AGCTS NEWSLETTER NOVEMBER ISSUE 2015

Australasian Gene and Cell Therapy Society

Message from the President

Dear AGCTS Membership,

At our last Society Annual General Meeting in March 2014, the membership unanimously voted for **a name change to the Australasian Gene and Cell Therapy Society (AGCTS)** to reflect the broader interests of our society members in cell biology, particularly the use of stem cells in delivering gene medicines. The name change of our Society was finalised earlier this year, announced to our membership and affiliates via email (and our website can now be found at www.agcts.org.au).

My goal for our society is to improve the interaction between the cell therapy and gene therapy research communities in Australia and we are off to a good start with the exciting program developed for this conference.

I would like to acknowledge the enormous contribution of the AGCTS Conference Organising Committee who have volunteered their time to make the latest meeting a success. This year the AGCTS Executive Committee have partnered with Benitec Biopharma Ltd to assemble an exciting panel of invited International and National speakers. I'd like to take a moment to individually thank our VP Jim Vadolas, Treasurer Ann Simpson, Secretary Samantha Ginn, Exec Members Paul Gregorevic, Sharon Cunningham and Marguerite Evans-Galea, Ex-officio member Steve Wilton and Benitec Biopharma's Peter French and Carl Stubbings. I would also like to thank our 12 invited speakers for their participation in our conference proceedings, Mark Kay (Stanford University), Markus Grompe (Oregon Health Sciences University), Philippe Leboulch (University of Paris), Maria Kavallaris (CCIA), Christina Mitchell (Monash University), Melissa Little (Murdoch Childrens Research Institute), Peter French (Benitec), David Schaffer (University of California USA), Anand Hardikar (University of Sydney), Marnie Blewitt (WEHI), Kevin Francis (PerkinElmer USA) and David Suhy (Benitec USA). Looking toward our next conference, we will likely meet in Sydney at the UTS Aerial Conference Centre again at the end of April 2017.

I am very proud to be leading a dedicated society which has continued to provide advocacy for Australian research in the development of molecular

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medicines, cell and gene therapies. Our membership works tirelessly to reduce the impact of some of Australia's largest health problems and improve the well being of those diagnosed with acquired or genetic disease. Focus areas of our membership are broad and include cancer, viral infection (HIV, Hepatitis B & C), autoimmunity, immunodeficiency, diabetes, metabolic disease, blood, eye, ear and muscle disorders.

Although there have been considerable funding challenges of late, momentum is clearly building thanks to the commitment, perseverance and support from our researchers, clinicians, industry leaders, regulators and the public. The Executive Committee and I feel privileged to represent you and our sector in this exciting journey and witness first-hand the continued progress of our field into the clinic.

Finally, the AGCTS Executive is committed to promoting the growth and success of our membership. For example, the AGCTS Best Paper Prize seeks to acknowledge and reward the quality of research published by our young and senior members (see below for 2014 and 2015 prize winners to date).

I also welcome your suggestions for how we can strategically grow our membership in order to ensure the survival of our Society in years to come.

With warm regards,

Rosetta Martiniello-Wilks PhD
President, Australasian Gene Therapy Society www.agcts.org.au

"Best paper" Prize by an AGCTS Member

Congratulations to 2014 "best paper" prize winners (as above):

1. A/Prof Frank Alderuccio (Dept. Immunology, Monash University), for "Gene therapy delivery of MOG via haematopoeitic stem cell transfer induces MOG specific B cell deletion" (The Journal of Immunology);
2. Dr Kane Greer (Centre for Comparative Genomics, Murdoch University) for "Targeted Exon Skipping to Correct Exon Duplications in the Dystrophin Gene" (Molecular Therapy — Nucleic Acids);
3. Dr Claire Deakin (Gene Therapy Research Unit, Children's Medical Research Institute) for "Impact of next-generation sequencing error on analysis of barcoded plasmid libraries of known complexity and sequence" (Nucleic Acids Research).

Congratulation to the "best paper" prize winners for 2015 (Jan — June):

1. Dr Paul Gregorevic (Baker IDI) for "Development of novel activin-targeted therapeutics" (Molecular Therapy);
2. Prof Ann Simpson (UTS) for "Reversal of diabetes following transplantation of an insulin-secreting human liver cell line: Melligen cells (Molecular Therapy—Methods & Clinical Development).

Don't Forget to Send us Your Papers!

To encourage our early and not so early career scientists and disseminate information among members, the AGCTS Executive is offering up to two $250 awards twice a year. These will be offered in each 6 month period of a calendar year to the first or corresponding author of a gene therapy or RNA therapeutic publication. Only current AGCTS members may apply and the award is open to all AGCTS members (the young as well as the wise). Please send your paper details to our Secretary at sginn@cmri.org.au for consideration.

2015 Premier's Awards for Outstanding Cancer Research

Geoff McCowage, Belinda Kramer and Ian Alexander were awarded the Excellence in Translational Cancer Research Award ($20,000) at the recent 2015 Premier's Awards for Outstanding Cancer Research, hosted by the Cancer Institute NSW:

http://www.cancerinstitute.org.au/events/i/2015-premiers-awards-for-outstanding-cancer-research

https://youtu.be/O_I7RL5nZYE

Dr McCowage is a paediatric oncologist at the Sydney Children's Hospital Network (SCHN) Westmead, with a particular interest in neuro-oncology and sarcomas of bone and soft tissue. He is SCHN Westmead's Principle Investigator for clinical trials of the international Children's Oncology Group.

The Children's Cancer Gene Therapy team started a Phase I study in June 2012 for the treatment of paediatric brain tumours using a combined gene therapy/pharmacological approach. The approach involves gene modification of haematopoietic stem cells, so that the cells produce a DNA repair protein and become resistant to the harmful effects of methylating chemotherapy. This trial is a world-first study demonstrating the safety and feasibility of infusing gene-modified haematopoietic stem cells in children. Success is due to the combined efforts and expertise of clinician researchers at The Children's Hospital at Westmead, cancer and genomics researchers from the Children's Cancer Research Unit and Gene Therapy Unit of the Kids Research Institute (KRI), members of Sydney Cell and Gene Therapy, RadPharm Scientific, as well as ongoing support and funding from The Kids Cancer Project.

From left: Professor Ian Alexander (Gene Therapy Research Unit, Kids Research Institute and Children's Medical Research Institute); Assoc Professor Jennifer Byrne, Dr Geoff McCowage and Dr Belinda Kramer (Children's Cancer Research Unit, Kids Research Institute); Prof Roger Reddel, (Director, Children's Medical Research Institute and head of the Cancer Research Unit); Assoc Prof Luce Dalla Pozza, (Head of the Oncology Unit at The Children's Hospital at Westmead). All are members of the Kids Cancer Alliance.

Dates for your Diaries

The BSGCT annual conference will be held in London in April 2016. More details will be available at www.bsgct.org closer to the meeting date.

The 19th Annual ASGCT meeting will take place in Washington DC from 4 to 7 May 2016. Please visit the ASGCT website at www.asgct.org for more details.

The International Society for Cellular Therapy annual meeting will be held in Singapore from 25 to 28 May, 2016. For more details, see www.celltherapysociety.org.

The 7th International Conference on Drug Discovery and Therapy" and 4th Biotechnology World Congress will both be held in Dubai UAE, from 15 to 18 February, 2016. Please visit www.icddt.com and www.biotechworldcongress.com for more details.

The 9th Biennial AGCTS Conference

The time since our biennial meeting, held at University College, University of Melbourne on 29th April to 1st May 2015, seems to have flown by. With the help from our sponsors, we were able to invite an impressive lineup of International and National speakers; Professors Mark Kay, Markus Grompe, Philippe Leboulch, Christina Mitchell, Melissa Little, Maria Kavallaris and David Schaffer, A/Professor Anandwardhan Handikar, Drs David Suhy, Marnie Blewitt and Kevin Francis and Peter French. The meeting was opened with an acknowledgement to the traditional owners the Kulin Nation on which the University of Melbourne stands. Proceedings were opened by AGCTS President Dr Rosetta Martiniello-Wilks, pictured in the centre of the front row.

Again, with help from our sponsors, we were able to award prizes to our student members Timothy Colgan (VIC), Astrid Glaser (VIC), Rosaline Habib (NSW) and Lauriel Earley (USA). Dr Chantelle McIntyre (School of Paediatrics and Reproductive Health, University of Adelaide) received the Panos Ioannou Young Investigator Award. Professor Christina Mitchell presented an excellent Greg Johnson Memorial Oration, and following the election at the Annual General Meeting, the Executive Committee remained unchanged.

The conference abstracts have been published in the Journal of Gene Medicine, and can be found in the following link:
http://onlinelibrary.wiley.com/doi/10.1002/jgm.2834/abstract

National and International delegates at the 9th Biennial Australasian Gene and Cell Therapy Society Meeting, 29th April to 1st May 2015, University College, University of Melbourne, Victoria.

Meeting Sponsors, without whom this conference would not have been possible

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Dr Ee Cheng Khor and Anna Megalogenis from Sigma-Aldrich

Ivor Butler, STEMCELL Technologies

Michael Keir from Lonza, with Aurelien Bore, Wei Lee and Astrid Glaser

Greg Johnson Memorial Oration by Professor Christina Mitchell

Regulation of PI3K/Akt-dependent breast cancer growth and metastasis

Lisa M. Ooms[1], Lauren C. Binge[1], Parvin Rahman[1], James R. Conway[2], Daniel T. Ferguson[1], Clare G. Fedele[1], Rajendra Gurung[1], Jessica L. Vieusseux[1], Ryan C. Chai[1], John T. Price[1], Tony Tiganis[1], Paul Timpson[2], Catriona A. McLean[3], Christina A. Mitchell[1]

[1] Department of Biochemistry and Molecular Biology, Monash University, Clayton, Victoria 3800, Australia; [2] Invasion and Metastasis Group, The Kinghorn Cancer Centre, Garvan Institute of Medical Research, Darlinghurst, New South Wales 2010, Australia. [3]Department of Anatomical Pathology, Alfred Hospital, Prahran, Victoria 3181, Australia

Professor Christina Mitchell, Academic Vice-President and Dean, Department of Biochemistry and Molecular Biology, Faculty of Medicine, Nursing and Health Sciences, Monash University.

Breast cancer is the most common cancer in women. However, despite advances in treatments metastatic disease remains the leading cause of breast cancer death. The phosphoinositide 3-kinase (PI3K) signalling pathway is frequently hyperactivated in breast cancer and represents a significant target for novel therapies. PI3K-generated PtdIns(3,4,5)P_3 activates Akt which promotes breast cancer cell proliferation. Akt1, but not Akt2, inhibits cell migration and metastasis. PI3K signaling is terminated by phosphoinositide phosphatases such as the tumor suppressor, PTEN, which hydrolyzes PtdIns(3,4,5)P_3 to form PtdIns(4,5)P_2 and thereby suppresses Akt signaling. PTEN loss is observed in 30-40% of sporadic cases of breast cancer associated with hyperactivation of Akt signaling and tumor progression. Interestingly, an alternative pathway for the termination of PI3K signaling is mediated by inositol polyphosphate 5-phosphatases (5-phosphatase), which degrade PtdIns(3,4,5)P_3 to form PtdIns(3,4)P_2, and in turn 4-phosphatases such as INPP4B hydrolyze PtdIns(3,4)P_2 to form PI(3)P. Although we and others have identified INPP4B as a tumor suppressor in breast cancer, there is little evidence that any of the ten mammalian 5-phosphatases suppresses PI3K/Akt signaling in breast cancer. Here we identify an inositol polyphosphate 5-phosphatase suppresses oncogenic Akt signaling in breast cancer and shows loss of expression in triple negative breast cancers. Using mouse knockout models and shRNA knockdown in breast cancer cell lines, we demonstrate loss of the 5-phosphatase leads to enhanced cell proliferation and tumour growth, but paradoxically suppression of metastasis via regulation of cell migration and invasion. Collectively these studies identity a novel regulator of PI3-kinase signalling in breast cancer.

Dr Chantelle McIntyre: Recipient of the 2015 Panos Ioannou Young Investigator Award

On April 14th, 2005 the Executive Members of the AGTS on behalf of its Members established the Panos Ioannou Young Investigator Award in recognition, appreciation and thanks to Panos for his founding, passionate and sustained support for young scientists in the society.

At the closing session of the 9th AGCTS meeting, Dr Chantelle McIntyre (School of Paediatrics and Reproductive Health, University of Adelaide) received the Panos Ioannou Young Investigator Award for conference travel expenses up to the value of $2000, presented by AGCTS Vice President Jim Vadolas (see photo at right).

AGCTS Student Prizes

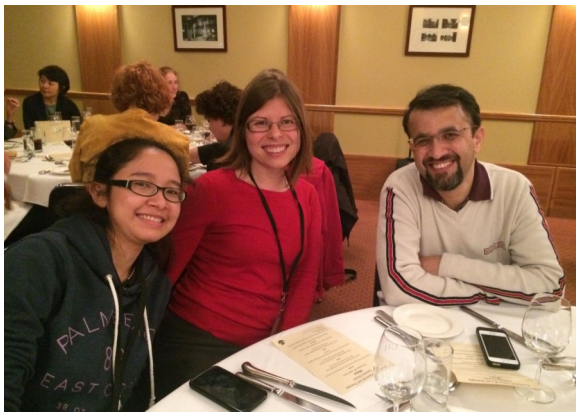
Congratulations to our AGCTS student members for their presentations (from left): Timothy Colgan (Baker IDI Heart and Diabetes Institute, Melbourne) was awarded the $250 Journal of Gene Medicine Student Presentation Prize (oral); Rosaline Habib (UTS Translational Cancer Research Group, Sydney) was awarded the $250 AGCTS Student Presentation Prize (oral); Lauriel Early (Oregon Health & Science University, Portland) was awarded the $250 Journal of Gene Medicine Student Presentation Prize (oral); Astrid Glaser (Murdoch Childrens Research Institute, Melbourne) was awarded the AGCTS Student Presentation Prize (poster).

Conference Dinner at University House

From left, Invited speaker Professor Philippe Leboulch (Harvard Medical School), AGCTS President Dr Rosetta Martiniello-Wilks (UTS) and Bob Atwill (Benitec)

From left, PhD candidate Anais Amaya (CMRI), AGCTS Life member Professor Ian Alexander (CMRI), Invited speaker Professor Mark Kay (Stanford University), Dr Grant Logan (CMRI) and Invited speaker Professor Markus Grompe (Oregon Health & Science University)

From left, Arron Magno (Lyons Eye Institute), Dr Glen Reid (Asbestos Diseases Research Institute), PhD candidate Hannah Pearce (Baker IDI), PhD candidate Rosaline Habib (UTS), Dr Rachael Richardson (Bionics Institute) and PhD candidate Lauriel Earley (Oregon Health & Science University)



From left, PhD candidates Tiwaporn Nualkaew and Astrid Glaser (both from Cell and Gene Therapy, MCRI) and Invited speaker Associate Professor Anandwarhan Hardikar (NHMRC Clinical Trials Centre)

Professor Ann Simpson (AGCST Treasurer) and Professor Steve Wilton (past President and ex-officio Committee member) with wife Sandy Wilton

From left, PhD candidate Niall Keegan, Dr May Aung-Htut, Dr Kristen West, and PhD candidate Ianthe Pitout (all from the Centre of Comparative Genomics, Murdoch University)

From left, Dr Anna Baoutina (National Measurement Institute) and PhD candidate Hwee Ong (Bruce Lefroy Centre, MCRI)

From left, Dr Belinda Kramer (Children's Cancer Research Unit, The Children's Hospital at Westmead) and members of the Gene Therapy Research Unit (Children's Medical Research Institute and The Children's Hospital at Westmead)

GENE THERAPY: IN THE NEWS

Towards the clinic - liver-targeted gene therapy

Professor Ian Alexander, AGCTS Life Member and head of the Gene Therapy Research Unit at the Children's Medical Research Institute (CMRI) and The Children's Hospital at Westmead (CHW).

Professor Ian Alexander spoke to the media recently about the research being undertaken in his laboratory towards the development of clinical vectors for urea cycle disorders, as an alternative to liver transplantation. The group has been focusing on adeno-associated viral (AAV) vector-mediated gene delivery to the liver, with the hope that one day this will replace the need for liver transplantation, or used as a bridging therapy. The media release coincided with the Jeans for Gene Day CMRI fundraising campaign, with news articles appearing in Daily Telegraph (Sydney), Herald Sun (Melbourne), Courier Mail (Brisbane) and the Adelaide Advertiser (Adelaide). An interview also aired on Channel Seven:

http://www.cmri.org.au/News/Videos/Channel-7-News-Prof-Ian-Alexander-interview-07-08

"Sarepta Therapeutics Announces Collaborative Research Agreement with Murdoch University Researchers Steve Wilton and Sue Fletcher"

Professor's Sue Fletcher and Steve Wilton, Murdoch University, Perth, WA.

On the 1st of October, Sarepta Therapeutics (NASDAQ:SRPT), a developer of innovative RNA-targeted therapeutics, announced a four-year collaborative research agreement to establish the Sarepta Translational Laboratory with Murdoch University, Perth, Western Australia. The Laboratory, led by professors Steve Wilton and Sue Fletcher, will explore the applicability of the Company's phosphorodiamidate morpholino oligomer (PMO) technology for disease targets beyond Duchenne muscular dystrophy (DMD), such as cystic fibrosis and spinal muscular atrophy. The first project to be targeted as part of the collaboration is multiple sclerosis. More information can be found in the following link:

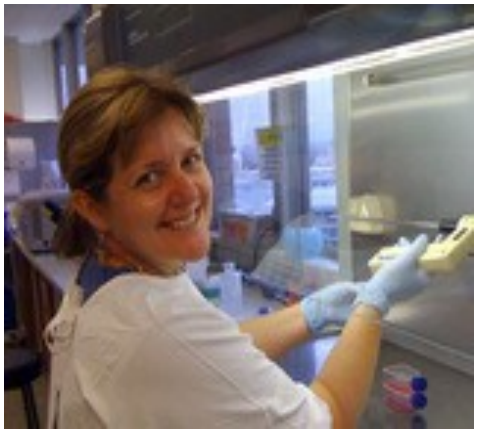
http://media.murdoch.edu.au/university-joins-forces-with-us-pharmaceutical-company-to-improve-drug-

SOCIAL MEDIA

The AGCTS is launching its Blog!

Gene and cell therapy is a rapidly growing field with significant potential for application in the clinic for many diseases. With mini-organs now being grown from patient-derived induced pluripotent stem cells, the capacity for modelling disease and evaluating the potential of gene correction has catapulted this field into the spotlight. So it's important to talk about what you do – with everyone. Not just your lab mates, colleagues and collaborators, but also the broader scientific community, industry leaders, Parliamentarians and most of all, the general public.

One way you can engage more broadly is to blog about your research.



The AGCTS has recently launched its blog and you are invited to contribute! We welcome articles that discuss your latest research or share the goals of your research program. You might want to share your career journey with students and fellows, or the latest technique you have developed. Perhaps you have a strong view about a recent publication or a meeting you attended – personal perspectives are welcome. A quick online search will provide plenty of great tips on good science communication. Contact us if you are keen to contribute!

Dr Marguerite Evans-Galea, Murdoch Childrens Research Institute

SAVE THE DATE!

The 10th Biennial AGCTS Conference will be held in Sydney, NSW from the 24th—26th May 2017

Australasian Gene and Cell Therapy Society