Co-organized by

Department of Anaesthesiology
The University of Hong Kong

The Hong Kong Pain Society

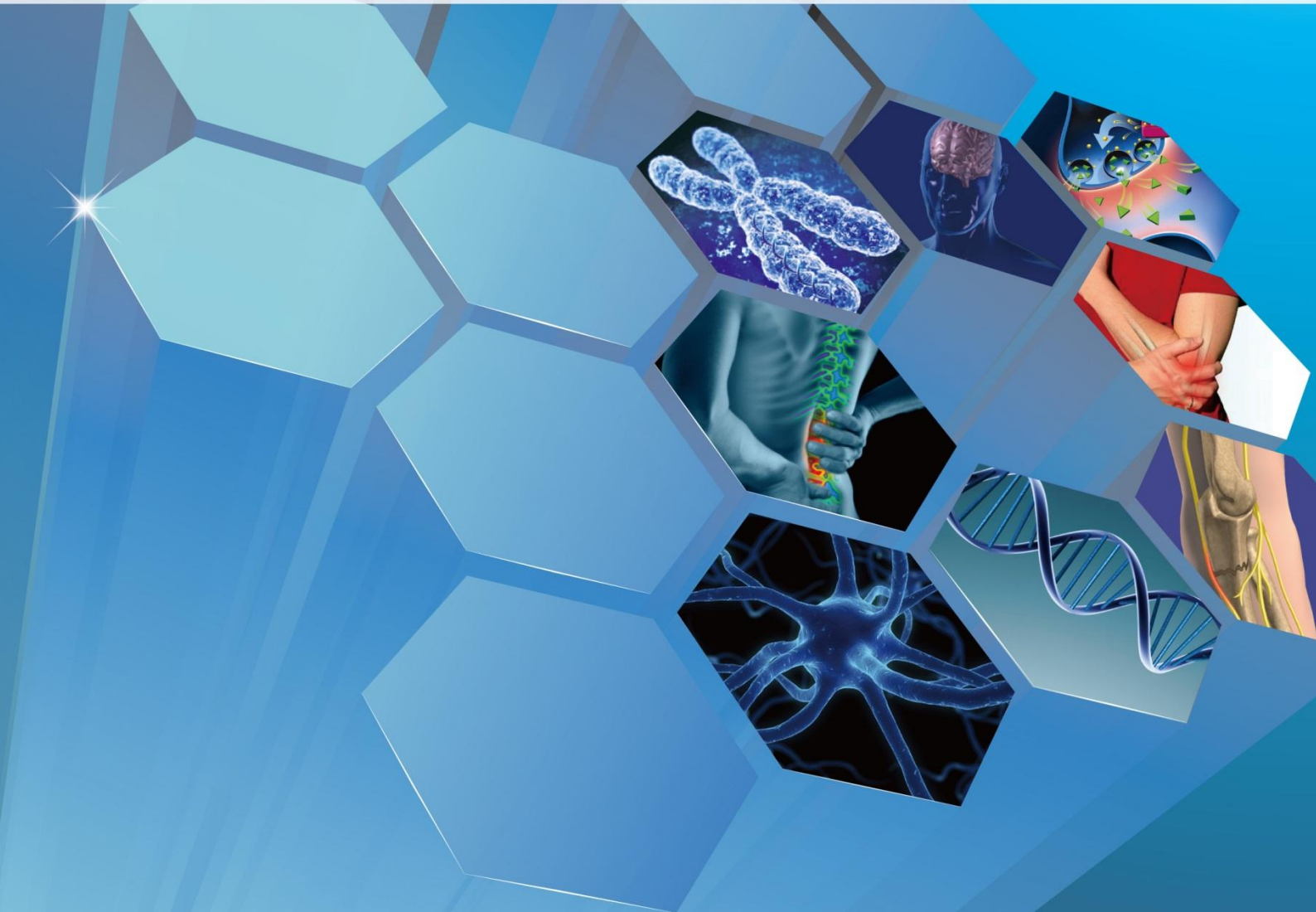
Pain Genetics Symposium

From Basic Science to Clinical Applications

9 June 2012, Saturday (09:00-18:00)

William MW Mong Block, Li Ka Shing Faculty of Medicine, The University of Hong Kong
21 Sassoon Road, Pokfulam, Hong Kong

Chairpersons: Dr Dino SAMARTZIS & Dr Steven WONG



Program Book

ADVANCING HEALTH FOR 125 YEARS

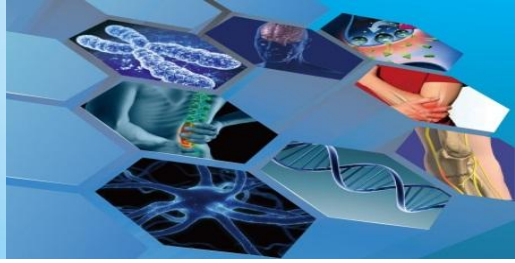
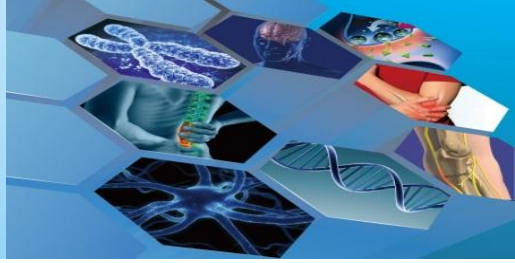


Table of Contents



Welcome Message

Dear Friends,

Pain is a complex and multi-dimensional process. There is increasing evidence to suggest that pain may have a genetic predisposition. Understanding the genetics of pain will broaden our knowledge of pain development, treatment, and outcomes; therefore, leading to more personalized medical care and better quality of life.

The **Pain Genetics Symposium: from Basic Science to Clinical Applications** is the first of its kind in Asia. The symposium will bring together a multidisciplinary faculty of scientists and clinicians to discuss pain, genetic tools/designs and analyses, pain genes, and the clinical applications of pain genetics. This event will endeavor to bridge collaborations, and establish a common language between basic scientists and clinicians that will further broaden research and applications of pain genetics.

Equally important during this event, we will commemorate the start of the **Laboratory and Clinical Research Institute for Pain** at the University of Hong Kong. Such an institute is the first of its kind in Hong Kong and in our region in Asia. This institute will consist of a multidisciplinary group of pain specialists with the focus of addressing novel treatment, preventative measures, and prognostic methods to address and alleviate pain in our society.

We would like to sincerely thank our organizing committee, our sponsors, and invited speakers/moderators for their time and support of this symposium. More importantly, we want to thank - you! Without your involvement and continued interest in pain, this event would not have been made possible.

Sincerely,

Dr. Dino SAMARTZIS
Co-chairperson

Dr. Steven Ho-Shan WONG
Co-chairperson

Organizing Committee

Chairpersons

Dr. Dino SAMARTZIS
The University of Hong Kong

Dr. Steven Ho-Shan WONG
The Hong Kong Pain Society

Members

Dr. Danny CHAN
The University of Hong Kong

Dr. Gladys CHEING
The Hong Kong Pain Society

Dr. Chi-Wai CHEUNG
The University of Hong Kong

Ms Mary Man-Lai CHU
The Hong Kong Pain Society

Dr. Victor HUNG
The University of Hong Kong

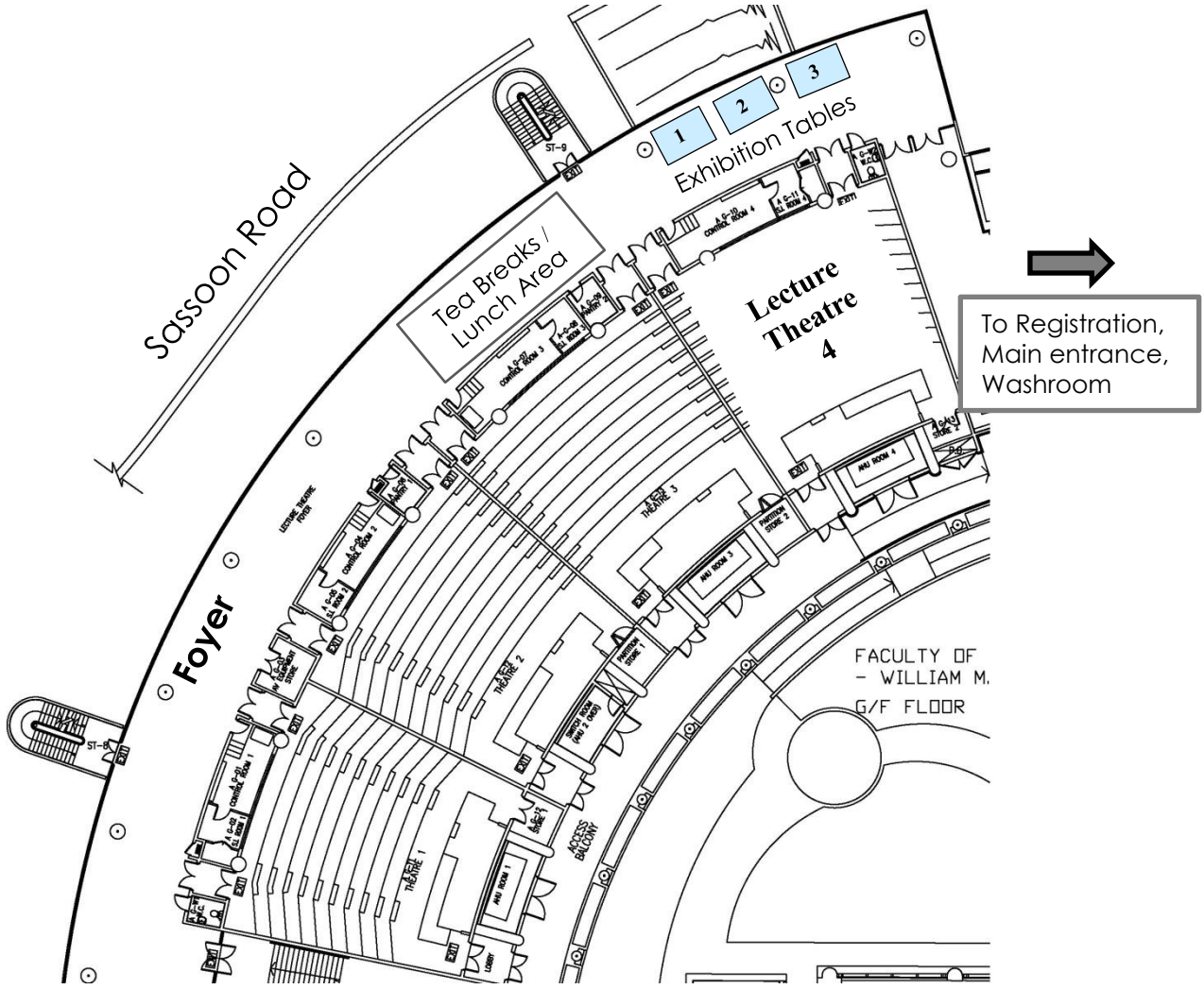
Prof. Michael G. IRWIN
The University of Hong Kong

Ms Yvonne LEE
The University of Hong Kong

Ms Joyce NG
The University of Hong Kong

Dr. Kam-Hung WONG
The Hong Kong Pain Society

Meeting Venue & Exhibition

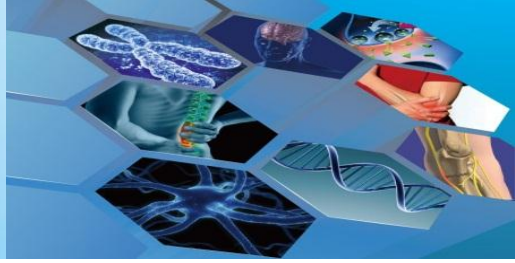


G/F, Cheung Kung Hai Conference Centre, William MW Mong Block

- Lecture Theatre 4: Main meeting room
- Foyer: Exhibition tables, tea breaks and lunch area

Exhibition Tables

Table No.	Company
1	Eli Lilly Asia, Inc.
2	Janssen Hong Kong
3	Pfizer Corporation Hong Kong Ltd.



Symposium Information

Symposium venue
Lecture Theatre 4, Cheung Kung Hai Conference Centre
William MW Mong Block, Li Ka Shing Faculty of Medicine
The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong

Minibus, taxi and other kinds of public transport are readily available to get to the HKU Medical Campus.

Language
English is the official language of the Symposium.

Registration and information
Symposium registration starts on Saturday, 9-June 2012 at 08:30-17:00. Upon arrival, please approach the Registration counter located at Ground Floor, William MW Mong Block, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, to collect your name badge and conference materials.

Tea breaks
Coffee and tea will be served at the Foyer of the Lecture Theatre 4 at designated times.

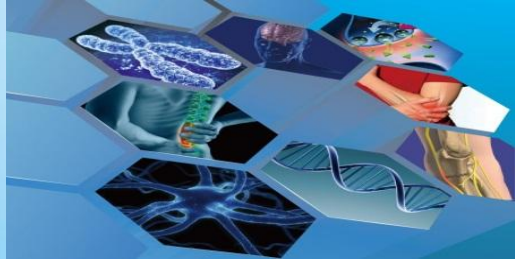
Lunch
Sandwich lunch box will be provided at the Foyer of the Lecture Theatre 4 at designated time.

Identification badge
All participants will receive an identification badge upon registration. Please wear your name badge at all times during the Symposium for identification purpose and admission.

Internet service
Free wifi is available within the Conference Centre.

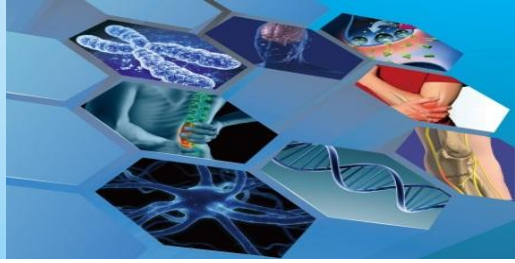
Mobile telephones / pagers
Please ensure that you switch off all mobile telephones and pagers during lectures.

Video-taping and photo-taking
Please note video and audio taping as well as photographs of the presentations during the Symposium is not allowed.



Programme

Time	Programme
08:30-17:00	Registration
09:00-09:30	**Opening Ceremony**
	Greetings **Prof. Sum-Ping LEE,** Dean, Li Ka Shing Faculty of Medicine, The University of Hong Kong **Prof. Ying-Shing CHAN**, Department of Physiology, The University of Hong Kong
	Welcome Address & Global Burden of Pain **Dr. Dino SAMARTZIS** Department of Orthopaedics & Traumatology, The University of Hong Kong **Dr. Steven WONG**, Department of Anaesthesiology, Queen Elizabeth Hospital
	Introduction of the Laboratory and Clinical Research Institute for Pain, The University of Hong Kong **Dr. Chi-Wai CHEUNG**, Department of Anaesthesiology, The University of Hong Kong
Session 1: Pain Mechanisms, Assessment and Treatment Moderator: **Prof. Michael IRWIN** Department of Anaesthesiology, The University of Hong Kong	
09:30-09:50	**Cortical Plasticity in Chronic Visceral Pain Pathogenesis** **Prof. Ying LI,** Department of Biology and Chemistry, The City University of Hong Kong
09:50-10:10	**Pain: Nature VS. Nurture** **Prof. Peter LEE**, Department of Psychiatry, The University of Hong Kong
10:10-10:30	**Hidden Facts about Pain Assessment** **Dr. Gladys CHEING** Department of Rehabilitation Sciences, The Hong Kong Polytechnic University
10:30-10:50	**Pharmacotherapy for Pain** **Dr. Steven WONG**, Department of Anaesthesiology, Queen Elizabeth Hospital
10:50-11:00	Discussion
11:00-11:20	Tea Break



	Session 2: Genetics Moderator**: Prof. Pak SHAM,** Department of Psychiatry, The University of Hong Kong
11:20-11:40	**Genes and Diseases: Basic Concepts** **Dr. Danny CHAN**, Department of Biochemistry, The University of Hong Kong
11:40-12:00	**Genetic Approaches to Complex Phenotypes** **Prof. Pak SHAM**, Department of Psychiatry, The University of Hong Kong
12:00-12:20	**Mouse as a Model for Functional Genetic Studies** **Prof. Kathy CHEAH**, Department of Biochemistry, The University of Hong Kong
12:20-12:40	**Molecular Basis for Painful and Painless Neuropathy** **Prof. Sookja CHUNG**, Department of Anatomy, The University of Hong Kong
12:40-12:50	Discussion
12:50-13:50	Lunch Break
13:50-14:30	**Keynote Lecture** **Pain Genetics: Past, Present, and Future** **Dr. Inna BELFER,** Department of Anesthesiology, The University of Pittsburgh, USA
	Discussion
	Session 3: Pain Genes and Clinical Applications Moderator**: Prof. Kenneth CHEUNG** Department of Orthopaedics and Traumatology, The University of Hong Kong
14:30-15:10	**Keynote Lecture** **Labor Pain Model: from Mice to Human** **Prof. Pamela Dru FLOOD,** Department of Anesthesia/Perioperative Care, UCSF, USA
	Discussion
15:10-15:30	Tea Break
15:30-15:50	**Postsurgical Chronic Pain** **Dr. Chi-Wai CHEUNG**, Department of Anaesthesiology, The University of Hong Kong
15:50-16:10	**Paroxysmal Extreme Pain Disorder** **Dr. Edmond CHUNG**, Department of Anaesthesiology, Queen Elizabeth Hospital
16:10-16:30	**Spine Disorders, Pain Genes, and Personalized Medicine** **Dr. Dino SAMARTZIS** Department of Orthopaedics & Traumatology, The University of Hong Kong
16:30-16:50	**Pharmacogenetics: Opioids & Personalized Health-Care** **Prof. Michael IRWIN,** Department of Anaesthesiology, The University of Hong Kong
16:50-17:00	Discussion & Closing Remarks

Special Guests

Prof. Sum-Ping LEE

Professor and Dean
Li Ka Shing Faculty of Medicine
The University of Hong Kong

Prof. Ying-Shing CHAN

Professor
Department of Physiology
The University of Hong Kong

Keynote Speaker

Pain Genetics: Past, Present, and Future

Dr. Inna BELFER
Associate Professor of Anesthesiology & Human Genetics
Department of Anesthesiology
The University of Pittsburgh, USA

Dr. Belfer has started her career as a licensed clinical neurologist, and then got extensive training in neurobiology and human genetics. She has appointments in Anesthesiology and Human Genetics at the University of Pittsburgh, and leads the Molecular Epidemiology of Pain Program at Pittsburgh Center for Pain Research. Since 2001, her primary interest has been the relationship between the genotypes and complex phenotypes such as pain, psychiatric disorders, and addictions. Her research focuses on biobehavioral aspects of acute and chronic pain, phenomics of human pain and genetic association studies in human pain cohorts. Specifically, she studies the transformation of acute pain into chronic condition and genetic factors contributing to this process. More recently, her program focuses on the effect of genotype on the neurobiology of primary afferent neurons in human dorsal root ganglia using a combination of molecular techniques on post-mortem nerve tissues from organ donors. Dr. Belfer collaborates with over 15 research groups around the world establishing new standards in clinical pain data collection and genetic approaches for clinical research in human pain.

Abstract

An estimated 15-50% of the population experiences pain at any given time, at great personal and societal cost. Pain is the most common reason patients seek medical attention, and there is a high degree of individual variability in reporting the incidence and severity of symptoms. Research suggests that pain sensitivity and risk for chronic pain are complex heritable traits of polygenic origin. Animal studies and candidate gene testing in humans have provided some progress in understanding the heritability of pain, but the application of the genome-wide association methodology offers a new tool for further elucidating the genetic contributions to normal pain responding and pain in clinical populations. Although the determination of the genetics of pain is still in its infancy, it is clear that a number of genes play a critical role in determining pain sensitivity or susceptibility to chronic pain. The talk will provide an update of the latest findings that associate genetic variation with variability in human pain and an overview of the candidate gene studies with the highest translational potential.

Keynote Speaker

Labor Pain Model: from Mice to Human

Prof. Pamela Dru FLOOD
Professor
Department of Anesthesia / Perioperative Care
University of California at San Francisco (UCSF), USA

Prof. Flood graduated from medical school and trained in anesthesia at Columbia University, New York. She has a Master's degree in Neurobiology from Columbia University. She spent the majority of her career as a faculty member in the division of Obstetric Anesthesia at Columbia University until July 2011 when she began her current position as Professor of Anesthesia and Perioperative Care and Professor of Obstetrics, Gynecology and Reproductive Sciences at UCSF. She is the Director of Obstetric Anesthesia and of the Obstetric Anesthesia fellowship program at UCSF. Prof. Flood's translational research program is focused on pain and analgesia ranging from molecular pharmacology of novel analgesic drugs in model systems and animals to clinical trials of novel analgesic treatments. Her current research program is directed toward understanding patient level variability in labor and post-operative pain and in the progress of labor. She has recently identified linked demographic and genetic variables that are predictive of differences in labor pain and progress.

Abstract

The process of labor is highly variable among women. There is variability in the progress of labor and in the experience of pain. Familial aggregation analysis and studies of twins have concluded that the time course of labor and the likelihood of failure of vaginal delivery is heritable. There are polymorphic areas in the oxytocin receptor beta-2-adrenergic receptor that may be responsible for at least some portion of the variability in labor progress. Multiple genetic polymorphisms have been identified that are predictive of differences in baseline sensitivity to pain. Some of these including polymorphisms in the beta-2-adernergic receptor and the COMT gene are predictive of labor pain. Since the beta-2-adrenergic responds to intrinsic catecholamines and COMT is important for catecholamine metabolism, adrenergic activity appears to be important in the expression of labour pain.

Cortical Plasticity in Chronic Visceral Pain Pathogenesis

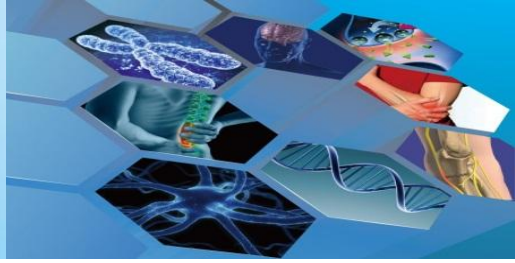
Prof. Ying LI

Professor Neuroscience Laboratory
Department of Biology and Chemistry
The City University of Hong Kong

Prof. Li was educated in Beijing medical University (1962 – 1968). He was a general surgeon at the Qinghai, and oral-maxillofacial surgeon at Nanjing Medical School, China. He completed post-doctoral fellowship in department of internal medicine Hypertension, University Michigan, and then joined Gastroenterology at the University of Michigan, where he was appointed Assistant Research Scientist in 1997, and Research Professor in 2002. Prof. Li joined Department Biology and Chemistry City University of Hong Kong in December 2009. Prof. Li is also a Fellow of the American Gastroenterological Association, Member of the American Pancreatic, Gastroenterological, Neurogastroenterology & Motility, and Physiology Association, serves on the scientific grant review board of the Health and Health Services Research Fund of Hong Kong, and is an Honorary Professor at the Faculty of Dentistry and the University of Hong Kong.

Abstract

Human brain imaging studies demonstrated the importance of cortical neuronal networks in the perception of pain in chronic pain disorders. We demonstrated that persistence of a heightened visceral afferent nociceptive input to the anterior cingulate cortex (ACC) induces ACC sensitization. The ACC plays a critical role in the modulation of pain responses in viscerally hypersensitive (VH) rats. This process appears to be mediated by enhanced activities of NR2B glutamate receptors. Further, VH together with ACC sensitization persisted for 2 months even though colonic mucosal inflammation has subsided within the first week suggesting neuroplasticity changes are responsible for pain memories in VH state.
ACC field potentials elicited by electrical stimulation of the medial thalamic nuclei were used as a quantitative measure of synaptic strength. We showed enhancement of basal synaptic transmission within the ACC. Theta burst stimulation was used to induce long-term potentiation (LTP), we identified the induction and enhancement of LTP in the ACC synapses occurred, which appear to be an important mechanism for learning and triggering of pain memories in the VH states.



Pain contains both sensory and affective dimensions, we measured a learned behavior that directly reflects the affective component of pain (conditioned place aversion) in rats, and show that ACC activation is critical for the memory processing involved in long-term negative affective state and prediction of aversive stimuli by contextual cue.

In vivo electroporation of CaMKII siRNA produced inhibition of colorectal distension-induced pain response. Western blotting following co-immunoprecipitation showed that phosphorylation of CaMKII at Thr286, which binds to NR2B is required for NR2B stabilization at post-synaptic site, and modulates visceral pain.

Pain: Nature VS. Nurture

Prof. Peter W. H. LEE
Hon. Professor
Department of Psychiatry
The University of Hong Kong and Hong Kong Sanatorium & Hospital

Prof. Lee has been involved with academics for over 30 years. After obtaining his undergraduate and graduate education at the University of Hong Kong, he went on to become honorary Professor in the Department of Psychiatry at the University of Hong Kong and Adjunct Professor in the Department of Psychology at the Chinese University of Hong Kong. He is the Director of the Clinical Health Psychology Centre of the Hong Kong Sanatorium & Hospital. With over 100 publications, Prof. Lee continues to maintain clinical and research interests in various psychological domains, all striving to improve patient quality of life.

Abstract

There is no doubt that subjective felt pain and pain related behaviours, feelings, perceptions and outcomes are complex and of multi-aetiological origins. In appreciating the broad meanings and implications of pain, instead of considering nature “vs.” nurture, it seems more appropriate and clinically realistic, to consider nature “AND” nurture. Ample evidence points to the “nature and nurture” interactions being potentially present right from the early days of birth. Experimental animal studies of neonatal stress have implicated a clear pronociceptive effects of early life stress, e.g. demonstrating muscle hyperalgesia and nociceptive sensitization in adult rats exposed to neonatal limited bedding paradigm. In human pain responses, male-female differences highlight the intricate interconnectedness between nature and nurture factors. The presentation will review representative conceptions relevant to understanding the influences of nature and nurture, from “discordance” in pain presentations to the more clinically relevant parameters including (but not limiting to) neuroticism, fear avoidance, pain catastrophising, and kinesiophobia. Implications for better management and coping with chronic pain based on understanding of nature and nurture factors will also be discussed.

Hidden Facts about Pain Assessment

Dr. Gladys CHEING
Associate Professor
Department of Rehabilitation Sciences
The Hong Kong Polytechnic University

Dr. Cheing received her education in Hong Kong and Canada. She now works as Associate Professor at The Hong Kong Polytechnic University. Dr. Cheing is keen in teaching and obtained Outstanding Teaching award from Department of Rehabilitation Sciences, PolyU in 2006. She is an active researcher and her main research area is on pain management. She also conducts studies to evaluate the influence of psychosocial factors on the management of chronic pain. In recent years, Dr. Cheing has received major research grants that apply new technology in the assessment and management of peripheral diabetic neuropathy. Also, she examines the efficacy of electrophysical therapy in managing diabetic ulcer.

Dr. Cheing has published over 50 papers in high impact scientific journals. She serves on the editorial board of Journal of Orthopaedics & Sports Physical Therapy and The International Journal of Therapy and Rehabilitation. She is now the Vice President of the Hong Kong Pain Society and The Hong Kong College of Physiotherapy.

Abstract

Pain is a complex experience that composed of multiple dimensions. An accurate assessment of the pain experienced by a patient is essential for making the diagnosis, determining the appropriate intervention, and evaluating the effectiveness of treatment.

Simple pain rating scales are commonly used in clinical setting, but it has limited role in registering a multi-dimensional experience. Multi-item instruments are often used in clinical research, but they are lengthy and time-consuming to use. The selection of pain assessment instruments should consider the issues of validity, reliability, and responsiveness to change. Validity refers to the fact that the measurement made by the instrument should be comparable to that made by the gold standard, which truly reflect the level of pain and hopefully the contents could cover the multi-dimensional components of pain. Inter-rater reliability represents the repeatability of results performed by various assessors using the same instrument. High level of reliability depends on careful instructions and standardized

procedures of assessment. Responsiveness to change represents that the instrument should be sensitive enough to detect small differences made after an intervention.

To document the treatment efficacy, clinicians may request patients to recall their pain level experienced in the past (e.g. immediately after the injury), and patients' reports of pain relief after receiving an intervention. They assume that the extent of pain relief can be derived by calculating the difference made between the pretreatment pain and the present pain level. However, various factors may interfere with the accuracy of the recall of subjective pain, which may potentially lead to recall bias. We need to acknowledge the contribution of recall bias in clinical management of pain.

Various studies have reported that there are discrepancies in patients' self report of pain versus clinician's judgments after delivering certain intervention. We may acknowledge that the findings in subjective report of pain can be different from that obtained from objective clinical assessment of pain conditions. Overall, there is no single comprehensive method available to assess pain. The context of pain assessment may vary considerably from clinical to research use, and it may vary for measuring acute or chronic pain.

This presentation will provide an overview of the pros and cons of adopting various pain assessment instruments. The criteria of adopting an appropriate assessment instrument of pain in clinical practice will also be discussed.

Pharmacotherapy for Pain

Dr. Steven WONG
Consultant
Department of Anaesthesiology
Queen Elizabeth Hospital

Dr. Wong is the Consultant Anaesthesiologist of the Department of Anaesthesiology, Queen Elizabeth Hospital. Dr. Wong graduated from the University of Hong Kong, and has attained the Fellowships of the Hong Kong College of Anaesthesiologists, Australian and New Zealand College of Anaesthetists and the Hong Kong Academy of Medicine (Anaesthesiology); as well as the Diploma in Pain Management of the Hong Kong College of Anaesthesiologists. His main clinical interest lies in management of pain and in particular interventional pain management. He is the Head of the Pain Management Team of Queen Elizabeth Hospital. He is the Chairman of Board of Pain Medicine of the Hong Kong College of Anaesthesiologists. He is the Immediate Past President of the Society of Anaesthetists of Hong Kong and is currently the President of the Hong Kong Pain Society.

Abstract

Effective pharmacotherapy for pain cannot be achieved without a good understanding of the mechanisms and neurophysiology of pain. It is now known that pain circuitry consists not only a peripheral system with wide spread distribution of nociceptors in the body responding to actual or potential tissue damage by release of an inflammatory soup of chemical agents, but also a central system with neural pathways and foci in the brain and spinal cord that is responsible for further processing and modulation of the pain signals. The phenomenon of sensitization occurs in both peripheral and central neural pathways and results in the development of persistent pain states.

The final perception of pain is a subjective experience that is unique to the individual biological setup which is genetically determined, under the influence of the emotional state of the individual, and in turn interacts with the environment in a number of ways. This is the now widely accepted bio-psycho-social model of pain. Thus, pharmacotherapy only forms a part of the total person management of pain. Nevertheless, targeting of pharmacological agents against specific mechanisms of nociception can be very effective in temporary relief of suffering, as well as prevention of development of chronic pain states.

Genes and Diseases: Basic Concepts

Dr. Danny CHAN
Associate Professor
Department of Biochemistry
The University of Hong Kong

After graduating from the University of Melbourne with a Bachelor of Science (with honours), Master of Science and a PhD, Dr. Chan continued research at his alma mater on heritable skeletal disorders with a focus on extracellular matrix proteins. His research contributed significantly to the understanding of the molecular consequences in many forms of the human osteochondrodysplasias. In recognition, he was presented with an award for "Excellence in Medical Research" by the State Premier of Victoria, Australia. He joined the University of Hong Kong in 1998, maintaining his research in skeletal biology using mouse as a model to address disease mechanisms in vivo, as well as human genetic studies to define genetic risk factors for common degenerative skeletal conditions such as intervertebral disc degeneration. Key findings in his laboratory included the consequence of cellular stress in chondrocytes allowing matured chondrocytes to be "rejuvenated", and how the capacity and range of a signaling molecule, Indian hedgehog, are regulated in development, published in PLoS Biology and Nature, respectively. Recently, he published in the Am. J. Human Genetics a significant discovery of a genetic risk factor for intervertebral disc degeneration and osteoarthritis that regulates TGF signaling, providing the potential of a new therapeutic target and preventive strategies. In 2010, he received a Research Output Prize from the University of Hong Kong.

Abstract

Genetics is an area connecting genes with functions, variations with phenotypes; and of most interest to scientists and clinicians, mutations with diseases. According to the Online Mendelian Inheritance in Man (OMIM), an online catalog for human genes and Mendelian disorders, over 3,000 known "genotype-phenotype" pairs have been recorded. A direct application of such knowledge is diagnosis, of which prenatal testing and newborn screening of rare conditions are common nowadays; but would ideally be extended in future for disease prevention or the development of personalized medicine. It is clear that our understanding of disease mechanism of rare disorders have come directly from knowing the genes involved, allowing detailed in vitro and in vivo functional studies. While it will be more difficult for common disorders such as intervertebral disc (IVD) degeneration and back pain, the same principle can be applied bearing in mind of the effect size, the number of genes involved and the contribution from environmental factors. These are some of the issues that will addressed, to provide the basic concepts of what genetic studies can achieved, and the road map for future studies in specific areas such as pain.

Genetic Approaches to Complex Phenotypes

Prof. Pak SHAM
Chair Professor
Department of Psychiatry
The University of Hong Kong

Prof. Sham is currently Chair Professor of Psychiatric Genomics, Head of the Department of Psychiatry, and Acting Director of the Centre of Genomics Sciences, the University of Hong Kong. He attended Cambridge and Oxford Universities, and trained in Psychiatry at the Northwick Park and Shenley Hospitals, and the Bethlem Royal and Maudsley Hospitals, UK. After being awarded a Wellcome Trust Training Fellowship (1990), he obtained an MSc in Applied Statistics from Birkbeck College London (1991) and visited the Virginia Commonwealth University, USA (1992). He was appointed Professor of Psychiatric & Statistical Genetics (2000-06) at Institute of Psychiatry, King's College London. Prof. Sham's research interests include the genetics and epidemiology of psychiatric disorders, and the statistical methodology for genetic and epidemiological studies. Prof. Sham is the author "Statistics in Human Genetics" published by Arnold, and an editor of "Analysis of Multifactorial Disease" (2000) published by Bios. Prof. Sham has also published over 400 articles in peer-reviewed journals.

Abstract

This talk will give a general overview of genetic approaches to complex phenotypes, including family studies, twin studies, linkage studies and association studies. The statistical methodologies involved, and the impact of recent developments in genomic technologies, will be discussed.

Mouse as a Model for Functional Genetic Studies

Prof. Kathy CHEAH
Chair Professor
Department of Biochemistry
The University of Hong Kong

Prof. Cheah is Chair Professor of Biochemistry at The University of Hong Kong and an expert on understanding gene regulation and function and how mutations cause disease, with an emphasis on the skeletal system and the inner ear. She has contributed insights into the regulation and function of genes in vivo and the molecular pathogenesis of disease by generating transgenic mice and mouse models and by studying human degenerative skeletal disorders especially degenerative intervertebral disk disease (DDD). She is the Director of an Hong Kong University Grants Council Area of Excellence Programme "Developmental Genomics & Skeletal Disease' an 8 year multidisciplinary programme involving scientists and clinicians combining molecular, biochemical, cellular, developmental and in vivo models with genomic, genetic and clinical studies, to address key issues in skeletal biology. In the area of public service, she served on the Biology and Medicine Panel of the Research Grants Council of Hong Kong for 6 years. She is the founding President of Hong Kong Society for Developmental Biology and was the President of the International Society for Matrix Biology 2006-2008. She actively promotes public understanding of science in the region. (2000/2001)

Abstract

With the availability of complete genome sequence information for many individual humans comes the challenge of interpreting the functional impact of genetic variations detected. The mouse has long been a favorite model for functional genomic studies and is commonly used for preclinical studies in drug development. I will illustrate the power of genetic manipulation of mice to understand gene function, discover disease genes and to create models of human disease. The advantages and limitations of such models will be discussed.

Molecular Basis for Painful and Painless Neuropathy

Prof. Sookja Kim CHUNG
Professor
Department of Anatomy
The University of Hong Kong

Prof. Chung received her doctoral degree under the supervisions of Prof. Rochelle Cohen at the University of Illinois at Chicago, Chicago, IL and Prof. Donald Pfaff at The Rockefeller University, where she worked on estrogen and the mechanisms underlying rodent female reproductive behavior. She was the first to show the estrogen-induced changes in postsynaptic density parameters related to plasticity, which has far-reaching implications even beyond mechanisms related to female reproduction, including memory and learning. After her graduate work, she joined Prof. Kevin McKenna's laboratory at Northwestern University Feinberg School of Medicine as a NIH Postdoctoral Fellow and published the first report on the sexual reflex in animal model, which was reported in Science section of New York Times. After her postdoctoral fellowship at Northwestern, she joined Prof. Donald W. Pfaff, Laboratory of Neurobiology and Behavior The Rockefeller University, New York, NY as the Winston Foundation Fellow. Here, she was one of the first to apply molecular biology to brain areas key to female reproductive behavior and also was trained to generate genetically engineered animals. Then, she joined Institute of Molecular Biology at The University of Hong Kong in March, 1991, and also served as an honorary lecturer and Associate Professor until she transferred to Department of Anatomy in 2006 as a full Professor. She is also Visiting Professor at the Fourth Military Medical University at Xian, China. She has generated numerous conventional and conditional transgenic and knockout mice to understand the pathogenesis of human diseases in order to search for novel diagnostic tools and effective treatments. She has the international reputation in the research area of diabetes and its complications including painless and painful neuropathy, retinopathy, cataract, nephropathy, and stroke.

She has secured numerous grants as Principal or Co-investigator (total of 88 grants: 49 as PI and 39 as co-I). She has also been involved in several group projects, such as RGC Central Allocation Grants, and Area of Excellence Program for Basic Neuroscience and drug discovery for Parkinson's disease, stroke, Alzheimer's disease and depression from the Chinese Medicine and synthetic chemicals. She also has been participating in Applied

Research to discover potential drugs by contracting research grants from Biotech companies, such as Pfizer, USA; Sanwa, Japan; Hybrigenic, France/HKU; TA Therapeutic Ltd. (a joint venture between Geron Corporation, U.S.A. and Biotechnology Research Corporation, HKUST); Merck & Co.

Abstract

Mouse genome has been manipulated to understand the pathogenesis of human diseases by employing the state-of-art technology, i.e., conventional, conditional and inducible transgenic and knockout mouse technology. The genetically manipulated mouse models are powerful reagents for understanding the genes' function and their role in complex disease processes. We have been focusing on the function of genes that are involved in hypoxic/ischemic, osmotic and oxidative stress and their dysfunctions in the pathogenesis of diseases, such as diabetes insipidus, hypertension, stroke, dementia, Parkinson's disease, obesity, and diabetes mellius and its complications including diabetic neuropathy, nephropathy, cardiopathy, embryopathy, and retinopathy. The role of these genes in the molecular basis of painful and painless neuropathy, which are often observed in diabetic neuropathy patients, will be discussed in more detail. The understanding of downstream signaling pathways of these genes would lead to devise novel diagnostic tools and effective therapies for prevention of human diseases in order to improve the quality of life.

Postsurgical Chronic Pain

Dr. Chi-Wai CHEUNG
Clinical Assistant Professor
Department of Anaesthesiology
The University of Hong Kong

Dr. Cheung is currently the Clinical Assistant Professor, Department of Anaesthesiology at the University of Hong Kong. He is also the Assistant Dean of Li Ka Shing Faculty of Medicine, at the University of Hong Kong since 2009 and responsible for academic networking and student affairs. His current research interests include pain management (acute, chronic and cancer), pain relief in maxillofacial surgery, and sedation medications and techniques. Apart from his work at University, he is also very active in his medical specialty. He is currently the President, the Society of Anaesthetists of Hong Kong. He has also been elected as the Vice President, the Hong Kong College of Anaesthesiologists. Recently, he has established the Laboratory and Clinical Research Institute for Pain at the University of Hong Kong and taken up the directorship of the Research Institute.

Abstract

It has been recognized that the development of chronic pain after surgery is not uncommon. A significant number of patients suffer from pain months or even years after surgery even though the wound has apparently healed. Chronic pain after surgery is defined as pain lasting for at least three months after the surgical procedure where other potential causes for the pain have been excluded. The incidence of chronic postsurgical pain ranges from 9% to 80%. Even though risk factors for the development of chronic postsurgical pain been suggested, it is difficult to predict if postsurgical pain would develop in individual patients. Genetic susceptibility is one of the key factors accounting for the different pain experience and response to analgesics. Postsurgical pain would be introduced. Challenges and difficulties of studies in genetics of postsurgical pain would also be discussed.

Paroxysmal Extreme Pain Disorder

Dr. Edmond Kin-Nam CHUNG
Associate Consultant
Department of Anaesthesiology
Queen Elizabeth Hospital

Dr. Chung is an Associate Consultant at the Department of Anaesthesiology & Operating Theatre Services at Queen Elizabeth Hospital. He also practices pain management, both acute & chronic, in his hospital & cluster.

Abstract

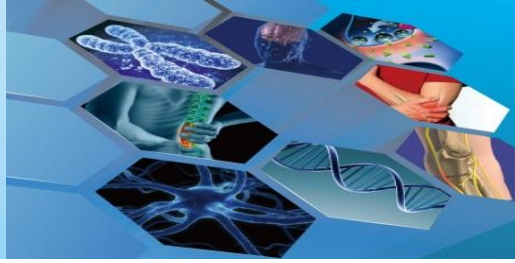
A case of Paroxysmal Extreme Pain Disorder (PEPD) in a 60-year-old Chinese male and his family is presented and discussed. This is a rare familial neuropathic pain disorder with autosomal dominant inheritance. It was first described in 1959. It was initially named "familial rectal pain". Previously, the genetic basis was not known. The condition was once thought to be the result of an abnormality of the autonomic nervous system, due to the presence of autonomic manifestations. It has also been considered as a form of reflex epilepsy, due to the association with tonic seizures and the response to carbamazepine. Only in recent years, genetic linkage studies showed that PEPD is caused by mutations in the SCN9A gene, which encodes an alpha subunit of the voltage-gated sodium channel Nav1.7. This finding has significant implication in the development of the field of pain genetics. It triggers new questions in this rapidly developing field such as in prenatal diagnosis, screening and treatment.

Spine Disorders, Pain Genes, and Personalized Medicine

Dr. Dino SAMARTZIS
Research Assistant Professor
Department of Orthopaedics & Traumatology
The University of Hong Kong

Dr. Samartzis was born in Chicago, Illinois. He attended Loyola Academy high school in Wilmette, Illinois and went on to obtain his undergraduate degree from Northwestern University in Evanston, Illinois. Dr. Samartzis further pursued graduate studies in biological sciences, evidence-based health care, clinical epidemiology, medical sciences, and international studies at Harvard University in Cambridge, Massachusetts, the University of Oxford in Oxford, England, the University of Cambridge in Cambridge, England, Erasmus University in Rotterdam, The Netherlands, Charles University in Prague, Czech Republic, and the London School of Economics and Political Science in London, England. Dr. Samartzis completed a postdoctoral fellowship at the Department of Biochemistry at the University of Hong Kong in Hong Kong. Furthermore, he was a Gilbert Beebe Fellow of the Radiation and Nuclear Board of the National Academies of Science in Washington D.C., the Radiation Epidemiology Branch of the National Institutes of Health in Bethesda, Maryland, and at the Radiation Effects Research Foundation (a.k.a. Atomic Bomb Casualty Commission) in Hiroshima, Japan addressing the effects of atomic nuclear power/radiation and their health-related risks upon the musculoskeletal system.

Since having started his career in spine at the Division of Spine Surgery, Department of Orthopaedic Surgery at Rush University Medical Center in Chicago, Illinois, Dr. Samartzis has published over 200 research articles, book chapters, and other educational material in peer-reviewed journals, textbooks, etc. Dr. Samartzis has also been the Editor-in-Chief and/or Section Editor for several textbooks and journal theme issues, such as The Cervical Spine, Intervertebral Disc Degeneration, Disc Degeneration, Minimally Invasive Spine Surgery, Orthopaedic Surgical Approaches, and others. Dr. Samartzis is actively involved on the Editorial, Advisory, and Review Boards of nearly two dozen medical journals, such as SPINE, Journal of Spinal Disorders and Techniques, The Spine Journal, Journal of Orthopaedic Surgery & Research, Journal of Bone and Joint Surgery, and the British Medical Journal. In particular, he serves as Deputy Editor for the Global Spine Journal, the most



circulated spine journal in the world. In addition, Dr. Samartzis is also an elected member of various organizations, such as the American Academy of Orthopaedic Surgeons, North American Spine Society, International Society for the Study of the Lumbar Spine, Orthopaedic Research Society, AOSpine, Hong Kong Orthopaedic Association, and the American College of Epidemiology. In particular, Dr. Samartzis serves as the Research Chair for AOSpine East Asia. In addition, Dino has been the recipient of over 30 awards related to his research and his work has been featured in over 200 media forums worldwide.

Dr. Samartzis is currently a Research Assistant Professor at the Division of Spine Surgery at the Department of Orthopaedics & Traumatology, Honorary Assistant Professor for the Department of Anesthesiology, and Deputy Director of the Laboratory and Clinical Research Institute for Pain at the University of Hong Kong. Dr. Samartzis is an evidence-based clinical spine epidemiologist whose main research interests are non-genetic and genetic factors related to intervertebral disc degeneration and spine pain, cervical spine disorders and management, and spine deformities. He also has expertise in complex statistical modeling, population-based studies, and evidence-based health-care.

Abstract

Low back pain is one of the world's most debilitating conditions, affecting every population. Treatment of low back pain can entail conservative measures or surgical interventions, often times with dubious outcomes. Although low back pain is multifactorial, such pain may have a genetic predisposition. The following lecture will address the complexities of low back pain, its potential genetic determinants, and pain genetics can alter its clinical management.

Pharmacogenetics: Opioids & Personalized Health-Care

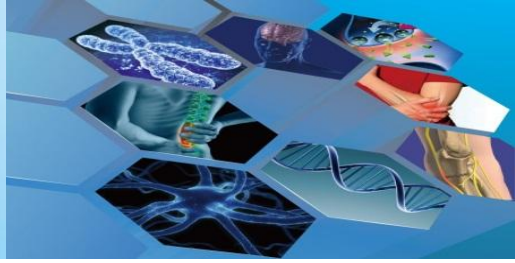
Prof. Michael G. IRWIN
Professor and Head
Department of Anaesthesiology
The University of Hong Kong

Prof. Irwin is Professor and Head of the Department of Anaesthesiology at the University of Hong Kong and Chief of Service in Anaesthesia at Queen Mary Hospital. He is Past President of the Hong Kong College of Anaesthesiology, where he is also a member of the education and examination committees and is chief censor. Prof. Irwin has published more than 130 articles in peer reviewed scientific journals and is a regular invited journal reviewer. He is an editor of Expert Opinion on Pharmacotherapy, Perioperative Medicine, CPD Anaesthesia (UK), Pain Research and Treatment, Hong Kong Medical Journal, Acta Anaesthesia Taiwanica, Case Reports in Medicine, Anaesthesia and Intensive Care Medicine and is on the International Advisory Panel for Anaesthesia. Research interests include anaesthetic pharmacology, acute pain management and organ preconditioning. He is part of the Faculty of 1000 Medicine in the field of Cardiovascular medicine in anaesthesia: basic science.

Abstract

Polymorphism derives from a single base mutation in DNA that substitutes one nucleotide for another. This is called a single nucleotide polymorphism or an SNP. The pivotal importance of SNPs was recognized soon after their discovery, and it has become a key objective to map all of these variants across the entire human genome. The effect of any particular SNP i.e. the resulting phenotype, will, however, depend on the impact of the resulting substitution of the encrypted amino acid on the respective protein. This effect will vary depending on both amino acid substituted and its position.

In pain management it is apparent that patients' respond differently to opioid therapy and current evidence suggests that this is related to genetic variability. Genetic factors regulate opioid pharmacokinetics (metabolizing enzymes, transporters) and pharmacodynamics (receptors and signal transduction elements) and contribute to such variability. Single-nucleotide polymorphisms in the mu opioid receptor gene are associated with



increasing morphine, but not methadone dosage requirements and altered efficacy of mu opioid agonists and antagonists. Genetic variability in non-opioid systems may also indirectly influence clinical opioid efficacy e.g. genetic inactivity of cytochrome P450 (CYP) 2D6 occurs in about 8% of the Caucasian population (only 1-2% of Chinese) and renders codeine ineffective (lack of morphine formation), decreases the efficacy of tramadol (lack of formation of the active O-desmethyl-tramadol) and slightly decreases the clearance of methadone. Another 5% have multiple copies of the CYP2D6 gene and are ultrarapid metabolisers. Opioid bioavailability can be altered by the function of membrane transporters e.g. P-glycoprotein, thereby affecting CNS distribution and elimination and even drug uptake into metabolising organs/cells. Polymorphisms in enzyme systems also affect the formation of active metabolites e.g. M-6-G, or opioid clearance. Variability in an enzyme-degrading catecholamine (COMT) gene may alter the efficacy of morphine. ABCB1 genotypes also inconsistently influence opioid pharmacodynamics and dosage requirements.

Receptor binding and a wide range of pharmacological studies have proposed several μ receptor subtypes, but only one μ opioid receptor (Oprm) gene has been isolated. These variants all show the same selectivity for μ opioids but major differences in binding affinity, potency and efficacy among these variants as well as in their anatomical localization. These variants may provide insights into the wide range of opioid responses among these agents observed clinically and opens new avenues in designing selective drugs based upon their efficacy and potency rather simple binding affinity.

Pharmacogenetics may be able to individualize pharmacotherapy and improve care by predicting the optimal dose and avoiding side effects and toxicity in individual patients.

Take home messages:

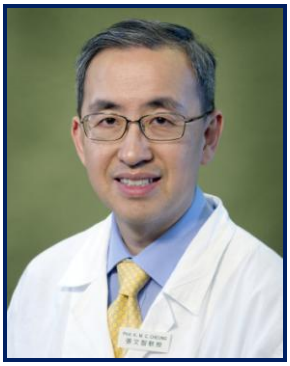
1. Virtually every aspect of drug bioavailability, metabolism, receptor interaction and movement can be affected by a person's genetic make up
2. Opioid effects and side effects vary markedly between sexes, races and individuals
3. It is currently not possible to predict these differences although research may help us to do this in the future
4. Codeine is ineffective in approximately 3% of Asians
5. Titration and multimodal techniques are important in pain management

Moderators

Prof. Michael G. IRWIN
Professor and Head
Department of Anaesthesiology
The University of Hong Kong

Prof. Pak SHAM
Chair Professor
Department of Psychiatry
The University of Hong Kong

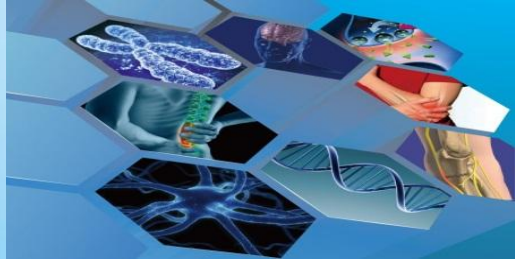
Prof. Kenneth CHEUNG
Jessie Ho Professor in Spine Surgery
Department of Orthopaedics & Traumatology
The University of Hong Kong



Accreditations

CME, CPD and CNE accreditations have been sought from following colleges / programmes. Registered participants can be accredited CME, CPD and CNE as follows:

	Whole Symposium (9-June 2012)	Category and Remarks
CME		
Hong Kong College of Anaesthesiologists	5.68	*ANA – Passive*
Hong Kong College of Community Medicine	6	
College of Dental Surgeons of Hong Kong	5.5	*Cat. B*
Hong Kong College of Emergency Medicine	5.5	
Hong Kong College of Family Physicians	pending	
Hong Kong College of Obstetricians and Gynaecologists	5	*O&G*
College of Ophthalmologists of Hong Kong	2.5	*Passive*
Hong Kong College of Orthopaedic Surgeons	5	*Cat. B*
Hong Kong College of Otorhinolaryngologists	3	*Cat. 2.2*
Hong Kong College of Paediatricians	6	*Cat. E*
Hong Kong College of Pathologists	5	*PP*
Hong Kong College of Physicians	5	
Hong Kong College of Psychiatrists	5	*PP/OP*
Hong Kong College of Radiologists	5.5	*Cat. B*
College of Surgeons of Hong Kong	5.5	*Passive*
MCHK CME Programme (The Medical Council of Hong Kong CME Programme)	6	*Passive* *Accredited by HKU*
CPD		
Hong Kong Physiotherapy Association	5	*MC1200178*
Hong Kong Occupational Therapists Board	pending	
CNE		
The University of Hong Kong Nursing	5.5	



Acknowledgements

The Organizing Committee would like to extend their heartfelt thanks to the following sponsors for their unfailing support and generous contribution.

Eli Lilly Asia, Inc.

Janssen Hong Kong

Pfizer Corporation Hong Kong Ltd

Bio-rad Pacific Ltd

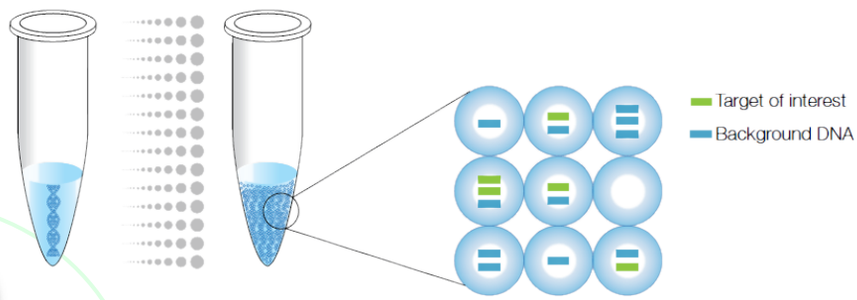
Joinhands Tech Ltd

Life Technologies

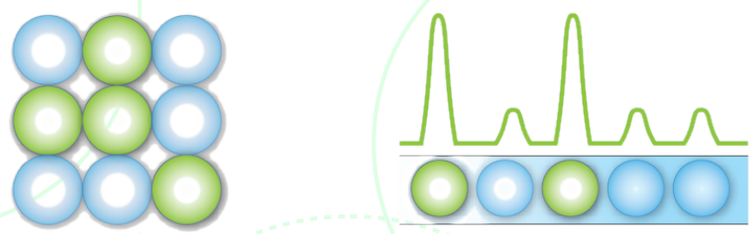
QX100™ Droplet Digital™ PCR System

Detect single cell by 3rd generation PCR technology

Droplet Digital PCR



The sample is partitioned into 20,000 droplets, with target and background DNA randomly distributed among the droplets.



After PCR amplification, each droplet provides a fluorescent positive or negative signal indicating the target DNA was present or not present after partitioning. Each droplet provides an independent digital measurement.

Application

- Enrich for rare target sequences
- Detect small differences in target concentration
- Determine copy number without standard curve
- Rare event detection, includes SNP
- Prenatal and Cancer Diagnosis

BIO-RAD *Web site: www.bio-rad.com Email: sales.hongkong@bio-rad.com Tel: (852) 2789 3300*