basic cancer metastasis, as well as identifying actionable targets for precision medicine to improve clinical outcomes.

Publications:

Refereed publications

1. Decleve A, Lieberman M, Ihle JN, Rosenthal PN, Lung ML, Kaplan HS. Physiochemical, biological, & serological properties of a leukemogenic virus isolated from cultured RadLV-induced lymphomas of C57B/Ka mice. *Virology* 90:23-35, 1978.
2. Lung ML, Hering C, Hartley JW, Rowe WP, Hopkins N. Analysis of the genomes of mink cell focus-forming murine type-C viruses: a progress report. *CSH Symposia on Quantitative Biology* XLIV: 1269-74, 1979.
3. Kelly M, Holland CA, Lung ML, Chattopadhyay SK, Lowy DR, Hopkins N. Nucleotide sequences of the 3' end of MCF 247 murine leukemia virus. *J Virol* 45:291-8, 1983.
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5. Lung ML, Lam WK, So SY, Lam WP, Chan KH, Ng MH. Evidence that respiratory tract is major reservoir for Epstein-Barr virus. *The Lancet* i: 889-892, April 20, 1985.
6. Yam WC, Lung ML, Ng MH. Evaluation and optimization of the DNA filter assay for direct detection of enterotoxigenic Escherichia coli in the presence of stool coliforms. *J Clin Microbiol* 24:149-151, 1986.
7. Yam WC, Lung ML, Yeung CY, Tam JS, Ng MH. Escherichia coli associated with childhood diarrhoeas. *J Clin Microbiol* 25:2145-2149, 1987.
8. Lung ML, Chang RS, Jones J. Genetic polymorphism analysis of EBV isolates from infectious mononucleosis patients and healthy carriers. *J Virol* 62:3862-3866, 1988.
9. Yam WC, Lung ML, Ng MH. The clonal origin, restricted natural distribution of Escherichia coli O126. *J Clin Microbiol* 26:1477-1481, 1988.
10. Lung ML, Chan KH, Lam WP, Kou SK, Choy D, Chan CW, Ng MH. In situ detection of Epstein-Barr virus markers in nasopharyngeal tissue sections. *Oncology* 46:310-317, 1989.
11. Yam WC, Lung ML, Ng KY, Ng MH. Molecular epidemiology of Vibrio cholerae in Hong Kong. *J Clin Microbiol* 27:1900-1902, 1989.
12. Zheng BJ, Lam WP, Yan YK, Lo SK, Lung ML, Ng MH. Direct identification of serotypes of natural human rotavirus isolates by hybridization using cDNA probes derived from segment 9 of the rotavirus genome. *J Clin Microbiol* 27:552-7, 1989.
13. Lung ML, Chang RS. Longitudinal study of Epstein-Barr virus genotypes associated with infectious mononucleosis patients. *J Inf Dis* 162:994-995, 1990.
14. Lung ML, Chang RS, Huang ML, Guo HY, Choy D, Sham J, Tsao SY, Cheng P, Ng MH. Epstein-Barr virus genotypes associated with nasopharyngeal carcinoma in Southern China. *Virol* 177:44-53, 1990.
15. Lung ML, Lam WP, Sham J, Choy D, Zong YS, Guo HY, Ng M.H. Detection and prevalence of the "f" variant of Epstein-Barr virus associated with nasopharyngeal carcinoma in Southern China. *Virol* 185: 67-71, 1991.

16. Lung ML, Li S, Chang RS. Study of Epstein-Barr virus transmission by EBV genotyping. *J. Inf Dis* 164: 213, 1991.
17. Yam WC, Lung ML, Ng MH. Restriction fragment length polymorphism analysis of Vibrio cholerae strains associated with an outbreak in Hong Kong in 1989. *J Clin Microbiol*. 29: 1058-1059, 1991.
18. Chen HL, Lung ML, Sham J, Choy DT, Griffin BE, Ng MH. Transcription of Bam HI A region of the EBV genome in NPC tissues and B cells. Virology 191: 193-201, 1992.
19. Lung ML, Chang G. Detection of distinct EBV genotypes in NPC biopsies from Southern Chinese and Caucasians. *Int J Cancer* 52: 34-37, 1992.
20. Lung ML, Lam WP, Chan KH, Li SB, Sham J, Choy D. Direct detection of Epstein-Barr virus in peripheral blood and comparison of Epstein-Barr virus genotypes present in direct specimens and lymphoblastoid cell lines established from nasopharyngeal carcinoma patients and healthy carriers in Hong Kong. *Int J Cancer* 52: 174-177, 1992.
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45. Leung CS and Lung ML. Detection of p53 mutations in Hong Kong colorectal carcinomas by conventional PCR-SSCP analysis versus p53 yeast functional assays. *Anticancer Research* 19: 625-628, 1999.
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52. Chan KT, Hsieh DP, Lung ML. In vitro aflatoxin B1-induced p53 mutations. *Cancer Letters* 199: 1-7, 2003.
53. Cheng Y, Ko JM, Lung HL, Lo PH, Stanbridge EJ, Lung ML. Monochromosome transfer provides functional evidence for growth-suppressive genes on chromosome 14 in nasopharyngeal carcinoma. *Genes Chromosomes Cancer* 37: 359-368, 2003.
54. Kwong FM, Wong PS, Lung ML. Genetic alterations detected on chromosomes 13 and 14 in Chinese non-small cell lung carcinomas. *Cancer Letters* 192: 189-198, 2003.
55. Lung ML. Functional approaches to localize and identify tumor suppressive regions required for development of nasopharyngeal carcinoma. *Cancer Reviews: Asia Pacific* 1: 21-30, 2003.
56. Yang LC, Tang CM, Lau KW, Lung ML. Frequent loss of heterozygosity on chromosome 9 in Chinese esophageal squamous cell carcinomas. *Cancer Letters* 203: 71-77, 2003.
57. Chan KT and Lung ML. Mutant p53 expression enhances drug resistance in a hepatocellular carcinoma cell line. *Cancer Chemotherapy and Pharmacology* 53: 519-526, 2004.
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63. Ko JM, Yau WL, Chan PL, Lung HL, Yang L, Lo PH, Tang JC, Srivastava G, Stanbridge EJ, Lung ML. Functional evidence for decreased tumorigenicity associated with monochromosome transfer of chromosome 14 in esophageal cancer and mapping of tumor suppressive regions to 14q32. *Genes Chromosomes Cancer* 24: 697-705, 2005.
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chromosome transfer (XMMCT) and involvement of *alpha b-crystallin (CRYAB)* in nasopharyngeal carcinoma. *Int J Cancer* 122: 1288-96, 2008.
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Major Research Grants

Croucher Foundation

research grant 1985-1988 $1,093,500 co-principal investigator
"The cell biology and molecular biology of Epstein Barr virus latency"

research grant 1989-1995 $1,691,000 principal investigator
Epstein-Barr virus as a cause of NPC and genetic predisposition to NPC"

research grant 1990-1995 $812,500 principal investigator
"The role of oncogenes in lung carcinomas in Hong Kong"

research grant 1993-1996 $1,250,940 principal investigator
"Molecular and cytogenetic analysis of the role of tumour suppressor genes and oncogenes in the development of esophageal carcinomas in Hong Kong"

senior research fellowship 2005-2006 $800,000

Biotechnology Research Institute, HKUST
research grant 1991-1995 $1,768,100 principal investigator
"Development of new laboratory tests based on the use of novel & conventional markers and assay methods for the diagnosis and prognostic evaluation of nasopharyngeal carcinoma"

Research Grants Council
CERG research grant 1992-1994 $652,000 principal investigator
"Genetic etiology of lung carcinomas among women in Hong Kong"

CERG research grant 1995-1997 $310,000 principal investigator
“A molecular and clinical investigation of colorectal carcinomas in Hong Kong patients”

CERG research grant 1996-1998 $692,000 principal investigator
“Functional analysis of the role of tumor suppressor genes in nasopharyngeal carcinomas”

CERG research grant 1999-2001 $580,000 principal investigator
“Functional analysis of the role of tumor suppressor genes in nasopharyngeal carcinomas”

CERG research grant 2000-2003 $941,850 principal investigator
“Functional analysis of the role of tumor suppressor genes in esophageal carcinomas”

CERG research grant 2001-2004 $1,296,000 principal investigator
"Identification of tumor suppressor genes on chromosome 11q in naspharyngeal carcinomas and esophageal carcinomas"

CERG research grant 2004-2007 $1,806,000 principal investigator
“Identification of key tumor suppressor genes mapping to 3p21.3 and global gene expression changes resulting from their critical loss in NPC”

CERG research grant 2005-2008 $1,084,957 principal investigator
“Investigation of the DEC1 candidate tumor suppressor gene (TSG) and other candidate TSGs associated with critical loss of 9q33-q34 in esophageal carcinoma”

CERG research grant 2006-2009 $932,500 principal investigator

"Molecular and functional investigation of two thrombospondin type 1 repeat candidate tumor suppressor genes mapping to critical regions involved in esophageal carcinoma"

CERG research grant 2007-2010 $1,726,995 principal investigator
"Molecular and functional studies of the role of chromosome 14q candidate genes, CRIP2 and MIPOL1, in nasopharyngeal and esophageal carcinomas"

CERG research grant 2008-2011 $1,578,830 principal investigator
"Molecular and functional investigation of the role of two metalloproteinases in nasopharyngeal carcinoma tumorigenesis"

CERG research grant 2010-2013 $1,437,500 principal investigator
"Role of DNAJB6 epithelial-mesenchymal transition in esophageal squamous cell carcinoma tumorigenesis and metastasis"

GRF research grant 2013-2016 $952,636 principal investigator
"Elucidating the functional role of a metastasis-associated extracellular matrix gene, ECM1, in esophageal cancer"

GRF research grant 2014-2017 $1,122,210 principal investigator
"Secretory NID2, a basement membrane protein facilitating cell adhesion, migration, and metastasis in human cancers"

GRF research grant 2015-2017 $1,168,311 principal investigator
"Functional and mechanistic investigation of frequent p53 gain-of-function mutations in esophageal squamous cell carcinoma"

GRF research grant (Competitive Earmarked Research Grant) 2015-2018 $971,461
(transferred from PI to Co-I, due to departure of PI)
"Functional and mechanistic characterizations of a Candidate Tumor Suppressor Gene, Mirror Image Polydactyly 1, in Nasopharyngeal Carcinoma"

GRF research grant 1/2018-12/2020 $971,720 Co-investigator
"Genomic and functional study of rare deleterious germline mutations in candidate genes associated with familial risk for esophageal carcinoma"

GRF research grant 1/2019-12/2022 $956,853 Co-investigator
"Genomic and functional study by targeting MST1R and its related chromosome 3p21.3 regions associated with genetic susceptibility in NPC"

Mass Transit Railway Corporation
service contract 1995-2008 $3,402,582 project manager
"Total viable counts and *Legionella* testing at MTR cooling towers"

Platform Technology Funding
"Establishing platform technology for use of circulating tumor cells for cancer diagnostics & drug testing" $1,000,000 2017-2019

Central Allocation/Collaborative Research Fund Group Research Grant
research grant 2000-2002 $3,500,000 Principal investigator
"Cooperative Nasopharyngeal Carcinoma Research Center"

research grant 2004-2007 $2,400,000 Principal investigator
"Cooperative Nasopharyngeal Carcinoma Research Center"

research grant 2007-2010 $5,200,000 Principal investigator
"Esophageal Carcinoma Research Center"

research grant 2016-2019 $7,570,304 Principal investigator
"Targeted Genomics and Functional Studies of Novel Cancer Predisposing Genes for Esophageal Squamous Cell Carcinoma"

Area of Excellence Group Research Grant
Research grant 2010-2018 $80,000,000 Project coordinator
"Center for Nasopharyngeal Carcinoma Research"

Theme-based Research Group Grant
Research grant 2017-2021 $33,330,000 Project coordinator
"Translational studies for elucidating the tumor heterogeneity and molecular evolution in metastatic gastrointestinal tract cancers for personalized medicine"

Advanced Studies Institute: Croucher Foundation
Grant 2000-2001 $592,000 ASI Director
"Molecular Genetic Basis of Cancer"
"Functional Genomics in Cancer Research"

Grant 2005-2006 $591,000 ASI Co-Director
"Epstein-Barr Virus and Nasopharyngeal Carcinoma"
"Viruses and Cancer"

Grant 2010-2011 $600,000 ASI Co-Director
"Molecular genetics and clinical advances in the study of esophageal and gastric cancers"

Grant 2014-2015 $600,000 ASI Director
"Advances in Nasopharyngeal Carcinoma Studies"
"Advances in Cancer Genomics, Cell Signaling, and Translational Studies"

Asian Cancer Research Fund
Research grant 2013-2015 $800,000, Principal investigator
Research grant 2014-2015 $345,000
"Genomic studies of esophageal squamous cell carcinoma familial genetic susceptibility and diagnostic biomarkers"

Hong Kong Cancer Fund
Research grant 2013-2015 $2,155,000 Principal Investigator
"Genetic studies of NPC"

Health Medical Research Fund
Research grant 2013-2015 $1,000,000 Principal Investigator
"Elucidating the genetic basis for early-age onset NPC in Hong Kong"

Research grant 2013-2015 $785,624 Co-investigator
"The SAA1 polymorphism vs risk factors in ESCC"

Research grant 2015-2017 $1,000,000 Co-investigator
"The effects of IKKbeta-specific inhibitor PS1145 on tumor formation and metastasis in NPC"

Research grant 2015-2017 $997,845 Co-investigator
"The clinical relevance of telomere attrition and NPC genetic susceptibility"

Research grant 2017-2019 $946,064 Co-investigator
"Optimizing the selection of patients with metastatic colorectal cancer for liver resection - An immuno-clinical scoring system incorporating circulating tumor cell enumeration and clinical factors"

Research grant 2018-2020 $1,199,732 Principal Investigator
"Clinical application of enumeration and genomic characterization for non-invasive detection and real-time monitoring of circulating tumor cells for esophageal carcinoma"

Gordon Research Conference (2016, alternative years)
NPC Research Conference, Chair
$19,125 USD

Technology Start-up Support Scheme for Universities
OncoSeek $650,000 Dec 2014-Mar 2015
$300,000 April 2015-Mar 2016

Hong Kong Science Park Incubator program ***2015-7***
OncoSeek $860,000

Innovation and Technology Commission
Corporate Sponsor: Lee's Pharmaceutical (HK) Ltd.
"Regulation and clinical implication of PD-L1 expression in esophageal tumor cells subjected to chemotherapy" $2,598,540 2015-2017

SK Yee Medical Foundation HK$$956,000 2018
"Non-invasive real-time monitoring and next-generation sequencing of circulating tumor cells for improved personalized treatment of metastatic colorectal cancer patients"

Graduated Postgraduate Students at HKUST (1991-2009)
Master of Philosophy degree (10) and Doctor of Philosophy degree (6)

Graduated Postgraduate Students at HKU (2009- now)
Master of Philosophy degree (5) and Doctor of Philosophy degree (14)

Sep 21, 2018