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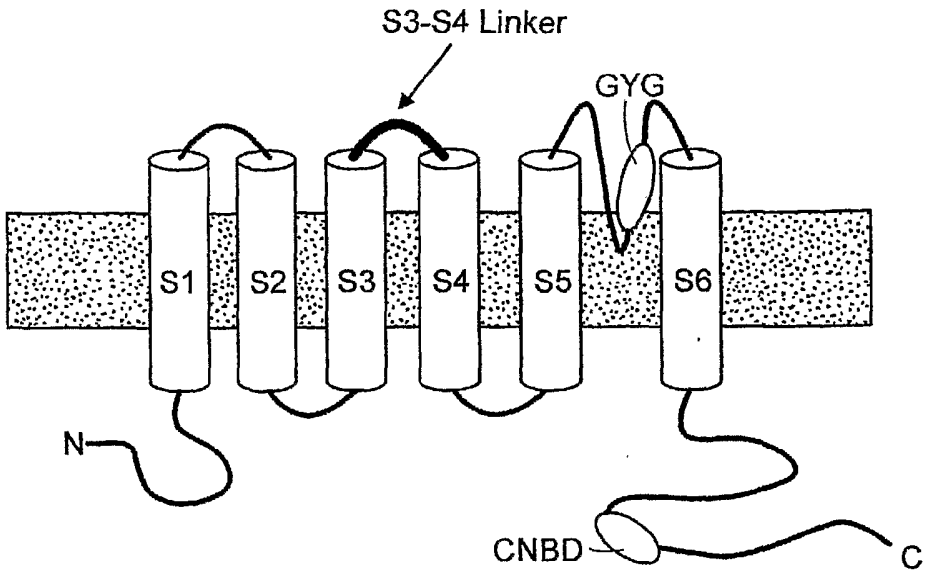
[Continued on next page]

(54) Title: MODULATION OF BIO-ELECTRICAL RHYTHMS VIA A NOVEL ENGINEERING APPROACH



(57) Abstract: The present invention relates to novel compositions and methods to induce , and/or' modulate bio-electrical rhythms (e.g. in cardiac, neuronal and pancreatic cells) by fine-tuning the activity of HCN-encoded pacemaker channels via a novel protein- and genetic-engineering approach to augment or attenuate the associated physiological responses (e.g. heart beat, neuronal firing, insulin secretion, etc) for achieving various therapeutic purposes (e.g. sick sinus syndrome, epilepsy, neuropathic pain, diabetes, etc).

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International application No.
PCT/US05/27549

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A01N 63/00**(2006.01);**A61K 31/711**(2006.01);**C12N 15/63**(2006.01),**15/85**(2006.01),**15/87**(2006.01)

USPC: 424/93.1;514/44;435/455
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/93.1; 514/44; 435/455

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
US-PGPUB; USPAT; EPO; JPO; DERWENT; Medline, Embase, Biosis, Caplus

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Qu, J. et al., "Expression and Function of a Biological Pacemaker in Canine Heart", Circulation, 04 March 2003, Vol. 107: pp. 1106-1109	1, 3, 6, 8, 10, 11, 17, 18, 21, 27, 28 --- 15, 16
X --- Y	Qu, J. et al., "HCN2 Overexpression in Newborn and Adult Ventricular Myocytes", 2001, Circ. Res., Vol. 89: pp. e8-e14.	1, 3, 6, 8, 10, 11 --- 15, 16
X --- Y	Potapova, I., et al., "Human Mesenchymal Stem Cells as a Gene Delivery System to Create Cardiac Pacemakers", Feb 26 2004, Circ. Res., Vol . 94: pp. 952-959	1, 2, 6, 8, 10, 17, 21, 22, 27, 28, 33, 34, --- 15, 16

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Plotnikov, A., et al., "Biological Pacemaker Implanted in Canine Left Bundle Branch Provides Ventricular Escape Rhythms That Have Physiologically Acceptable Rates", Jan 20 2004, Circ. Res., Vol. 109: pp. 506-512.	1, 3, 6, 8, 10, 11, 17, 18, 21, 27, 28 --- 15, 16
X, P	WO 2005/062958 (MEDTRONIC) 14 July 2005, see entire document	1-4, 6, 8, 10-12, 15--19, 21-24, 26-28, 33, 34
A	Accili, E., et al., "From Funny Current to HCN Channles: 20 Years of Excitation", 2002, News Physiol. Sci., Vol. 17: pp. 32-37	1-38