



Singapore - Australia

Joint Symposium on Stem Cells and Bioimaging

Date : 24 - 25 May 2010

Time : 8.30am - 6.00pm

Venue : Breakthrough and Discovery Theatrettes, Level 4, Matrix, Biopolis

Jointly organised by



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Convenors of Symposium



Dr Alan Colman

Executive Director, Singapore Stem Cell Consortium
Principal Investigator, Institute of Medical Biology

Alan Colman is currently the Executive Director of the Singapore Stem Cell Consortium and Principal Investigator in the A*STAR Institute of Medical Biology. He was involved in cloning Dolly, the world's first cloned sheep from an adult somatic cell in 1996 when he was the research director of the company PPL Therapeutics in Edinburgh, UK. Dr Colman's research will involve the differentiation of human and mouse embryonic or embryonic-like (induced pluripotent stem cells) stem cells that harbor deleterious mutations known in humans to cause distinctive pathological conditions. Neurodegenerative disease will also comprise a major focus.



Professor Robert (Bob) Williamson

Faculty of Medicine
University of Melbourne

Professor Bob Williamson was appointed Professor of Molecular Genetics at St Mary's Hospital Medical School, Imperial College, University of London from 1976 until 1995, when he moved to Melbourne as Director of the Murdoch Institute and Professor of Medical Genetics. He retired in 2004, and now is an Honorary Senior Principal Fellow of the Murdoch Institute, the University of Melbourne, and Monash University. He was involved in the identification of genes for cystic fibrosis, Friedreich ataxia, craniofacial abnormalities, heart disease and Alzheimer disease. More recently he has taken a major interest in national science policy and medical and scientific ethics.

Background

As part of the aim to foster greater collaborations between researchers in Singapore and Australia, the idea of joint symposia between Singapore's Agency for Science, Technology and Research (A*STAR) and the Australian Department of Innovation, Industry, Science and Research (DIISR) was initiated in 2008 by Chairman A*STAR and Minister Kim Carr, Minister for Innovation, Industry, Science and Research (IISR).

In 2009 and 2010, A*STAR and Australian Academy of Sciences (AAS) organize two symposia in the areas of common interest of Energy as well as Stem Cells and Bioimaging.

The 1st Singapore-Australian Joint Symposium on Energy was held on 15-16 June 2009 in Canberra, Australia with Prof Andrew Holmes (Member of AAS Council) and Mr Peter Laver (Vice-President, Australian Academy of Technological Sciences & Engineering) as the co-convenors. This year, A*STAR is happy to host the 2nd Singapore-Australia Joint Symposium on Stem Cells and Bioimaging at Biopolis, Singapore and we are glad to have Prof Robert (Bob) Williamson (Honorary Senior Fellow and Professor of Medical Genetics, University of Melbourne, Fellow of AAS and the Royal Society) and Dr Alan Colman (Executive Director, Singapore Stem Cell Consortium) to be co-convenors of this joint symposium. We hope that this symposium will further strengthen the existing good relations between Singapore and Australia and create more opportunities for exchange of ideas as well as collaborations in the areas of Stem Cells and Bioimaging.

Day 1 Programme

08.30 - 09.00	Arrival of Participants and Registration
09.00 - 09.10	Welcome Address by: Prof Lee Eng Hin, Executive Director, Biomedical Research Council, A*STAR
09.10 - 09.20	Welcome Address by: Prof Robert (Bob) Williamson, Faculty of Medicine, University of Melbourne
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Overviews	
09.20 - 09.30	Introduction: Dr Alan Colman, Executive Director, Singapore Stem Cell Consortium
09.30 - 10.00	S01: Megan Munsie, Australian Stem Cell Centre Delivering On The Promise – Progress In Stem Cell Science During The Last Decade
10.00 - 10.30	S02: Alan Colman, Singapore Stem Cell Consortium Use of Induced Pluripotent Stem Cells (iPSC) To Model A Human Premature Aging Disease
10.30 - 11.00	Tea Break
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Session on Neurology Issues and Potentials	
11.00 - 11.30	S03: Perry Bartlett FAA, Queensland Brain Institute Stimulation of Latent, Neurogenic Stem Cells In The Hippocampus By Synaptic Activity
11.30 - 12.00	S04: Sohail Ahmed, Institute of Medical Biology Quantitative Analysis Of Neural Stem Cells And Neural Progenitors Through High Content Imaging
12.00 - 12.30	S05: Gary Egan, Howard Florey Institute MRI Translational Research in Neurodegenerative Diseases Using Ultrahigh Field MRI
12.00 - 13.00	Discussion
13.00 - 14.00	Lunch
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Session on Cardiology and Ion Channels	
14.00 - 14.30	S06: Lim Sai Kiang, Institute of Medical Biology Reducing Myocardial Ischemia/Reperfusion Injury Via Exosomes Secreted From Mesenchymal Stem Cells
14.30 - 15.00	S07: Pankaj Sah, Queensland Brain Institute Calcium Signalling In Dendritic Spines In The Basolateral Amygdala
15.00 - 15.30	S08: Richard Harvey, The Victor Chang Cardiac Research Institute Endogenous Cardiac MSC-Like Stem Cells: Biology And Origins
15.30 - 16.00	Tea Break
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Session on Organogenesis	
16.00 - 16.30	S09: David Elliott, Monash Immunology and Stem Cell Laboratory Multipotent NKX2-5+ Cardiac Progenitors Derived From Human Embryonic Stem Cells
16.30 - 17.00	S10: Ray Dunn, Institute of Medical Biology Signals Governing Definitive Endoderm Formation In Mouse And Human Embryonic Stem Cells
17.00 - 17.30	S11: Melissa Little, Institute for Molecular Bioscience, University of Queensland Starting The Kidney All Over Again: A Number Of Stem Cell Options
17.30 - 18.00	Discussion
19.00 - 21.00	Welcome Dinner Restaurant 1827 1 Old Parliament Lane, Level 1, Old Parliament House

Day 2 Programme

08.30	Introduction
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Session on Cancer and Stem Cells	
08.35 - 09.00	S12: Andrew Laslett, CSIRO Molecular and Health Technologies Avoiding Teratoma When Using ESC or iPS Cells For Therapy: Development of New Tools
09.00 - 09.30	S13: Andre Choo, Bioprocessing Technological Institute Characterization Of Prohibitin As A Novel Surface Marker On Human Embryonic Stem Cells And Induced Pluripotent Stem Cells
09.30 - 10.00	S14: Jane Visvader, Walter and Eliza Hall Institute of Medical Research Delineation Of The Mammary Epithelial Hierarchy And Cell Types Predisposed To Breast Oncogenesis
10.00 - 10.30	Tea Break
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Session on Advanced Concepts in Imaging	
10.30 - 11.00	S15: Kishore Bhakoo, Singapore Bioimaging Consortium Assessing Stem Cell Efficacy In Vivo Using Multi-Modal Imaging
11.00 - 11.30	S16: Tamil Selvan Subramanian, Institute of Materials Research and Engineering Multifunctional Fluorescent Nanoparticles For Bioimaging Applications
11.30 - 12.00	S17: Caroline Rae, Prince of Wales Medical Research Institute Magnetic Resonance Approaches In Interdisciplinary Brain Research
12.00 - 12.30	S18: Young-Tae Chang, Singapore Bioimaging Consortium LuminoGenomics Using Diversity Oriented Fluorescence Library Approach (DOFLA)
12.30 - 14.00	Lunch¹ <i>*¹Networking Lunch for Australian speakers, selected PhD students/ Post-Docs and other invited guests to be held at Onaka Café and Juice Bar, Immunos (Biopolis), Level 1, 8A Biomedical Grove.</i>
14.00 - 14.30	S19: William Hughes, The Garvan Institute of Medical Research Imaging Regulated Exocytosis: Total Internal Reflection Fluorescence Microscopy Of The Last Steps Of Glucose Transporter Exocytosis
14.30 - 14.45	Discussion
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Session on Basic Developmental Biology of Stem Cells	
14.45 - 15.15	S20: Bing Lim, Genome Institute of Singapore Factors Modulating Reprogramming Of Somatic Cells To Pluripotent Stem Cells
15.15 - 15.45	S21: Nick Barker, Hubrecht Institute Lgr5 Stem Cells In Self-Renewal and Cancer
15.45 - 16.15	S22: Ng Huck Hui, Genome Institute of Singapore Deciphering And Reconstructing The Embryonic Stem Cell Transcriptional Regulatory Network
16.15 - 16.30	Discussion
16.30 - 17.00	Tea Break
17.00 - 17.30	S23: Robert (Bob) Williamson, Faculty of Medicine, University of Melbourne The Ethics Of Embryonic Stem Cell Research
17.30 - 18.00	General Discussion Led by Bob and Alan on future perspectives, both in general and in terms of collaboration between Singapore and Australia.
18.00	Networking Reception Biopolis Epicentre
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Day 3 (26 May 2010, Wednesday)	
10.00 - 11.30	Presentation on Institute of Medical Biology (IMB) and Tour of IMB's Microscopy Unit
11.30 - 13.00	Presentation on Bioimaging in Singapore and Tour of Singapore Bioimaging Consortium (SBIC)'s Labs
13.00	Lunch Hosted by Singapore Stem Cell Consortium (SSCC)

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S01: Dr Megan Munsie
Senior Manager – Research and Government
Australian Stem Cell Centre
Email: megan.munsie@stemcellcentre.edu.au

Biography

Dr Megan Munsie's career in stem cell research spans her proof-of-concept somatic cell nuclear transfer studies in mouse and her involvement in deriving one of Australia's first HESC lines; through to her participation in the reform of Australian legislation governing this area and her participation on the ISSCR Task Force on the Clinical Translation of Stem Cells. Megan is currently a member of the Australian Stem Cell Centre's management team where she is responsible for managing its diverse research portfolio and its government interactions. Megan received her undergraduate degree from QUT and a Masters and a Doctorate of Philosophy from Monash University.

Abstract

Delivering On The Promise – Progress In Stem Cell Science During The Last Decade

Around the globe stem cell science has captured the public's imagination like almost no other scientific field in recent times. Every breakthrough attracts immediate media interest, further heightening the community's expectation of new therapies to treat incurable diseases and illness. While the last decade has seen tremendous advances in stem cell research, translation of the discoveries into effective therapies is yet to fully deliver on such a promise. This presentation will place recent developments in stem cell science into context, highlighting ongoing challenges of clinical translation as well as delving beyond the direct therapeutic applications of stem cells to other important, and perhaps more immediate, applications of stem cells to medical research.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S02: Dr Alan Colman

Executive Director, Singapore Stem Cell Consortium
Principal Investigator, Institute of Medical Biology
Email: alan.colman@imb.a-star.edu.sg

Biography

Alan is currently the Executive Director of the Singapore Stem Cell Consortium and also a Principal Investigator in the A*STAR Institute of Medical Biology. His research will involve the differentiation of human and mouse embryonic or embryonic-like (induced pluripotent stem cells) stem cells that harbor deleterious mutations known in humans to cause distinctive pathological conditions. Neurodegenerative disease will comprise a major focus.

Alan Colman obtained a BA degree in Biochemistry in Oxford (1971) and a PhD under John Gurdon, a pioneer of the field of nuclear transfer, at the MRC Laboratory of Molecular Biology in Cambridge, UK (1974). After a series of academic appointments in Oxford and Warwick Universities, he became Professor of Biochemistry in the University of Birmingham, UK. The focus of his academic career was the area of eukaryotic protein secretion, with a particular emphasis on the use of frog oocytes and eggs as in vivo test tubes.

From 1987 until March 2002, he was research director of the company PPL Therapeutics in Edinburgh, UK. This company specialized in the production of transgenic livestock that produced human therapeutic proteins in their milk. PPL attracted considerable media attention because of its participation, together with the Roslin Institute, in the technique of somatic nuclear transfer. This work led to Dolly, the world's first sheep cloned from an adult somatic cell (1996), Polly and Molly, the first cloned transgenic livestock (1997), Diana and Cupid, the first livestock with targeted genetic changes (2000), Millie et al., the first cloned pigs (2000) and, finally, Austin and crew, the first homozygous alpha-gal-transferase knock-out pigs (2003).

From April 2002 - June 2007, he worked for the Singapore - based company, ES Cell International (ESI), first as its Chief Scientific Officer (April 2002 - February 2005) and then its Chief Executive Officer (February 2005 - June 2007). ESI specialized in the development of human embryonic stem cell-based therapies for the treatment of diabetes and congestive heart failure.

Abstract

Use of Induced Pluripotent Stem Cells (iPSC) To Model A Human Premature Aging Disease

The process for generating induced pluripotent stem cells (iPSC) from murine somatic cells was first reported in Kyoto in 2006. Since that time this field has burgeoned, and it seems that this technology works in many mammalian species and with many somatic cell types. iPSC research has permeated many different research areas. I will discuss its application to furthering our understanding of the early pathophysiology of specific human diseases. In these circumstances, iPSC generated from patients displaying genetic disease are used as a surrogate model to understand some of the early molecular correlates of that disease. There is an underlying assumption that a disease phenotype will be seen in the in vitro conditions. It is not clear that this assumption is a valid one for many human diseases. In my talk I will also discuss our own research on iPSC to study Hutchinson-Gilford Progeria Syndrome, a premature aging disease.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S03: Professor Perry Bartlett FAA
Director
Queensland Brain Institute (QBI)
Email: p.bartlett@uq.edu.au

Biography

Professor Perry Bartlett was appointed Foundation Chair in Molecular Neuroscience at The University of Queensland in 2002, and inaugural Director of the Queensland Brain Institute in 2003 - the same year he was elected a Fellow of the Australian Academy of Science.

He is internationally renowned in the field of cellular and molecular neuroscience. In 1992, his laboratory co-discovered the presence of stem cells in the adult brain that had the capacity to produce new neurons. His group was first to isolate and characterise these stem cells; they went on to reveal the presence of a latent hippocampal stem cell population that can be activated by synaptic stimulation and give rise to new neurons. These discoveries underpin the concept of functional stem cells in the adult mammalian brain and the burgeoning interest in their importance to learning and memory. Professor Bartlett has published extensively and received a number of prizes for neuroscience excellence.

Abstract

Stimulation Of Latent, Neurogenic Stem Cells In The Hippocampus By Synaptic Activity

The production of new neurons in the hippocampus is thought to underpin aspects of learning and memory, especially those associated with spatial memory formation. In addition, the rate of neurogenesis is influenced by environmental stimuli including learning activities, which, in turn, supplement learning capacity. Thus, defining how neurogenesis is regulated is central to our understanding of the learning process and to the future development of neurogenic-based therapeutics aimed at ameliorating cognitive loss.

Recently, we identified a large precursor pool in the dentate gyrus of the mouse hippocampus, including a small number of true stem cells, which is normally dormant but can be activated by depolarizing levels of K⁺ to produce large numbers of neurogenic neurospheres. In situ stimulation of the perforant pathway also activates this precursor population and leads to an increase in newly born neurons. Importantly, we have shown that this population can be activated in the aged mouse even though neurogenesis has declined dramatically, uncovering the potential for significant neurogenesis in the ageing brain.

Further studies have shown that synaptic activity stimulates precursor activity through the release of a number of soluble factors and the neurotransmitter, norepinephrine (NE). Clonal studies have shown that these factors act directly on the precursors with NE activating through a novel adreno-receptor pathway. Interestingly, we found that different stimuli led to the activation of different pools of precursors and stem cells, raising the possibility that this may lead to the production of hippocampal neurons in the dentate gyrus with distinct properties reflective of a specific stimulation process. This provides a mechanism by which the functional capacity as well as the number of newly generated neurons can be directly influenced by the type and complexity of the environmental stimuli.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S04: Dr Sohail Ahmed
Principal Investigator
Institute of Medical Biology
Email: sohail.ahmed@imb.a-star.edu.sg

Biography

Sohail Ahmed received his B.Sc. (University of London) in 1979 and Ph.D. (University of Aberdeen) in 1982, both in Biochemistry. He carried out his post-doctoral studies at the University of California, Berkeley (1983), the Institute Pasteur, Paris (1985) and UCL, London (1986). In 1989 he was appointed a Lecturer at the Institute of Neurology, UCL, and a Senior Scientist in the Glaxo-IMCB group. In 1998, he was appointed Senior Research Fellow at the Institute of Neurology, UCL. In 2002, he moved to Singapore and joined the Centre for Molecular Medicine (CMM) where he set up the Neural Stem Cell Laboratory within the Regenerative Medicine Programme. (CMM became part of the new IMB in April 2007.)

Sohail's research interests focus on trying to understand the molecular and cell biology of neural stem cells in the context of regenerative medicine. His laboratory is investigating fundamental aspects of neural stem cells and neural precursors, and how these cells grow, divide, differentiate and die. The group has a particular interest in the application of advanced imaging techniques such as time-lapse microscopy and the F-techniques (FRET, FRAP, FLIM, and FCS) to map cell signalling pathways responsible for controlling actin dynamics in growth cones. 3-D imaging techniques and GFP/RFP reporters are being used to investigate the formation of neurospheres. Sohail Ahmed has championed advanced light microscopy imaging techniques at Biopolis and has played a key role in establishing the IMB Microscopy Unit. Together with Ernst Stelzer (EMBL), he ran the first Singapore EMBO course in 2003.

Abstract

Quantitative Analysis Of Neural Stem Cells And Neural Progenitors Through High Content Imaging

Neural stem cells (NSCs) and neural progenitors (NPs) can be propagated as neurospheres in vitro culture. The neurosphere is a model for the central nervous system that can be used to investigate, neurodevelopment, disease states and drug screening. We use 3-D time-lapse optical imaging to follow the growth, activity and function of NSCs and NPs. Here I will present some of the high content screens and image processing tools we have developed. We are able segment the nuclei/cells in live neurospheres and can measure quantitatively, cell volumes, cell numbers and the extracellular space. A software package called StemCELL3D has been developed that is a powerful computational tool to segment and visualize the nuclei and cells in neurosphere assays. StemCELL3D is applicable to segment images generated from 3-D cell culture systems in general. Importantly, our high content assays will allow NSCs to be screened for anti-cancer drugs.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S05: Professor Gary Egan

Associate Director and Principal Research Fellow
Howard Florey Institute
Email: gary.egan@florey.edu.au

Biography

Gary Egan is a Senior Principal Research Fellow at the Howard Florey Institute, University of Melbourne and Associate Director and Professor in the Centre for Neuroscience, University of Melbourne, and Deputy Director of the National Imaging Facility. He has published over 140 papers and over 200 abstracts in peer reviewed journals. He leads the Neuroimaging and Neuroinformatics laboratory undertaking neuroscience imaging research in humans including studies of high resolution functional and structural brain mapping. He is head of the small animal Magnetic Resonance (MR) imaging and spectroscopy laboratory where he leads a translational research program using small animal models of human disease.

Abstract

MRI Translational Research In Neurodegenerative Diseases Using Ultrahigh Field MRI

Neuroimaging is an indispensable research tool in the neurosciences with major advances in our understanding of the human brain resulting from imaging studies over the past 20 years. The ongoing development of novel Magnetic Resonance (MR) imaging techniques continues to provide new insights into brain function in neurological and psychiatric disease processes. Techniques including blood oxygenation level dependent (BOLD) functional MR, cerebral blood flow or perfusion, diffusion weighted, susceptibility weighted, manganese enhanced contrast, and spectroscopy techniques provide unique in vivo measures of brain function and microstructure. Current developments in ultra high field strength magnets for human and animal model research have great potential to further revolutionise our understanding of the brain.

The use of MRI in translational research in Multiple Sclerosis (MS), Huntington's disease (HD) and Alzheimer's disease will be presented, including recent results using ultrahigh field (7 Tesla) MR in human studies that reveal microstructural changes in vivo. Whilst there remain many challenges to routine imaging at ultrahigh field strengths, the development of new imaging techniques such as phase contrast imaging provide exciting examples of new research opportunities at high field.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S06: Dr Lim Sai Kiang
Principal Investigator
Institute of Medical Biology
Email: saikiang.lim@imb.a-star.edu.sg

Biography

Sai-Kiang Lim graduated with B.Sc (Hons), NUS in 1985 and PhD (Molecular Biology) SUNY at Buffalo; in 1992. She was awarded the Most Meritorious Student Research Award by Sigma Xi Society (1989) and a NY State Predoctoral Fellowship (1989-91). She did her postdoctoral training at Columbia University first as a Cooley's Anemia Foundation Research Fellow (1992-94) and a Leukemia Society of America Special Fellow (1994-96) before leading independent research groups at NUMI, NUS (1996-2001), Genome Institute of Singapore (2002-2007) and Institute of Medical Biology (2007-present). She is also concurrently an Associate Research Professor in the Dept. of Surgery, YLL School of Medicine, NUS. Her research focus has been disease-related with emphasis on elucidating the underlying molecular and cellular mechanisms, and development of therapies.

Abstract

Reducing Myocardial Ischemia/Reperfusion Injury Via Exosomes Secreted From Mesenchymal Stem Cells

The therapeutic efficacy of mesenchymal stem cells (MSCs) in the treatment of cardiovascular disease is increasingly attributed to their paracrine secretion. Consistent with these observations, my lab has recently demonstrated that administration of culture medium conditioned by MSCs derived from human ESCs into a pig and mouse models of myocardial ischemia/reperfusion (MI/R) injury reduced infarct size by ~60% and ~50%, respectively. Size fractionation of the conditioned medium (CM) suggested that the active cardioprotective factor was a ~50-100 nm complex. Electron microscopy and ultracentrifugation studies confirmed the presence of 50-100 nm particles in the CM. Mass spectrometry and biochemical analysis of the CM identified exosome-associated proteins such as CD81, CD9 and Alix that also co-immunoprecipitated and small RNAs of <300 nt that included microRNAs. The exosome-associated proteins and RNA were found to be encapsulated in cholesterol-rich phospholipid vesicles. These vesicles was purified by HPLC size exclusion fractionation as a population of homogenously sized particles with a hydrodynamic radius of 55-65 nm and highly enriched in exosome-associated proteins. When administered to a mouse model of myocardial ischemia/reperfusion injury, these purified particles reduced infarct size by ~50%. Therefore, the cardioprotective component in MSC secretion is an exosome, a secreted bi-lipid membrane vesicle of endosomal origin.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S07: Professor Pankaj Sah
Deputy Director (Research)
Queensland Brain Institute (QBI)
Email: pankaj.sah@uq.edu.au

Biography

Pankaj Sah is a neurobiologist working at the Queensland Brain Institute at the University of Queensland. He graduated in Medicine from the University of NSW in 1983. Following an internship I became interested in the brain and did a PhD in Neuroscience. After my PhD I worked in the United States for two years and returned as a postdoctoral fellow to the University of Queensland. After 3 years there he was at the University of Newcastle, faculty of medicine. I moved to Canberra in 1998 to set up a lab at the John Curtin School of Medical Research and relocated to the Queensland Brain Institute as a founding member in 2003. He is Deputy Director (research) at the QBI. My lab works on the amygdala, a region of the brain involved in laying down emotional memory. I became interested in working on the amygdala as dysfunction of this structure underlie such mental disorders as panic attacks, anxiety and post traumatic stress disorder.

Abstract

Calcium Signalling In Dendritic Spines In The Basolateral Amygdala

Glutamatergic connections in the mammalian brain are largely made onto small compartments known as dendritic spines that express both ionotropic and metabotropic glutamate receptors. Calcium influx via NMDA receptors triggers cellular processes that mediate synaptic plasticity that underlies learning and memory formation. The spine neck restricts diffusion of calcium and other second messengers creating isolated biochemical compartments that is thought to underlie the synapse specificity of associative learning. In the basolateral amygdala, metabotropic receptors are present on spines and their activation is required for some forms of learning. In this talk I will show that activation of metabotropic receptors releases calcium in some dendritic spines and generates a propagating calcium wave. This propagating wave invades local spines that have short dendritic necks but is shielded from spines with long necks that are diffusionally protected from the dendritic shaft. These results show that activation of metabotropic receptors not only signals local events by raising spine calcium but also has more global actions on nearby spines and the nucleus.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S08: Professor Richard Harvey
Deputy Director
The Victor Chang Cardiac Research Institute
Email: r.harvey@victorchang.edu.au

Biography

Professor Harvey received his PhD in 1982 from the Department of Biochemistry, University of Adelaide, training under Julian Wells. After further training at Harvard University for 3 years and spending 10 years at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Professor Harvey joined the Victor Chang Cardiac Research Institute in 1998, where he is currently Co-Deputy Director and Head of the Developmental Biology Program. He holds the endowed Sir Peter Finley Professorship of Heart Research at the University of New South Wales. Professor Harvey's expertise is in developmental cardiology using the mouse as a genetic model. More recently has begun an exploration of the biology of adult cardiac stem cells and cardiac regeneration. In 2007, he was elected member of the Australian Academy of Science. He is an Associate Member of EMBO and an NHMRC Australia Fellow.

Abstract

Endogenous Cardiac MSC-Like Stem Cells: Biology And Origins

Our laboratory has developed a quantitative framework for characterising colonyforming cells from the adult mouse heart. Such cells (colony-forming units-fibroblast; CFU-F) are multipotent for a variety of mesodermal lineages in vitro and have a gene expression and cell surface receptor profile resembling bone marrow (BM) mesenchymal stem/progenitor cells (MSCs). MSC-like cells have recently been claimed to be a sub-fraction of pericytes. However, cardiac CFU-F with the highest self-renewal and broadest lineage differentiation potential do not express pericyte markers – nonetheless they exist in a continuum with pericytes which, along with myofibroblasts and smooth muscle cells, may be their preferred lineage descendants. The numbers and self-renewal characteristics of cardiac CFU-F have been explored in a mouse model of myocardial infarction as well as in aging. We have also explored the lineage origins of cardiac CFU-F using embryo studies, bone marrow transplantation and Cre recombinase lineage mapping. Data suggest an epicardial origin for cardiac CFU-F in development, with no contribution from bone marrow, even in the setting of myocardial infarction. Our ongoing work has highlighted the stable or semi-stable nature of the intrinsic states of self-renewal in CFU-F, and the possibility that growth factors such as Pdgf can regulate these states, which may prove useful in regeneration therapies.

Speakers' Biography and Abstract



S09: Dr David Elliott
Monash Immunology and Stem Cell Laboratory
Email: david.elliott@med.monash.edu.au

Biography

My PhD studies, supervised by Prof. Richard Harvey at the Walter and Eliza Hall and Victor Chang Cardiac Research Institutes, were on the genetic regulation of heart development. To broaden my technical skills, and pursue my interest in stem cells, I worked on the Drosophila nervous system in the laboratory of Prof. Andrea Brand at Cambridge University. My current project is the investigation of human heart development using the differentiation of human embryonic stem cells (hESC) as a model system. The goal of this program is to provide a sound understanding of the differentiation of human embryonic stem cells into cardiac precursors and onto mature cardiomyocytes, which may lead to the development of novel therapeutic approaches, both pharmacological and cell based, for heart disease.

Speakers' Biography and Abstract

Abstract

Multipotent NKX2-5+ Cardiac Progenitors Derived From Human Embryonic Stem Cells

Differentiation of human embryonic stem cells (hESCs) into cardiac progenitors is a powerful approach to dissect the molecular control of early human cardiogenesis. In order to identify, purify and characterise emerging cardiac progenitor cells (hESCCPCs) we engineered a hESC line, NKX2-5GFP/w, in which GFP replaced the coding region of the conserved cardiac transcription factor NKX2-5. Using this line we have optimised a protocol for the differentiation of hESC-CPCs and cardiomyocytes (hESC-CMs) from hESCs as embryoid bodies (EBs) in a 96-well plate format in serum free, chemically defined media. Contractile foci are found in almost all EBs and all beating areas are GFP positive. Flow cytometric analysis for GFP demonstrates that up to 30 % of cells within the EB are NKX2-5 positive. NKX2-5+ hESC-CPCs and CMs constitute developmentally distinct populations with both having gene expression profiles closer to foetal heart than adult heart. Clonal analysis shows that NKX2-5+ cells are capable of giving rise to the three major lineages in the heart, namely cardiomyocytes, smooth muscle and endothelium. This study will also form the basis of further investigations into the molecular mechanisms underlying both human CPC specification and the expansion and maturation of cardiac progenitors into cardiomyocytes.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S10: Dr Ray Dunn
Principal Investigator
Institute of Medical Biology
Email: ray.dunn@imb.a-star.edu.sg

Biography

Dr. Ray Dunn obtained his Ph.D. in Cell Biology in 1999 from Vanderbilt University under the supervision of Brigid Hogan, PhD FRS. His thesis described how the TGF β -related growth factor BMP4 controls primordial germ cell formation in the early mammalian embryo. He then completed a post-doctoral fellowship in the laboratory of Elizabeth Robertson, PhD FRS at Harvard University, where he studied the growth factor Nodal and its intracellular effector proteins Smad2 and Smad3 during early axis formation and early germ layer patterning in the mouse. In 2004, he joined ES Cell International Pte Ltd as a Research Scientist in the Diabetes Group, eventually being named Program Manager in 2005. In July of this year, he was appointed as a Principal Investigator in the Institute for Medical Biology and Singapore Stem Cell consortium.

Abstract**Signals Governing Definitive Endoderm Formation In Mouse And Human Embryonic Stem Cells**

The definitive endoderm (DE) is formed during gastrulation and is the parental lineage of such organs as the pancreas and liver. Studies in model organisms have established the obligate requirement for Nodal/Activin signaling in the specification of the DE. Thus, in the vast majority of in vitro differentiation protocols recombinant Activin is added to mouse and human ES cell cultures to stimulate the robust production of DE. We (and others) have previously shown that simultaneous addition of Activin and a related growth factor BMP4 to human ES cells promotes the rapid downregulation of pluripotency genes such as Oct4 and Nanog and increased expression of cardinal genes that identify DE such as Sox17 and Foxa2. FACS studies reveal that around day 4 we routinely achieve 70% DE cells. We propose that the addition of Bmp4 elicits numerous transcriptional changes and that differential gene expression profiles between Activin only and Activin and Bmp4-treated cultures would reveal the effects, direct or indirect, of Bmp4 on the formation of the DE in vitro. From our microarray studies, 19 of 92 genes have shown intriguing expression patterns in the mouse embryo with regard to DE formation. Some of these genes such as Smarcd3/Baf60c, Mcc, Igfbp5, Sema3e and Agtr1 are specifically expressed in the primitive streak, the site of DE production, or in the DE itself. Using a similar DE differentiation strategy, we have exploited mouse ES cell lines that are either wild-type or deficient in the Activin/Nodal downstream effector Smad2 in an effort to specifically identify transcriptional targets downstream of Activin/Nodal during DE formation. These parallel approaches using mouse and human ES cells have broadened our insight into the genes upregulated during DE formation in vitro, and at present we are "functionalizing" several novel genes using the Xenopus and zebrafish systems to better resolve which genes indeed operate in the DE specification pathway in vivo. An update on this initiative will be presented.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S11: Professor Melissa Little
Principal Research Fellow
Institute for Molecular Bioscience
University of Queensland
Email: m.little@imb.uq.edu.au

Biography

Professor Little is a Principal Research Fellow and leads the Renal Development and Disease Laboratory at the Institute for Molecular Bioscience, University of Queensland, Australia. She was also a Founding Scientist and Director of Nephrogenix Pty Ltd and held the position of Chief Scientific Officer at the Australian Stem Cell Centre from 2007-8. Her research focuses on the molecular genetics of kidney development and the causes of renal disease, with the aim of developing stem cell technology for use in kidney regeneration. Throughout her career, Professor Little's achievements have been recognised by awards such as the GlaxoSmithKline Award for Research Excellence (2005), the Australian Academy of Sciences Gottschalk Medal in Medical Sciences (2004), and a prestigious Eisenhower Fellowship, which recognises her contribution to both the commercial and academic sectors. Complementing her research and commercial endeavours, Professor Little has been strongly involved in the development of medical research in Australia through her contribution to the Health and Medical Research Strategic Review and in the development of National Research Priorities for Australia.

Abstract

Starting The Kidney All Over Again: A Number Of Stem Cell Options

Chronic renal disease is rising at the rate of 8% per annum due to increasing rates of obesity, diabetes and cardiovascular disease. Hence, there is an urgent need for novel therapeutic options in this organ. The functional units of the kidney, the nephrons, vary in number considerably and low nephron number is correlated with increased risk of postnatal renal disease. Nephrons are formed from a self-renewing renal progenitor population but this process ends in the first postnatal week in mice, presumably due to an exhaustion of the progenitor population of the kidney. In the absence of such a postnatal renal stem cell, we will present two options for renal regeneration; i) dedifferentiation of mature epithelial cells to a progenitor phenotype and ii) the generation of nephrons from human embryonic stem cells. To investigate the former, a screen for the dedifferentiation of the proximal tubule cell line using lentiviral-induced gene expression of genes expressed in the renal progenitor population has been performed. To investigate the later, we have commenced a screen of novel natural compounds seeking those able to direct the differentiation of the human embryonic stem cell line Mixl1-EGFP towards mesendoderm, the precursor mesodermal population for the kidney. Progress on both screens will be presented.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S12: Dr Andrew Laslett
Research Team Leader
CSIRO Molecular and Health Technologies
Email: andrew.laslett@csiro.au

Biography

Andrew and his team joined CSIRO Molecular Health Technologies in August 2009 and remain based at the Australian Stem Cell Centre (ASCC). Prior to this he was a Senior Scientist and Group Leader of the Human Embryonic Stem Cell Technology Laboratory at the ASCC. Dr Laslett's research compares human embryonic stem cells to human induced pluripotent stem cells and is focused on exploiting the basic biology of these cell types to create novel tools that enhance pluripotent cell research translation. He leads an independent program as well as having significant national and international collaborations. In September 2007, Dr Laslett was elected as a Board Member and Director of the Australian Society of Medical Research (ASMR). Dr Laslett's research is supported by the Australian Stem Cell Centre, the NHMRC (Australia), the Victoria California Stem Cell Alliance (Victorian Government and California Institute for Regenerative Medicine) and the NSW / Victorian Government Stem Cell Research Grant Program.

Abstract

Avoiding Teratoma When Using Human ESC Or iPS Cells For Therapy: Development Of New Tools

We have developed a FACS-based immunotranscriptional profiling system for identifying and isolating human embryonic stem cells (hESC) that express high levels of the cell surface antigens CD9 and GCTM-2 and have demonstrated that these cells represent a highly enriched population of hESC. This work has used multiple hESC lines (MEL1, HES2 & H9) and culture conditions (serum based culture, KOSR and MEFS, mTESR1 and matrigel) and combines immunotranscriptional and membrane polysome translation state analysis. These studies identified a refined genetic signature for hESC and have since been extended using multiple human induced pluripotent stem (iPS) cell lines. We are currently utilising these methodologies and information to produce and characterise new antibodies to novel cell surface markers for pluripotent cells for the detection and elimination of unwanted pluripotent cells.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S13: Dr Andre Choo
Senior Scientist, Stem Cells Group
Bioprocessing Technology Institute
Email: andre_choo@bti.a-star.edu.sg

Biography

Dr Andre Choo obtained his PhD in 2001 from the University of Technology Sydney focusing on the molecular engineering of antibody fragments and immunotoxins. He was also involved in the identification and characterization of a monoclonal antibody that induced apoptosis of λ -myelomas. This work has resulted in several patents which were recently granted in the US and Europe for its novel application and the formation of a spin-off company, Immune System Therapeutics Ltd, whose lead antibody has just successfully completed Phase I clinical trials in Australia.

Moving back to Singapore in 2002, he together with Dr Steve Oh nucleated the Stem Cell group at the Bioprocessing Technology Institute (BTI) focusing on developing gold standards for the characterization of human embryonic stem cells (hESC) and establishing scalable cell expansion technologies for regenerative medicine. Their group has been actively involved in developing serum-free and feeder-free culture platforms, generation of antibodies to novel cell surface antigens, understanding the signaling pathways controlling pluripotency and establishing new methods for hESC expansion in suspension. He currently holds the position of Senior Scientist and has been involved in more than 30 peer-reviewed publications/book chapters and 6 patent filings since entering into the field of hESC.

Abstract

Characterization Of Prohibitin As A Novel Surface Marker On Human Embryonic Stem Cells And Induced Pluripotent Stem Cells

Human embryonic stem cells (hESC) and induced pluripotent stem (iPS) cells are pluripotent cells with the potential to proliferate indefinitely in culture, but still retain their capacity for differentiation into a wide variety of cells. Our group has previously raised a panel of monoclonal antibodies (mAbs) specific to cell surface markers on hESC. Two of the clones identified (mAb 375 and mAb 529) binds to prohibitin (PHB) on hESC and iPS cells. PHB is a highly conserved protein in eukaryotic cells and is present in multiple cellular compartments such as the mitochondria, nucleus and plasma membrane. Its roles include acting as a chaperone protein in the mitochondria and modulating cell proliferation in cancer cells. However to date, the function of PHB on the cell surface of cells has not been defined.

In this study, the reactivity of antibodies to PHB on the cell surface of hESC and iPS cells was strongest in the undifferentiated state. Reactivity was significantly reduced when the cells were differentiated to embryoid bodies (EB). Furthermore, both mAb 375 and mAb 529 had no reactivity with embryonal carcinoma cells. By immunocytochemistry, we observed the PHB localizes to the nucleus during differentiation following deprivation of FGF-2. This was accompanied by the down-regulation of MAPK activity. Surprisingly, this down-regulation of PHB expression on the cell membrane can be reversed with FGF-2 addition following short term deprivation. This transient phenotype was abolished following longer term deprivation. Hence, these interesting preliminary findings warrant further investigation to elucidate the functional role of PHB in undifferentiated cells. In conclusion, we have identified PHB as a novel surface marker on pluripotent stem cells which can potentially be exploited for the enrichment or removal of undifferentiated hESC and iPS cells using the specific mAbs generated.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S14: A/Professor Jane Visvader
VBCRC Laboratory Head
Walter and Eliza Hall Institute of Medical Research
Email: Visvader@wehi.edu.au

Biography

Jane Visvader carried out her PhD studies in the Department of Biochemistry, University of Adelaide with Professor Robert Symons. She then went to the Salk Institute as a postdoctoral fellow in Prof Inder Verma's laboratory to work on the c-fos and c-jun oncogenes, followed by Prof Stuart Orkin's laboratory at the Children's Hospital in Boston to pursue transcription factors that regulate haematopoietic lineage commitment and differentiation. In 1997, she was recruited as a Group Leader to the Victorian Breast Cancer Research Consortium, based at the Walter and Eliza Hall Institute, to establish a laboratory focused on mammary gland development and dysregulated pathways leading to breast oncogenesis. In 2010 she was appointed as Joint Head of a new Division on Stem Cells and Cancer at WEHI. This Division will extend its studies to include other epithelial tumours, using paradigms established for breast tissue to further understand the development of different solid tumour types.

Abstract

Delineation Of The Mammary Epithelial Hierarchy And Cell Types Predisposed To Breast Oncogenesis

To further understand relationships between 'cells of origin' and cancer stem cells in breast cancer, it is necessary to dissect the normal mammary epithelial hierarchy. We have isolated discrete populations of mouse mammary epithelial cells on the basis of cell-surface markers and defined populations that are highly enriched for mammary stem cells as well as luminal progenitor cells. Analysis of different mouse models of mammary tumorigenesis using syngeneic transplantation assays has revealed potential 'cells of origin' in preneoplastic tissue and the presence of a definitive cancer stem cell subset in different mouse mammary tumors. These studies have now been extended to human breast tissue, leading to the identification of functionally analogous epithelial subsets.

The ovarian hormones estrogen and progesterone are known to profoundly influence breast cancer risk. Modulation of their levels through ovarian ablation or chemoprevention strategies significantly decreases breast cancer incidence. Conversely, there is an increased risk of breast cancer associated with pregnancy in the short-term. The cellular mechanisms underlying these observations, however, are poorly defined. We demonstrate that mouse mammary stem cells (MaSCs) are highly responsive to steroid hormone signalling, despite lacking the estrogen and progesterone receptors. Ovariectomy markedly diminished MaSC number and outgrowth potential in vivo. In contrast, pregnancy led to a large but transient increase in MaSC numbers. This augmented MaSC pool indicates a cellular basis for the short-term increase in breast cancer incidence that accompanies pregnancy. Overall, these findings suggest that breast cancer chemoprevention may in part be achieved through suppression of MaSC function.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S15: Dr Kishore Bhakoo

Head, Translational Molecular Imaging Group
Singapore Bioimaging Consortium
Email: kishore_bhakoo@sbic.a-star.edu.sg

Biography

Kishore Bhakoo obtained his BSc from the University of Kent at Canterbury in Medical Biochemistry (1978) and received his PhD from Institute of Neurology, University of London in 1983, with a thesis defining the inflammatory processes following cerebral stroke. He completed his postdoc training at the Ludwig Institute for Cancer Research (1986). In 1992 he was appointed a Wellcome Research Fellow at Royal College of Surgeons, Institute for Child Health, London, where he used Magnetic Resonance Spectroscopy for metabolic profiling of CNS tumours, specifically the role of oncogenes on cellular metabolism. Kishore was appointed as a Staff Scientist and University Research Lecturer at the MRC Magnetic Resonance Spectroscopy Unit, Department of Biochemistry, University of Oxford (1996), where he developed cell-based disease models of the CNS, for NMR spectroscopic analysis. He was also a Lecturer in Medical Biochemistry at Corpus Christi College, Oxford. In 2002, Kishore returned to London as a MRC Group Head and Senior Lecturer at the MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, to lead the Stem Cell Imaging Group. The group developed and implemented a programme of molecular imaging in preclinical models directed towards improving our understanding of stem cell migration in the context of the whole organism, in different tissues including the brain, spinal cord and heart.

More recently (2009), Kishore was appointed as the Head of the Translational Molecular Imaging Group, based within the Singapore Bioimaging Consortium (SBIC), where he is developing multi-modal imaging technologies to allow the monitoring of stem cell-based therapies, inflammatory processes and to interrogate cancer biology.

Abstract

Assessing Stem Cell Efficacy In Vivo Using Multi-Modal Imaging

Stem cells have significant therapeutic potential to replace diseased cells. The monitoring of cellular grafts, non-invasively, is an important aspect of the ongoing efficiency and safety assessment of cell-based therapies. Magnetic resonance imaging methods are potentially well suited for such an application as they produce non-invasive 'images' of opaque tissues. For transplanted stem cells to be visualised and tracked by MRI, they need to be tagged so that they are 'MR visible'. We are developing and implementing a programme of Molecular Imaging in preclinical models that is directed towards improving our understanding of stem cell behaviour in the context of the whole organism.

In order to achieve these goals we are engineering novel MRI contrast agents and developing specific tagging molecules to deliver efficient amounts of contrast agents into stem cells. The intracellular contrast agents are based on either superparamagnetic nanoparticles, such as polymer-coated iron oxide, or other paramagnetic MR contrast agents.

With its ability to precisely target cell delivery, track cell migration and non-invasively evaluate living subjects over time, this technique will help to bridge the gap between bench and bedside.

Development of multimodal imaging (MRI, PET, SPECT/CT and Optical) methodologies for monitoring implanted stem cells in vivo will greatly facilitate the clinical realisation and optimisation of stem cell based therapies.

Moreover, these multi-modal methodologies will also be used to interrogate a number of other pathologies, such as the Immune system and Cancer.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S16: Dr Tamil Selvan Subramanian
Research Scientist
Institute of Materials Research and Engineering
Email: subramaniant@imre.a-star.edu.sg

Biography

Dr. Subramanian Tamil Selvan is a Research Scientist at the Institute of Materials Research and Engineering (IMRE) since September 2008. Prior to this, he was with the Institute of Bioengineering and Nanotechnology (IBN, Singapore) for close to 5 years. Dr. Subramanian studied Chemistry and received his Ph.D from Madurai Kamaraj University, India in 1992. He is a recipient of the Alexander von Humboldt (AvH, Germany, 1995–1997) and Japan Society for the Promotion of Science (JSPS, Japan, 1997-1999) fellowships. He is a member of Materials Research Society, Singapore. He was also a member of the American Chemical Society and the Royal Society of Chemistry (2007-2008). Dr. Subramanian serves as a Reviewer for the American Chemical Society, Wiley-VCH, RSC and Elsevier Publications (2000–Present). Recently, he has earned a place as one of the top 20% of reviewers for ACS journal, Langmuir.

His research interests include metal, magnetic, semiconducting and multi-functional nanoparticles for optical and bioimaging applications. Dr. Subramanian is an author of about 45 publications and 3 invited book chapters. He has acquired over 1200 citations and his h-index is 18. To his credit, he has 2 granted U.S. patents and 3 filed patent applications. He has recently organized a symposium on Nanomaterials for Bioimaging and Biosensing within ICMAT 2009 in Singapore. Currently, he is leading a project on "Multifunctional Nanoparticles for Multimodality Bio-imaging and Targeted Drug Delivery Applications", funded by A* STAR Joint Council Office (JCO) in collaboration with SBIC and IMB, Singapore.

Abstract**Multifunctional Fluorescent Nanoparticles for Bioimaging Applications**

Hybrid multifunctional nanoparticles (NPs) are emerging as useful probes for magnetic based targeting, delivery, cell separation, magnetic resonance imaging (MRI), and fluorescence-based bio-labeling applications. Assessing from the literature, the development of multifunctional NPs for multimodality imaging is still in its infancy state. This talk would focus on our current work aiming to develop various multifunctional NPs (composed of either quantum dots or rare-earth NPs, and magnetic NPs – iron oxide or gadolinium oxide, and an anti-cancer drug) for multimodality imaging in a number of clinical pathologies such as early cancer diagnosis and cellular trafficking in stem cell therapy and immunological interventions. The combination of MRI and fluorescence would ally each other in improving the sensitivity and resolution, resulting in improved and early diagnosis of the disease.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S17: Professor Caroline Rae
Professor of Brain Sciences
Prince of Wales Medical Research Institute
Email: c.rae@powmri.edu.au

Biography

Caroline Rae is a research scientist with particular interest in multidisciplinary brain research. She holds undergraduate and doctoral degrees from The University of Sydney and underwent further training at The University of Oxford as holder of the 1992 Australian Nuffield Fellowship. On her return to Australia she held a number of short term competitive research fellowships, establishing her research program in brain biochemistry and function, with particular emphasis on brain imaging approaches. In 2005 she was appointed Chair of Brain Sciences at The University of New South Wales, a cross-faculty position in interdisciplinary brain research. She is currently also director of POWMRI Imaging at The Prince of Wales Medical Research Institute and an Australian National Health and Medical Research Council Senior Research Fellow. She is company secretary to the Australian and New Zealand Society for Magnetic Resonance (ANZMAG) and UNSW Node director for the National Imaging Facility.

Abstract

Magnetic Resonance Approaches In Interdisciplinary Brain Research

The brain is a complex organ with many inputs and outputs and multiple functions. Magnetic resonance approaches provide a range of perspectives on the brain and, when coupled with other assessments, provide a valuable tool for the study of disorders of complex etiology. Magnetic resonance imaging is often central in crossdisciplinary studies due to its ability to "see" non-invasively inside the brain. It is imperative, for optimal outcomes to be achieved, that the collaborating researchers involved understand one another's language and perspective. This talk will illustrate some of the information that MR approaches can provide when accomplished in a genuinely cross-disciplinary and collaborative environment.

Speakers' Biography and Abstract

Speakers' Biography and Abstract

**S18: Dr Young-Tae Chang**

Head, Laboratory of Bioimaging Probe Development
Singapore Bioimaging Consortium
Email: chang_young_tae@sbic.a-star.edu.sg

Biography

Young-Tae Chang was born in Busan, Korea, in 1968. He studied chemistry in Pohang University of Science and Technology (POSTECH, Korea) and received his B.S. in 1991. After one and half years of army service in Korea, he started his graduate study at POSTECH and received a Ph.D. in 1997 under the supervision of Prof. Sung-Kee Chung, working on the divergent synthesis of all possible regioisomers of myo-inositol phosphates. He did his postdoctoral work with Prof. Peter Schultz at UC Berkeley and The Scripps Research Institute. In 2000, he was appointed assistant professor at New York University and promoted to associated professor in 2005. He received the NSF Career award in 2005 and his research interests have been chemical genetics, molecular evolution, and artificial tongues. In September, 2007, he moved to National University of Singapore and Singapore Bioimaging Consortium. He is running Medicinal Chemistry Program of NUS as leader, and Lab of bioimaging Probe Development. To revolutionize the bioimaging field, he recently developed "diversity oriented fluorescence library approach (DOFLA)" platform at NYU and is trying to fully materialize the power of the new approach in Singapore.

Abstract**LuminoGenomics Using Diversity Oriented Fluorescence Library Approach (DOFLA)**

With the successful result of Human Genome Project, we are facing the problem of handling numerous target genes whose functions remain to be studied. In chemical genetics, instead of using gene knock-out or overexpression as in conventional genetics, a small molecule library is used to disclose a novel phenotype, eventually for the study of gene function. While a successful chemical genetics work will identify a novel gene product (target protein) and its on /off switch, the small molecule complement, and thus chemical genetics promises an efficient "two birds with one stone" approach, the most serious bottleneck of modern chemical genetics is the step of target identification. The currently popular affinity matrix technique is challenging because the transformation of the lead compound into an efficient affinity molecule without losing the biological activity is not easy, requiring intensive SAR studies. To surrogate the well known problem, our group has developed a linker tagged library and has successfully identified multiple target proteins so far. While successful, the affinity matrix technique requires a breakdown of the biological system to pool the proteins into one extract, which inherently introduce a lot of artifacts, such as dilution and abolishing the biological environment, etc.

As the next generation of tagged library, we are currently developing fluorescence tagged libraries for in situ target identification and a visualization of the biological events using Diversity Oriented Fluorescence Library Approach (DOFLA). The basic hypothesis is DOFLA of the same fluorescence scaffold, but with various diversity elements directly attached around the core, may selectively respond to a broader range of target proteins in intact biological system and facilitate the mechanism elucidation and target identification. The high throughput strategy using colorful chemical genetics for stem cell study will be discussed.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S19: Dr William Hughes
The Garvan Institute of Medical Research
Email: w.hughes@garvan.org.au

Biography

Will Hughes studied Microbiology at Bristol University in the UK. Uninspired, he joined the British Army before studying for a Masters and then a Ph.D in the Genetics Department at Leicester University (UK). Here he studied the genetics of drug sensitivity in the yeast *S. cerevisiae*. He continued aspects this study on moving to the I.C.R.F. labs in London as a post-doc with Prof. Peter Parker. Here he identified the prototype of the SAC class of phosphatidylinositol-phosphate phosphatase and then cloned and characterized human Phospholipase D. It was at the I.C.R.F. that he first developed novel imaging techniques to establish where and when the activity of signalling molecules was required in a cell.

This is the focus of his subsequent research on moving to the Garvan Institute in Sydney (2002). He has established the role of phospholipase D in vesicle trafficking critical for insulin exocytosis (from pancreatic b-cells) and is currently determining novel regulatory steps controlling exocytosis of the glucose transporter GLUT4.

Abstract

Imaging Regulated Exocytosis: Total Internal Reflection Fluorescence Microscopy Of The Last Steps Of Glucose Transporter Exocytosis

The insulin-stimulated trafficking of GLUT4 to the plasma membrane in muscle and fat tissue constitutes a central process in blood glucose homeostasis. The tethering, docking and fusion of GLUT4 vesicles with the plasma membrane represent the most distal steps in this pathway and have been recently shown to be key targets of insulin action. However, it remains unclear how insulin influences these processes to promote the insertion of the glucose transporter into the plasma membrane. We have identified a previously uncharacterised role for cortical actin in the distal trafficking of GLUT4. Using high frequency total internal reflection fluorescence microscopy (TIRFM) imaging we show that insulin increases actin polymerisation near the plasma membrane. Disruption of this process inhibits GLUT4 exocytosis. Using TIRFM in combination with probes that could distinguish between vesicle transport and fusion we found that defective actin remodelling was accompanied by normal insulin-regulated accumulation of GLUT4 vesicles close to the PM but the final exocytotic fusion step was impaired. These data resolve multiple steps of the final stages of GLUT4 trafficking, demonstrating a crucial role for actin in the final stage of this process. These data and our latest discoveries will be presented.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



Dr Bing Lim
Senior Group Leader
Genome Institute of Singapore
Email: limb1@gis.a-star.edu.sg

Biography

Dr Bing Lim is Senior Group Leader for Stem Cell and Developmental Biology group at the Genome Institute of Singapore. Dr Lim's research interest has been centered around the biology of Stem Cells, beginning with hematopoiesis at University of Toronto and retroviral-mediated gene transfer into stem cells at Harvard Medical School where he is currently also Associate Professor of Medicine. More recently, using genomic approach in studying mouse and human embryonic stem cells, he has sought to identify genes and molecular determinants of Stemness, Self renewal, Pluripotency and Reprogramming. Dr Lim sits on several research, educational and ethics committee responsible for charting research focus and efforts in Singapore. He also sits on review committees for research grants in major international institutions and is on the editorial board of several research journals.

Abstract

Factors Modulating Reprogramming Of Somatic Cells To Pluripotent Stem Cells

Recent studies have shown that a co-expression of a set of transcriptional factors can stably alter the epigenome of a somatic cell to that of a cell with pluripotent properties. These results demonstrate dramatically that the mammalian genome is quite plastic. This plasticity is further emphasized by the fact that the factors are interchangeable. Here we discussed our studies demonstrating that the reprogramming factors are interchangeable (e.g. Klf4 can be replaced by Esrrb, Oct4 can be replaced by NR5a2). Most interestingly we showed that the quality of iPS cells can be affected by the combination of factors used. This raises the question whether one common mechanism underlies the reprogramming to ES cells or are there more than one reprogramming route toward regaining pluripotency, dependant on the factors used. It is noteworthy that all the reprogramming factors identified thus far are hooked, one way or the other, to the core ES pluripotency gene network. Thus one would predict that any gene whose perturbation resulted in ES cell loss of pluripotency will have a role in reprogramming.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S21: Dr Nick Barker
Hubrecht Institute
Email: n.barker@hubrecht.eu

Biography

Since completing his PhD in 1995, Dr Nick Barker has worked as a senior scientist in the laboratory of Prof Hans Clevers (Utrecht, the Netherlands) focusing on the Wnt signalling pathway in development and carcinogenesis.

Dr Barker initially studied the role of TCF transcription factors in initiating colon carcinogenesis (Barker et al. (1997) Science). More recently, his significant achievements include the discovery that a TCF target gene, Lgr5, specifically marks stem cells in adult tissues, including the intestine (Barker et al. (2007) Nature) and the hair-follicle (Barker et al. (2008) Nature Genetics).

Ongoing lineage tracing experiments in the stomach and mammary gland strongly indicate that Lgr5 is also a marker for stem cells in these tissues. Using Lgr5-EGFP-ires-CreERT2 mice to selectively induce deletion of the tumour suppressor gene in the intestinal stem cells it was recently proved that Lgr5+ve stem cells are the cell-of-origin of colon cancer (Barker et al. (2008) Nature).

Abstract

Lgr5 Stem Cells In Self-Renewal and Cancer

Lgr5 is a Tcf/ β -catenin (Wnt) target gene specifically expressed on crypt-base columnar cells located at the base of the intestinal crypts. Using in-vivo lineage tracing we have proven these cells to be the stem cells of the small intestine and colon. Using a similar strategy we also demonstrated that Lgr5 marks cycling stem cells in the hair-follicle and stomach. Ongoing lineage tracing experiments in several other tissues, including kidney and brain strongly indicate that Lgr5 is also a bona-fide marker for adult stem cell populations in these tissues. Using Lgr5-EGFP-ires-CreERT2 mice to selectively induce deletion of the APC tumor suppressor gene in the intestinal stem cells we recently proved that these Lgr5+ve stem cells are the cell-of-origin of colon cancer. This work revealed the presence of a minor population of Lgr5+ve cells within intestinal tumors, which are candidate stem cells fuelling the growth of the cancer (the cancer stem cells). Deletion of Lgr5 and the highly-related family member Lgr4 using inducible knock-out mice causes rapid stem cell death, implying an essential in-vivo role in maintaining self-renewal in the intestine.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S22: Dr Ng Huck Hui
Senior Group Leader
Assoc Director, Biology
Genome Institute of Singapore
Email: nghh@gis.a-star.edu.sg

Biography

Huck-Hui NG is currently a Senior Group Leader at the Genome Institute of Singapore.

Huck-Hui NG graduated from the National University of Singapore and obtained his PhD from the University of Edinburgh. He spent the next few years working at the Harvard Medical School as a Damon Runyon-Walter Winchell research fellow.

His lab is studying gene regulation in stem cells. Specifically, his group is using genome wide approaches to dissect the transcriptional regulatory networks in embryonic stem cells and to identify key nodes in this network. More recently, his lab has begun to investigate the reprogramming code behind the induction of pluripotency in somatic cells.

Abstract

Deciphering And Reconstructing The Embryonic Stem Cell Transcriptional Regulatory Network

Embryonic stem (ES) cells are characterized by their ability to self-renew and remain pluripotent. Transcription factors have critical roles in the maintenance of ES cells through specifying an ES cell-specific gene expression program. Deciphering the transcriptional regulatory network that describes the specific interactions of these transcription factors with the genomic template is crucial for understanding the design and key components of this network. To gain insights into the transcriptional regulatory networks in ES cells, we use chromatin immunoprecipitation coupled to ultra-high-throughput DNA sequencing (ChIP-seq) to map the locations of sequence specific transcription factors. These factors are known to play different roles in ES cell biology. Our study provides new insights into the integration of these regulators to the ES cell-specific transcription circuitries. Collectively, the mapping of transcription factor binding sites identifies new features of the transcriptional regulatory networks that define ES cell identity. Using this knowledge, we investigate nodes in the network which when activated, will jump-start the ES cell-specific expression program in somatic cells.

Speakers' Biography and Abstract

Speakers' Biography and Abstract



S23: Professor Robert (Bob) Williamson
Faculty of Medicine
University of Melbourne
Email: r.williamson@unimelb.edu.au

Biography

Professor Bob Williamson was appointed Professor of Molecular Genetics at St Mary's Hospital Medical School, Imperial College, University of London from 1976 until 1995, when he moved to Melbourne as Director of the Murdoch Institute and Professor of Medical Genetics. He retired in 2004, and now is an Honorary Senior Principal Fellow of the Murdoch Institute, the University of Melbourne, and Monash University. He has over 400 refereed career publications, including about 40 in Nature, Nature Genetics, Cell and Lancet. He was involved in the identification of genes for cystic fibrosis, Friedreich ataxia, craniofacial abnormalities, heart disease and Alzheimer disease. More recently he has taken a major interest in national science policy and medical and scientific ethics. He still helps a small research group working on stem cells, cystic fibrosis and ataxia. He is a Fellow of the Australian Academy of Science (where he is Secretary for Science Policy), a Fellow of the Royal Society, and an Officer of the Order of Australia.

Abstract

The Ethics Of Embryonic Stem Cell Research

In Australia, as in Singapore, there is debate about the ethics of embryo stem cell research. Although surveys demonstrate that the great majority of persons in Australia support stem cell medical research (including the use of ES cells), there are vocal groups that oppose embryonic stem cell research for three broad reasons.

1. The creation of ES cell lines requires the destruction of embryos.
2. ES cells have the potential to become embryos, and therefore deserve respect for this potential.
3. ES stem cell research represents a class of biomedical research involving reproduction will be used in the interests of rich countries against poor countries, men against women, and those with money against the poor. None of these arguments has equivalent ethical force to the statement that we have an obligation to conduct research that has the potential to benefit people with physical needs due to illness, whether inherited or acquired. To fail to perform research that could be of value to those with diseases such as cancer, cystic fibrosis or Parkinson disease is unethical. Provided research has been approved by research ethics committees, the arguments commonly used against ES cell research are at best weak, and at worst spurious.

Note