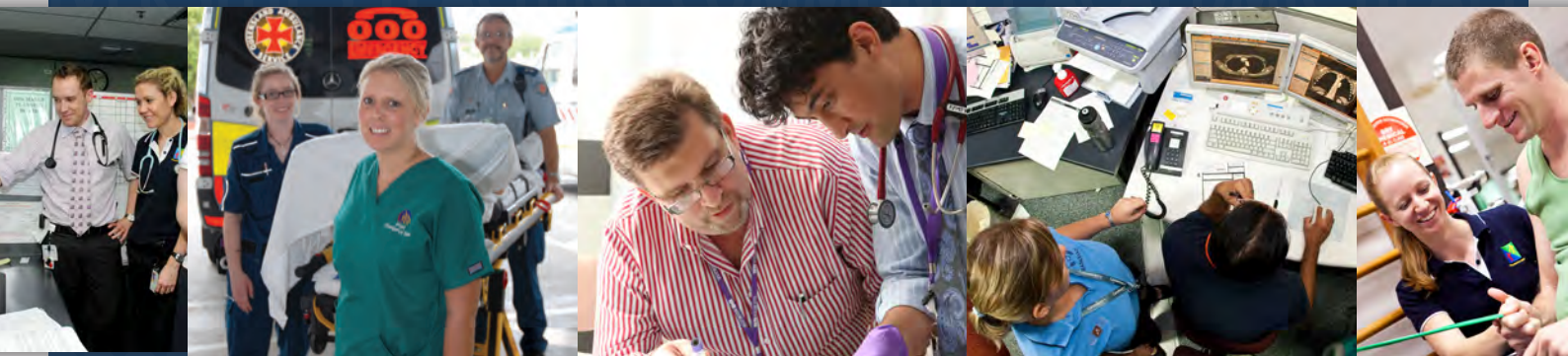


PRINCESS ALEXANDRA HOSPITAL

Health Research Alliance

in transforming care



2014 PAH Health Symposium
4 - 8 August • Brisbane Australia



Table of Contents

	Page
Welcome	3
Kurt Aaron Oration	4
Kurt Aaron Orator 2014	5
Past Kurt Aaron Orators	5
Past Young Investigator Award and Poster Expo Winners	6
The Covidien Prize for General Surgical Trainee Research	7
Past Covidien General Surgeons Surgical Trainee Research Winners	7
Award for Excellence in Resident Education	8
Past Award for Excellence in Resident Education Recipients	8
Award for Excellence in Allied Health Clinical Education	9
Past Award for Excellence in Allied Health Clinical Education Recipients	9
Award for Excellence in Nursing Education	9
Past Award for Excellence in Nursing Education Recipients	9
PA Health Symposium Speakers 2014	10
Information for Delegates and Presenters	41
Princess Alexandra Hospital Venue Map Layout	42
Program	
Monday	43
Tuesday	44
Wednesday	46
Thursday	48
Friday	50
Author Index	51
PAH Health Symposium Young Investigator Award Abstracts	52
Notes	98

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“Health Research Alliance in transforming care”

On behalf of the Organising Committee, I welcome you to the 2014 PAH Health Symposium, which carries the theme: Health Research Alliance in transforming care.

2014 marks the first anniversary of the Translational Research Institute and the second anniversary of Diamantina Health Partners (DHP), Queensland’s first academic health science centre. These strategic developments bring together research, teaching and treatment, to consolidate the Princess Alexandra Hospital campus at the forefront of shaping the future of health in Queensland, nationally and internationally.

Central to the Symposium program is Professor Boris Bastian, University of California, San Francisco, this year’s International Fellow. As an eminent clinical scientist, he will illustrate in his keynote address how interdisciplinary and global partnerships have advanced the understanding of the causes of skin cancers and are translating this new knowledge to novel therapies for their treatment. Professor Bastian is also this year’s Kurt Aaron Orator.

The core program this year is aligned to the flagship themes of DHP, whose mission it is to achieve better health globally through the integration of clinical care, research and education. The DHP themes are:

- Cancer
- Chronic Disease
- Trauma and Recovery
- Immunity and Inflammation
- Mental Health
- Health Innovation.

Symposium week will feature engaging educational forums covering mass media and consumer alliance. The program will be augmented by sessions on new technologies, by oral and poster communication, and by awards and will culminate in a special session entitled PAH Health Odyssey, showcasing a rich history of transforming health care delivery on campus.

Please come along to engage and enjoy a stimulating week of educational, research and clinical activities, reflective of the partnerships within the PAH community.

Professor Ken Ho
Convenor

Kurt Aaron Oration



Kurt Aaron

OBE (1976) MD Frankfurt (1935) LRCP LRCS Edin (1937) LRFP&S Glasgow (1937) MRCP Edin (1951) MRACP (1961) FRCP Edin (1971) FRACP (1971)

Born - 27th February, 1909

Died - 23rd August, 1986

Dr Kurt Aaron was born in Hamburg in 1909 and died in Brisbane in 1986. After receiving his secondary schooling at the Helmholtz Ober-Real Schule in Frankfurt, he attended universities in Munich and Cologne and graduated MD University of Frankfurt in 1935, completing his clinical undergraduate studies at the Stadtischen Krankenhaus in Frankfurt.

With his widowed mother, Kurt left Hitler's Germany in 1936, studied in Glasgow to qualify LRFP&S (Glasgow) and LRCP LRCS (Edin) in January, 1937. He then came to Australia and undertook his internship at the Brisbane General (now the Royal Brisbane) Hospital. In 1939, Kurt married Miss Sheila Cato, a nursing sister, and in time they raised five good looking children, three girls and two boys.

On completion of his senior residency in 1941 (and after the threat of being conscripted into the Civil Construction Corps in Central Australia) Kurt was directed under government wartime manpower control to a recently vacated medical practice in East Brisbane, and eventually established from that one man practice, the South Brisbane Clinic, a group practice of general practitioners and specialists. He was also appointed Assistant Visiting Physician to the BGH at that time. At the age of 42, Kurt went to Edinburgh where he gained his membership of their RCP. Ten years later, in 1961, he obtained the MRACP by examination and in 1971 was elected to Fellowship of the RACP and of the RCP (Edin).

In 1956, by now a Senior Visiting Physician to the RBH, Kurt Aaron was appointed as one of the original senior visiting physicians to Princess Alexandra Hospital, newly established as a teaching hospital at South Brisbane. It was there that he displayed his considerable skills in patient care, student teaching, residency training and hospital affairs. He wrote papers on matters scientific; other publications reflected his sensitivity to the importance of emotional factors in the causation of symptoms. He had a particular interest in renal disease, held membership of the Australasian College of Nephrology, and in 1968 was instrumental in obtaining a Kiil dialyser for PAH, as a donation from the Rotarians.

Kurt was considerably involved in workers compensation matters, being the Inaugural Chairman of the General Medical Board of the Workers Compensation Board of Queensland from 1967 to 1979. After his retirement as Visiting Physician in 1968, he continued to actively participate in hospital affairs, serving on the South Brisbane Hospitals Board from 1974 to 1979, assuming Chairmanship of the Princess Alexandra Hospital Society (the Hospital's social and educational Society) in 1973 and continuing as a committee member from 1974-1985, receiving life membership in 1978. In acknowledgement of his unique contribution to the PAH his friends had his portrait painted and hung in the medical staff common room on the 18th July, 1985 - only the second person to be so honoured at that time.

Outside of medical activities, Kurt was very involved in Rotary from 1957, being President in 1963 and 1964. Living in a spacious Queenslander with typical wide verandas, Kurt and his wife, Sheila entertained generously using their home for fund raising and other community social activities. In 1976 his work both in medicine and in citizenship was recognised with the award of an O.B.E.

Some years before his own death, Kurt was saddened by the loss of his wife. He continued in medical practice until the day before his death. His eulogy was delivered by his long-time colleague, Dr Keith Cockburn, to whom I am indebted for much of the information relating to Kurt Aaron's early years in this country. Keith Cockburn concluded with these words "He was a great citizen, a great father, a great physician and a great friend".

Kurt Aaron Orator 2014



Professor Boris Bastian

Dr Boris Bastian received his MD degree and Dr. med degree from the Ludwig-Maximilian University of Munich. After completing a residency in dermatology at the University of Wurzburg, he received additional training in dermatopathology and completed a postdoctoral fellowship at the University of California, San Francisco before joining the institution's faculty and starting his research laboratory at UCSF's Helen Diller Family Comprehensive Cancer Center. In 2010 he moved to the Memorial Sloan-Kettering Cancer Center to become Chairman of the Department of Pathology.

In 2011 he returned to UCSF, where he is currently the Leader of the Cutaneous Oncology Program and the Gerson and Barbara Bakar Distinguished Professor of Cancer Biology. His laboratory is in the Helen Diller Family Comprehensive Cancer Center and he has clinical responsibilities in the Dermatopathology Section of the Departments of Dermatology and Pathology, where he directs the molecular diagnostic laboratory of the Dermatopathology Section.

Dr Bastian's research focuses on the molecular genetics of cutaneous neoplasms, with a particular emphasis on the discovery of genetic alterations useful for diagnosis, classification, and therapy. His laboratory has contributed to the discovery of several genetic alterations in melanocytic neoplasia that are relevant for therapeutic and diagnostic purposes and for a molecular taxonomy of melanocytic neoplasia.

Past Kurt Aaron Orators

1997	The Most Reverend Peter Hollingworth AO
1998	Dr Owen Harris
1999	Dr Neville Davis
2000	Prof David Theile
2001	Dr Sam Mellick
2002	Prof Russell Strong
2003	The Honourable Justice Paul de Jersey
2004	Dr (Colonel) John Taske
2005	Prof John Pearn
2006	Prof Ian Frazer
2007	Prof Richard Larkins
2008	Prof Michael Lucey
2009	Colonel Georgeina Whelan
2010	Prof Matt Sanders
2011	Prof John Wass
2012	Prof Paul Stewart
2013	Professor Stephen Durham

Past Young Investigator Award and Poster Expo Winners

2010

YIA Research Presentation: Clinician	Dr Eduardo Pimenta
YIA Research Higher Degree	Kelly Brooks
YIA Poster Prize: Clinical	Dr Lillian Wong
YIA Poster Prize: Basic Science	Dr Michael Wagels
YIA People's Choice	Cassandra Budden / Michaela Antonia

2011

YIA Junior Scientists: Clinical	Paul Lee
YIA Junior Scientists: Basic	Dr Tony Kenna
YIA Research Students: Clinical	Graeme Rich
YIA Research Students: Basic	Kelly Brooks
Poster Expo: Clinical	Dr Rathika Krishnasamy
Poster Expo: Basic Science	Julie Burel
Poster Expo: People's Choice	Dr Amelia Granger

2012

YIA Junior Scientists: Clinical	Dr Lachlan Marshall
YIA Junior Scientists: Basic	Dr Linda Rehaume
YIA Research Students: Clinical	Dr Christine Jellis
YIA Research Students: Basic	April Choi
Poster Expo: Clinical	Dr Ingrid Hickman
Poster Expo: Basic Science	Dr Helen Benham
Poster Expo: People's Choice	Dr Peter Hendy

2013

YIA Junior Scientists: Clinical	Emma Taylor
YIA Junior Scientists: Basic	Linda Gallo
YIA Research Students: Clinical	Emma McMahon
YIA Research Students: Basic	Steven Taylor
Poster Expo: Clinical	Veronique Chachay
Poster Expo: Basic Science	Jana McKaskill
Poster Expo: People's Choice	Nathan Close

The Covidien Prize for General Surgical Trainee Research

The Covidien Prize Competition for general surgical trainee research commenced during PAH Week in 2006, the Golden Jubilee of Princess Alexandra Hospital, under the auspices of the PAH General Surgeons Group. It was certainly a success that year and has been held every year since, always during PAH Week, with up to 10 registrars presenting their projects each year.

The purpose of this competition is to stimulate innovative thinking and skilful presentation of research, both laboratory and clinical surgical research, in our general surgery trainees, and to give them a local forum to present their studies. The emphasis is towards junior trainees who may not have previously done any research or made presentations of their work. The format is a 10-minute Power Point presentation followed by up to 5 minutes of questioning by an erudite judging panel composed of PAH surgeons. This panel then selects winners for each of the two prizes at the end of the session.

Rather than reading an abstract, each submitted paper is audited by the impartial chairman individually in the preceding weeks, and is either rejected, or accepted for the competition with some expert advice on timing, structure and style. A single pre-competition audit is offered to all candidates. This process enhances the overall quality of the session without favouring any participant.

In former years before the company name change in 2010, this competition was sponsored generously by Tyco Healthcare. Their title has now become Covidien Healthcare and the very generous sponsorship continues, with an annual prize of \$1500 to the trainee presenting the best paper overall. In addition Professor Daryl Wall left a sum of money (now administered by the PAH Foundation) which finances a second prize of \$1000 each year for the trainee presenting the best clinical paper. It is therefore possible for a single trainee to win both prizes. The winners' names are engraved year by year on a plaque which hangs in the Doctor's Lounge at PAH.

Past Covidien General Surgeons Surgical Trainee Research Winners

- | | |
|-------------|---|
| 2008 | Dr Ben Lancashire
“How do the results of fundoplication compare between consultants and trainees at PAH?” |
| 2009 | Dr Jodi Hurst
“Five year survivors following oesophagectomy, and predictors of survival.” |
| 2010 | Dr Adam Frankel
“Morbidity of regional lymph node surgery in cutaneous melanoma.” |
| 2011 | Dr Adam Frankel
“Oesophageal adenocarcinoma – towards biomarkers of prognosis.” |
| 2012 | Dr Adam Frankel - Best Paper Overall
“Intra-tumour genomic heterogeneity in oesophageal adenocarcinoma”
Dr Kenneth Loon - Best Clinical Paper
“Quality of life outcomes from sacral nerve stimulation in the treatment of faecal incontinence” |
| 2013 | Anitha Karunairajah -1 st Prize - The Covidien Health Care Surgical Trainee Research Prize
“The Management of CMV Infection in Liver Transplant Patients at PAH”
Adrienne Wilson -2 nd Prize - The General Surgeons Group Surgical Trainee Research Prize
“Emergency Management of Small Bowel Tumours – A Review of Cases at PAH” |

Award for Excellence in Resident Education

This prestigious long-standing Award has been presented to exemplary teachers who have supported junior medical staff at this hospital for a period of 15 years. The previous generosity of Roche and PA Private Practice with sponsorship of \$1000 has enabled this award to be presented to the clinician voted as “best clinical teacher” by PAH junior doctors.

At the Princess Alexandra Hospital, resident education is recognised as a priority issue and this award not only highlights its importance but also promotes enthusiasm and excellence in clinical teaching in general. With the increase of numbers of medical students graduating from Qld universities, commitment to resident teaching is paramount in producing quality doctors. In addition to recognising one to two clinical teacher(s) and/or Departments as the winner(s) of the Award, the presentation ceremony during the PAH Health Symposium also acknowledges all clinical teachers who were nominated by the junior medical staff in that year. There has been one senior doctor as a result of him being consistently nominated year after year who has been inducted into the Award for Excellence in Resident Education Hall of Fame. His name is Dr Brian Miller. He has truly been honoured to be recognised in this way.

Past Award for Excellence in Resident Education Recipients

1994	Dr Winifred Lee
1995	Dr Luis Prado
1996	Dr Michael Sinnott
1997	Dr Daryl Wall, Dr Geoff Playford and Dr Gerald Feeney
1998	Dr Brian Miller
1999-2002	No Awards Presented
2003	Dr Sean Tolhurst
2004	Dr Michaela Cartner
2005	Dr Toby Tang
2006	Dr Shaun Pandy and Dr Michelle Murphy
2007	Dr Jonathon Isoardi
2008	Dr Merryn Thomae
2009	Emergency Department - Dr Andrew Churchman and Jonathon Isoardi
2010	Dr Kim Nicholls
2011	Dr Brian Miller
2012	Dr Kim Nicholls
2013	Dr Mark Deuble

Award for Excellence in Allied Health Clinical Education

This prestigious award is presented to exemplary allied health clinicians who contribute to clinical education who have, and continue to, support the professional education and development of allied health students and allied health clinicians at the PA Hospital.

Allied health clinicians who contribute to clinical education strive for continuous improvement in access to, and quality of clinical education for pre-entry students and new graduates. They employ a range of evidence based clinical education strategies underpinned by the principles of sustainability, consistency, efficiency and collaboration. Allied health clinicians who contribute to clinical education are committed to clinical education that is planned, managed and evaluated to make a contribution to the safe clinical care outcomes for the patients of PA Hospital services. It is an expectation that all allied health clinicians contribute to the education of students.

Excellence in allied health clinical education continues to become increasingly important due to a number of factors. These include:

- Allied health professional education programs requiring work integrated clinical education and therefore the support of allied health clinicians to manage, supervise and evaluate student performance.
- Growth in allied health education programs at Universities creating an increasing number of allied health students requiring clinical placements.
- Evidence supporting the contribution of clinical placements to the development of a highly skilled allied health workforce with allied health students contributing to achieving optimal patient outcomes.

The award for excellence in allied health clinical education is determined by the Executive Director of Clinical Support Services with support from the allied health workforce development team and the Chair of the Metro South Allied Health Clinical Educator Network.

Past Award for Excellence in Allied Health Clinical Education Recipients

2010	Jenny Lethlean (Speech Pathology)
2011	Tom Steffens (Medical Imaging)
2012	Karl Winckel (Pharmacy)
2013	Sarah Bowden (Social Work)

Award for Excellence in Nursing Education

The PA Hospital Award for Excellence in Nursing Education was first offered in 2009 in line with the Medical and Allied Health Award for Excellence in Education. This award was developed to recognise a nurse who has made a significant contribution to Nursing Education through his/her educational contribution to patients, colleagues or students. In addition it recognises a nurse who is an outstanding role model and has had a positive influence on his/her team.

This award is seen as a prestigious award to recognise a nurse with excellence in nursing education.

Past Award for Excellence in Nursing Education Recipients

2011	Leanda Ismail, Clinical Facilitator, NPDU
2012	Angela Henson, Renal Nurse Educator
2013	Andrea Thompson, Simulation Coordinator

PAH Health Symposium Speakers 2014



Ms Delena Amsters

Delena Amsters is the Senior Research Officer with the Spinal Outreach Team. Delena has worked primarily in the area of applied health service research but also has considerable experience in service development and project management. Delena has a Master of Physiotherapy by research and is a PhD candidate with the School of Human Services and Social Work at Griffith Health. She has a strong interest in the discipline of program evaluation and is a member of the Australasian Evaluation Society.



Ms Melissa Argent

Melissa Argent is the Assistant Director of Nursing (ADON), Division of Medicine, Princess Alexandra Hospital. Melissa received her Bachelor of Nursing from Griffith University, Brisbane and her Masters of Business Administration from Central Queensland University. Clinically Melissa worked in a variety of areas both in Australia and internationally, however specialised in Respiratory nursing with a particular interest in transplantation. As ADON, Melissa is committed to leading a culture of nursing excellence in providing person centred care, valuing professionalism, quality outcomes and collaborative practice.



Dr Richard Ashby

Dr Richard Ashby is one of the state's most experienced clinicians and clinical administrators. In 2010, Dr Ashby was awarded a Member of the General Division of the Order of Australia for service to emergency medicine, to medical administration, and to a range of professional associations. He is active across a broad range of medical areas, including teaching, research and consultancy.

Dr Ashby previously held the post of Executive Director and Director Medical Services at the Princess Alexandra Hospital. Dr Ashby is a University of Queensland graduate who undertook his internship at the Princess Alexandra Hospital and subsequently worked in provincial and rural centres and at the QEII Hospital. He was appointed Director of Emergency Medicine at the Royal Brisbane Hospital in 1989, a post he held until his appointment as Executive Director Medical Services at the Royal Brisbane and Women's Hospital in 2000. During this period, Dr Ashby spent a year as the Assistant Regional Director – Policy and Planning for the Brisbane North Regional Health Authority. Dr Ashby is a past President of the Australasian College for Emergency Medicine and was Chairman of the International Federation for Emergency Medicine from 1994 to 1996.

In the period 2000–2006, Dr Ashby also acted as District Manager at both the Royal Brisbane and Women's Hospital and Princess Alexandra Hospitals for lengthy periods. Dr Ashby was appointed Executive Director of Medical Services at PAH in September 2006 and, in 2008, was additionally appointed as Executive Director of the hospital.

PAH Health Symposium Speakers 2014



Dr Stephen Ayre

Dr Stephen Ayre was appointed to the position of Executive Director Princess Alexandra Hospital (PAH) and QEII Jubilee Hospital (QEII) Health Network, Metro South Hospital and Health Service, Brisbane on 5 May 2014. Stephen was previously the Executive Director Medical Services - The Prince Charles Hospital (TPCH).

Stephen is a graduate of the University of Queensland (UQ) Medical School, has a Masters in Health Administration from the University of NSW and is a Fellow of the Royal Australasian College of Medical Administrators (RACMA). He currently is the Jurisdictional Coordinator of Training for the College of Medical Administrators.

In the past Stephen has worked as a general practitioner on the Sunshine Coast after postgraduate experience in a number of Queensland Hospitals. During his work in general practice he developed an interest in Alcohol and Drug Medicine and Community Medicine and is a member of the Australasian Professional Society for Alcohol and Drugs.

His appointments with Queensland Health have included Director of Community Health - Sunshine Coast, Medical Superintendent - Caboolture Hospital, Deputy Executive Director Medical Services - Royal Brisbane Hospital and Medical Superintendent for the Royal Women's Hospital (RWH). In Tasmania, he was the CEO of the Launceston General Hospital (2004-2008) and acted as the CEO for all three northern Tasmanian Hospitals for a prolonged period.

His interests are in the areas of safety and quality in complex health environments, accelerated process redesign and the hospital community interface.



Associate Professor Andrew Barbour

Associate Professor Andrew Barbour is a Surgical Oncologist at the Princess Alexandra Hospital (PAH). He is a translational researcher at The University of Queensland (UQ) School of Medicine, PAH where his research has focused on using genomic, mRNA expression and next generation sequencing data to classify oesophageal adenocarcinoma (OAC) and identify biomarkers of outcome of OAC and melanoma. In addition, he is a James IV Travelling Fellow in 2013. He is the Principal Investigator for multicentre phase II trials in oesophageal and pancreatic cancer, funded by the NHMRC



Ms Kate Bell

Kate Bell has been working in the speciality of osteoporosis since being appointed as the first Osteoporosis Nurse in Qld back in Feb 2009. Her experience has centred on orthopaedics, with a special interest in the care and management of those with hip fracture. Kate successfully completed her Masters of Nurse Practitioner Studies and was appointed last month as the PA Hospital's Osteoporosis Fragility Fracture Nurse Practitioner. This position is the first of its kind in Queensland. She was given the honour of being acknowledged at the Queensland Health Australia Day awards for excellence in nursing in the field of osteoporosis and orthopaedics.

PAH Health Symposium Speakers 2014



Dr Helen Benham

Dr Helen Benham is a consultant rheumatologist at Princess Alexandra Hospital (PAH), post-doctoral researcher at the University of Queensland Diamantina Institute and deputy head of the PAH clinical school, UQ School of Medicine. She completed her medical degree at the University of Sydney in 2002 and subsequently gained her FRACP in 2009. In 2010 she spent a year as a research fellow in the UK at Addenbrooke's Hospital/Cambridge University investigating Th17 and Th22 cells in patients with Psoriasis and Psoriatic Arthritis.

Following her return to Australia Helen completed her PhD in Professor Ranjeny Thomas's lab focusing on IL-23 signalling in the SKG mouse model of Spondyloarthritis. The focus of her continuing research is the study of pre-clinical Rheumatoid Arthritis, to understand the relationships between genetics and environment in the development of RA, evaluate and explore hypotheses regarding disease initiation, develop predictive models of disease, evaluate pre-clinical interventions and novel immunomodulation including antigen-specific therapy.



Mr Robert R Bowen

Robert has an extensive background in the health care industry and technology commercialisation. As National Manager of a Commonwealth program Robert provided commercialisation advice and assistance and some initial funding to new technology companies.

Previously he was a founder director of the Triton foundation, a not-for-profit association providing assistance to start-up companies with a focus on youth assistance, and a consultant advisor to the Commonwealth on pharmaceutical industry research and development. In the health area Robert has been a board member of the Wesley Hospital, general manager of an Australian public listed medical biotechnology research and marketing company, director of a university-based biotechnology company and executive director of an international pharmaceutical company in Australia. Robert has a BSc degree from the University of NSW and a MBA degree from Macquarie University.



Dr Mary Boyd

Dr Mary Boyde is a Nurse Researcher in Cardiology and Nurse Educator in Nursing Practice Development Unit at the Princess Alexandra Hospital.

Mary's research has focused on investigating and developing effective patient education strategies. Mary has published in the fields of patient education, cardiology, resuscitation, and clinical practice development

PAH Health Symposium Speakers 2014



Professor Matthew Brown

Professor Matt Brown is currently the Institute Director and Professor of Immunogenetics at The University of Queensland, based at the Diamantina Institute and Institute of Molecular Biosciences, a position he has held since September 2005. Prior to that he was Professor of Musculoskeletal Sciences, University of Oxford, where he worked since 1994. He initially trained in rheumatology in Sydney, and remains clinically active, with a special interest in ankylosing spondylitis (AS).



Professor Donald Cameron

Graduated from University of Sydney. Resident and Registrar RPAH. Moved to Melbourne to train in Endocrinology – Alfred Hospital Diabetes and Metabolic Unit and Medical Research Centre Prince Henry's Hospital. This was followed by a Research Fellowship at the University of Geneva. On return to Australia became Senior Research Fellow Prince Henry's Hospital and spent some time as Visiting Professor University of Louvain. Moved to PAH in 1978 as Director of Diabetes and Endocrinology and held this Post until 1998. Appointed first Chair of Centres for Health Research and remained in this position until 2005.



Dr Katrina Campbell

Dr Katrina Campbell is a Senior Research Fellow in the Department of Nutrition and Dietetics at Princess Alexandra Hospital. Having developed a track record in clinical nutrition research focused on the nutritional management of renal disease, Katrina is the principal investigator on a number of clinical trials and multi-centre investigations, with a keen interest in factors influencing food intake, including taste. She is funded by fellowships from Office of Health and Medical Research and Lions Medical Research Foundation.



Ms Veronica Casey

Veronica is currently the Executive Director, Nursing and Midwifery Services, Metro South Health and Executive Director of Nursing Services. Her previous experience includes the Nursing Director Division of Medicine at PAH, Executive Director of Aged and Disability Services at The Prince Charles Hospital, Director of Nursing at the Royal Women's Hospital, redevelopment positions, Quality Facilitator and clinical positions across a number of medical nursing specialties.

In 2010 she was appointed as an American Nurses Credentialing Centre (ANCC) Commissioner – Magnet Recognition Program, one of three inaugural International Commissioners. Her special interests are in safety and quality in patient care, care of the aged and rehabilitation nursing.

Veronica has been appointed as a Member of the Nursing & Midwifery Board of Australia (NMBA) National Board from 2014 until 2017.

PAH Health Symposium Speakers 2014



Mr Patrick Condren

Patrick Condren is an Australian journalist that has been in the industry for over 25 years. Making a start with broadcasting with the ABC Rockhampton, Patrick went on to a 10+ year career with ABC News and current affairs. This included a year's stint presenting the ABC 612 morning program.

Patrick broadened his horizons when he left for a 12 month stay in London, with his wife Margaret. This visit to old Blighty in 1997, led him to a producer position with the BBC's radio 4 Today program. Patrick also spent a couple of years presenting a weekly program on the BBC's world service, also in London.

His eventual return to Australian shores has seen him spending the last 11 years as a political reporter with Channel 7. This worldly experience gives Patrick Condren more than 20 years broadcast experience as a journalist/ presenter having worked for the ABC, BBC, ITN and the 7 Network.



Dr Georga Cooke

Dr Georga Cooke is the Director of Clinical Training within the Medical Education Unit at the Princess Alexandra Hospital. She is a fellow of the RACGP and is pursuing a fellowship with the RACMA. Georga has a research appointment with the Centre for Research in Evidence-Based Practice at Bond University. Her research interests include burnout, uncertainty in medicine and diagnosis, systematic reviews and medical workforce.



Professor David Crompton

Professor David Crompton was awarded an Order of Australia (OAM) for development of community based mental health services for veterans, and the development of community Post Traumatic Stress Disorder (PTSD), and anxiety and substance abuse treatment services. Professor Crompton worked in private practice as a rural general practitioner prior to commencing psychiatry training and spent 12 years in private psychiatry practice. Professor Crompton has subsequently held leadership roles in Queensland Health and New South Wales Health Mental Health Services.

Research interests include:

- impact of disasters on psychological and physical health in Queensland
- clinical redesign
- recovery
- health economics
- Suicide.

Professor Crompton contributes to a significant number of organisations/committees. His roles include and have included: Member of Australian Expert Advisory Disaster Committee and Queensland Health Psychosocial Disaster Committee

- Member of Centre of Excellence in Relapse Prevention
- Chair Southern Queensland Mental Health Clinical Cluster (Queensland Health)
- Project lead for the activate: mind & body initiative
- Australian Council on Health Standards (ACHS) surveyor
- Head of Centre Trauma, Loss and Disaster Recovery
- Board member for Stepping Stones Clubhouse.

PAH Health Symposium Speakers 2014



Ms Kym Dalmaso

Kym Dalmaso obtained her nursing degree from Griffith University and commenced her career in the Orthopaedic Unit of the PAH. She moved into a Trauma High Dependency Unit after her time in Orthopaedics. For the past 5 years, she has been a Registered Nurse in the Emergency Department at PAH. During this time I have had the opportunity to work for the Disaster Response Service as a Clinical Facilitator. She was the Principal Investigator in the Trauma Nursing Round study.



Dr Michael Daly

Michael graduated from University College Dublin, where he trained in the Mater Hospital. After internship, he moved to Queensland and in 2000 he became Deputy Director Medical Services at Toowoomba Hospital.

Michael was appointed Executive Director, Medical Services in West Moreton in 2002 and with the Health Reforms of 2005-6, Michael founded the Southern Area Clinical Governance Unit.

In 2008 Michael was appointed Executive Director, Clinical Governance, Metro South Hospital and Health Service.



Dr Goce Dimeski

Goce is the Chief Scientist of Chemical Pathology at Princess Alexandra Hospital, Pathology QLD and an Adjunct Research Fellow with the School of Medicine, University of QLD. He has been the instigator in many innovative processes for Chemical Pathology that have resulted in positive patient care outcomes across the state, and received acknowledgement internationally via a sound publication record. His research focus is on practical aspects that have immediate impact on delivering change for the better and this has been either in his Chief Scientist role or in collaboration with many clinical units at PAH as well as with UQ teams. Currently one of his major research interests is the development of a much improved serum collection tube for biochemical analysis, now under the management of the newly formed company via UQ, Q-Sera by using clotting complex isolated from the taipan and brown snakes' venoms.



Dr Mark Elcock

Dr Mark Elcock PSM (MBChB, FACEM, FCEM) is Senior Director, Retrieval Services and Counter Disaster Unit, Queensland Department of Health and Assoc Professor (Adjunct) Schools of Medicine and Public Health, Tropical Medicine & Rehabilitation Sciences, James Cook University. He has provided the clinical leadership behind the development and establishment of Australia's first fully integrated adult, paediatric, neonatal and high risk obstetric retrieval system, providing >20,000 retrievals/transport per year across Queensland. He has a strong interest in prehospital and retrieval medicine, trauma care, telehealth, clinical governance and rural/remote Emergency Medicine.

PAH Health Symposium Speakers 2014



Dr Devakar Epari

Dr. Devakar Epari is the Leader of the Trauma Research Group at the Queensland University of Technology and the co-ordinator of the Medical Engineering undergraduate program. Dr. Epari has degrees in Mechanical and Biomedical Engineering from the University of New South Wales and a PhD from the Technical University of Berlin.

In addition, to Dr Epari's research interests in the treatment of fractures and the mechanics of bone healing, Dr Epari has an interest in Biodesign and frugal innovation. He is supporting student programs to place medical engineers in clinical observation to facilitate the identification of health needs in Australia and Asia-Pacific to stimulate medical device innovation locally.



Professor David Evans

David Evans is the new Professor of Statistical Genetics and Head of Genomic Medicine at the Diamantina Institute. He obtained his PhD at the University of Queensland in 2003, before undertaking a four year post-doctoral fellowship in statistical genetics at the Wellcome Trust Centre for Human Genetics, University of Oxford. In 2007 he moved to take up a Senior Lecturer then Reader position at the University of Bristol where he has led the genome-wide association studies work in the Avon Longitudinal Study of Parents and Children cohort (ALSPAC).

His research interests include the genetic study of several complex traits and diseases including atopic dermatitis, ankylosing spondylitis, and osteoporosis. He co-leads the world's largest genetic study of atopic dermatitis involving ~300,000 participants. His other main research interest is in the development of statistical methodologies in genetic epidemiology including approaches for gene mapping, individual risk prediction, causal modelling and dissecting the genetic architecture of complex traits.



Ms Naomi Ford

Naomi has more than 20 years' experience in the journalism and public relations field. She began her career in NSW working as journalist on various newspapers before moving to Brisbane in 1998 to work with Quest Newspapers. Naomi has worked in various government departments as a media advisor, manager and director for the past 13 years, including at Transport and Main Roads, Treasury and Queensland Health.



Dr Judy Flores

Dr Judy Flores graduated from The Johns Hopkins University School of Medicine and completed her training in Internal Medicine at the University of California, San Francisco. She was appointed as Chief Resident at UCSF before joining the faculty as Assistant Professor in the Division of General Internal Medicine. Moving to Brisbane in 1996, she gained her FRACP and was appointed Director of Medicine at the QEII Hospital in 1998. She was recruited as Chair of the Division of Medicine at PAH in 2009 and additionally as Clinical Stream Leader for Medicine and Chronic Disease Services in 2013. In addition to her administrative roles she has continued clinical practice in general medicine at the QEII. Her clinical interests include care of the complex medical patient, clinical redesign and quality improvement.



Dr Geoff Garrett AO

Geoff Garrett was appointed Chief Scientist to the State Government of Queensland in January 2011. In this role he is accountable for science policy, providing strategic guidance across a range of government departments, and has also been involved with or led a number of reviews and enquiries, covering inter alia, the science of floods, uranium mining, bat derived horse viruses, underground coal gasification and innovation in government.

Formerly he was, for eight years, Chief Executive and member of the Board of Australia's Commonwealth Scientific and Industrial Research Organisation. CSIRO is one of the world's largest and most diverse national research organisations, with close to 6 500 staff across 55 sites in Australia and an annual turnover exceeding Aus\$1 billion.

Prior to joining CSIRO, Geoff led South Africa's national science agency, the CSIR, as President and Chief Executive from 1995, following five years as Executive Vice President: Operations. He was named South Africa's 'Boss of the Year' in 1998, and 'Engineer of the Year' by the South African Society of Professional Engineers in 1999.

Educated in the United Kingdom, Geoff is a graduate of Cambridge University where he completed a doctorate in metallurgy. He was also a university boxing blue. He then took up a lecturing position at the University of Cape Town. Prior to joining the CSIR in 1986 to head up South Africa's National Institute for Materials Research, he was Professor and Head of Department at the University of the Witwatersrand in Johannesburg. He held visiting positions at Brown University (RI, USA), and at Oxford and Sheffield Universities. His research interests centred around the fracture and fatigue behaviour of engineering materials.

On joining CSIRO, Dr Garrett and his team undertook a program of major strategic and operational transformation, seeking to achieve greater focus through their Flagship Programs on the major scientific challenges for Australia, including water, clean energy, health and climate change, and opportunities in minerals and mining, manufacturing, new food technologies and ocean science. Key to this was developing stronger partnerships across the innovation system, and growing the organisation's impact through a more unified 'One-CSIRO' approach. In December 2008 CSIRO's Flagship Programs received the top Prime Minister's Award for Excellence in Public Sector Management.

Geoff is a Fellow of the Australian Academy of Technological Sciences and Engineering, the Royal Society of South Africa and the Australian Institute of Company Directors, and served on the Prime Minister's Science, Engineering and Innovation Council in Australia for eight years. From 2002 he also served as a founder Principal and subsequently as an Executive Committee member of the Global Research Alliance, a group which brings together some of the world's most significant R&D organisations, spanning five continents.

Dr Garrett is a recipient of the Centenary Medal for service to Australian society through science, and was named by the Australian Financial Review as one of Australia's 2008 'True Leaders'. In June 2008 he was appointed as an Officer of the Order of Australia (AO) in the Queen's Birthday Honours list.

PAH Health Symposium Speakers 2014



Ms Areti Gavrilidis

Areti Gavrilidis has a business, health and science background. She has over 30 years of experience in the public and private sectors including health, education, business consulting and charity. She has a keen interest in mentoring, supporting and facilitating research to deliver outcomes. In 2002 she moved from Austin Health to the PAH Centres for Health Research to support, facilitate and strengthen health and medical research within the hospital campus and district.

In 2007 she was appointed as the Principal Researcher of a Smart State Council Working Group to research and prepare a report to advance Queensland's health and medical research and development (R&D) outcomes. This led to the establishment of the QH Office of Health and Medical Research. In 2008 she was a recipient of a Scholarship from the Australasian Research Management Society – International Network of Research Management Societies (ARMS -INORMS). In the same year Areti was awarded a Churchill Trust Fellowship to look at models facilitating translational research. She visited over 40 prestigious leading research Academic Health Science organisations in the USA, Canada and the UK and interviewed over 130 key individuals. Her scientific background is strengthened and augmented by her interest and experience in business management.

In late 2011 Areti moved from her position as PAH Director, Research Development, Ethics & Policy to manage and enable the development of the Diamantina Health Partners, Queensland's first Academic Health Science Centre. Areti holds academic undergraduate and post graduate qualifications in science, applied science, and business administration.



Associate Professor Devinder Gill

Dr Gill is the Director of Haematology and the founding Chair of Cancer Collaborative Group at Princess Alexandra Hospital (PAH) and Associate Professor of Medicine at University of Qld. He is also an Adjunct Principal Research Fellow of the Diamantina Institute and is currently a member of TRI Caucus and the TRI Research Committee. Dr Gill Chaired the Aggressive and Hodgkin's Lymphoma for the Australasian Leukaemia and Lymphoma Group (ALLG) and until recently was a member of the ALLG Board. He was the Founding Co-Chair of the International Meeting "New Direction in Leukaemia Research Meeting" in 2006 which is now held every 2 years. Apart from the Clinical Trials, his other research interests include biology of Chronic Lymphocytic Leukaemia (CLL). Dr Gill was also the Founding Member and currently the Vice-President of the CLL Australian Research Consortium



Dr David Gillis

Dr David Gillis is a clinical immunologist at PA / Pathology Queensland having worked at the Royal Adelaide Hospital / IMVS over many years as Head of the clinical and diagnostic laboratory over there. He has an ongoing interest in diagnosis and management of vasculitis, primary immunodeficiency and allergic disease. He is a former president of the Australasian Society of Clinical Immunology and Allergy.

PAH Health Symposium Speakers 2014



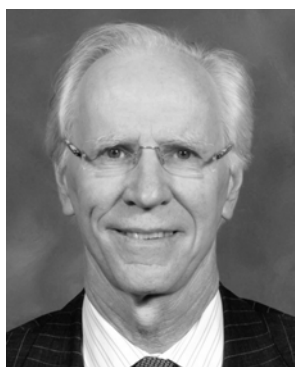
Professor Nicholas Graves

Nicholas Graves is Professor of Health Economics with a joint appointment in the Institute of Biomedical and Health Innovation, School of Public Health, Queensland University of Technology and the Centre for Healthcare Related Infection Control and Surveillance, Queensland Health, Australia.

Nicholas Graves is the Academic Director for The Australian Centre for Health Services Innovation (AusHSI), Queensland University of Technology / Institute of Health and Biomedical Innovation. Nick is the Academic Director for the Centre of Research Excellence in Reducing Healthcare Associated Infections (CRE-RHAI), Queensland University of Technology / Institute of Health and Biomedical Innovation.

His applied research brings economics to the study of healthcare. He has a programme of research that uses Bayesian methods for the synthesis of diverse sources of data that are subsequently used to inform parameters in decision models that address questions about the value of competing investments in healthcare sector alternatives.

Nick supervises PhD students, teaches economics to postgraduate students and has made research contributions of international significance publishing in the journals *Nature*, *BMJ*, *AIDS*, *Health Economics*, *Lancet Infectious Diseases*, *The Journal of Infectious Diseases* and *Emerging Infectious Diseases*.



Professor Len Gray

Professor Len Gray is Professor of Geriatric Medicine at the University of Queensland where his current academic appointments are as Director of the Centre for Research in Geriatric Medicine and the Centre for Online Health. He holds clinical appointments as Senior Consultant Geriatrician, Princess Alexandra Hospital, Brisbane and Visiting Physician (Geriatrician) at Toowoomba Base Hospital, Dalby Hospital and Mater Misericordiae Hospital, Rockhampton.

He is a Board Member of the interRAI Research Collaborative, an international working group of researchers developing assessment protocols, data sets and quality tools for aged care and related fields.

His research interests focus on aged care policy, models of aged care service delivery, assessment and care planning systems, and e-Health and telemedicine strategies. He has secured over \$6m in competitive research grants in the last 5 years and has led 6 NHMRC grants as principle investigator. Most recently, he led a successful application for a NHMRC Centre for Research Excellence (CRE) which will encompass an extensive 5 year program of research in Telehealth commencing in 2013.

PAH Health Symposium Speakers 2014



Professor Peter Gray

Professor Peter Gray was appointed the inaugural director of the Australian Institute of Bioengineering and Nanotechnology (AIBN) at the University of Queensland in 2003. Previously he was Professor of Biotechnology and Director of the Bioengineering Centre at UNSW, and a Senior Principal Research Fellow at the Garvan Institute of Medical Research in Sydney. Professor Gray has had commercial experience in the USA working for Eli Lilly and Co and for the Cetus Corporation as well as previously holding academic positions at University College London, and at the University of California, Berkeley. His research interests are focussed on engineering mammalian cells to produce the complex proteins called biologics which are gaining rapid acceptance as human therapeutics, and on developing human stem cells bioprocesses suitable for clinical application. Professor Gray was one of the founders and

is a past President of the Australian Biotechnology Association, AusBiotech. He is a Fellow of the Australian Academy of Technological Sciences and Engineering (ATSE) and of the Australian Institute of Company Directors, and has been named as one of Australia's 100 Most Influential Engineers.

He is a Vice-President of ATSE, and serves on the Boards of Biopharmaceuticals Australia Pty Ltd, Institute for Photonics and Advanced Sensing (IPAS), ACYTE Biotechnology Pty Ltd, Stem Cells Ltd, ECI Inc, New York, and a number of State and Federal Government Councils and Committees.



Professor Amanda Henderson

Professor Henderson has an extensive career in nursing education, research and leadership in both academic and clinical settings. Her scholarship is focused on the establishment of clinical settings that promote learning in practice. She is an Australian Learning and Teaching Fellow, Discipline Scholar (Health) and received numerous grants for promoting scholarship in teaching and learning. She has written extensively on learning in clinical practice and evaluated many initiatives, including student placement models. She has over 100 publications in international refereed journals, written ten book chapters and co-edited two books.



Dr Michelle Hill

Dr Michelle Hill is an Australian Research Council Future Fellow. Dr Hill obtained her PhD from The University of Queensland (UQ) in 2000. She undertook two post-doctoral positions before returning to UQ. Supported by a National Health and Medical Research Council (NHMRC) Career Development Award, Dr Hill chose to establish the Cancer Proteomics Group at The UQ Diamantina Institute (UQDI) in 2009, based on its location on the Princess Alexandra Hospital campus and its translational research focus. Collaborative research was further enhanced with the relocation of the UQDI to the Translational Research Institute (TRI) building on the same campus in December 2012. Dr Hill is a member of the TRI caucus and the academic lead of the TRI Proteomics Core Facility.

PAH Health Symposium Speakers 2014



Professor Ken K.Y. Ho

Ken took up the positions of Chair, Centres for Health Research, Princess Alexandra Hospital, Professor of Medicine University of Queensland and Adjunct Professor Queensland University of Technology, Brisbane in 2011. He graduated in medicine at the University of Sydney, obtained a doctorate degree from the University of New South Wales and undertook postdoctoral studies at the University of Virginia.

His research focuses on hormones and metabolism, investigating the causation of and treatments for obesity, muscle loss and physical frailty. The work is strongly translational closely integrating laboratory and clinical studies, directed at understanding how hormones act on cells and on the whole body. He has published over 200 scientific papers and written editorial commentaries for the Lancet. He serves or has served on the Editorial Boards of leading endocrinology journals including Journal of Clinical Endocrinology and Metabolism, Endocrinology, Growth Hormone and IGF Research and Best Practice in Endocrinology and Metabolism and as Section Editor of the Oxford Textbook of Endocrinology.

He received the inaugural 2011 Senior Plenary Award of the Endocrine Society of Australia, the 2000 Visiting Trust Professor and the 2008 Asia Oceania Medal of the British Endocrine Society. He is a past-president of the Endocrine Society of Australia and of the International Growth Hormone Research Society and President Elect of the Pituitary Society. He has served on NHMRC discipline review panels and was deputy chair in 2006. He is a member of the Specialist Medical Review Council, Australian Government.



Professor Gerald Holtmann

Professor Holtmann is Director of Gastroenterology and Hepatology at the Princess Alexandra Hospital, and Associate Dean Clinical at the University of Queensland. He is a Sub-Stream leader in both the Medical and Surgical Metro South Health Clinical Streams - being responsible for Endoscopic Services and Medical Specialties throughout the region. He was born in Essen, Germany. He graduated from the Medical School of the University of Essen. He completed his clinical training in Internal Medicine and Gastroenterology at the University Hospital of Essen, Germany, and completed a Fellowship at the Mayo Clinic, Rochester, Minnesota, USA. At the age of 38 he was appointed Professor of Medicine at the University Hospital of Essen in Germany. In 2004 he was appointed Director of Gastroenterology & Hepatology at the Royal Adelaide Hospital, and Professor of Medicine at the University of

Adelaide. From 2007 to 2010 he served a term as Chief Executive Officer and Medical Director of the University Hospital Essen. Professor Holtmann is a Fellow of the Royal College of Physicians in London and fellow of the Royal Australasian College of Physicians. His research is focused in the field of Neurogastroenterology and has continuously attracted peer reviewed funding from national and international funding bodies such as the National Health and Medical Research Council, and the German Research Foundation. He has published more than 300 articles and book chapters in leading journals including the NEJM, Lancet and Gastroenterology. Besides his clinical and academic activities he completed a Master in Business Administration (MBA) at the University of South Australia.



Dr Patrick Honasia

Dr Houasia completed his MBBS at University South Pacific, Fiji, and concluded his orthopaedic training with the Australian Orthopaedic Association. He was awarded a Fellowship of the International College of Surgeons in orthopaedics in 2008 and was also awarded fellowships in Switzerland, Australia, Taiwan.

Dr Houasia is currently is the head of Orthopaedic & Trauma unit at the national referral hospital in Honiara, Solomon Islands.



Dr Ruth E. Hubbard

Dr Ruth E. Hubbard moved to Brisbane, Australia from her native Wales in September 2011, having been appointed to a joint position as Senior Lecturer in Geriatric Medicine at the University of Queensland and Consultant Physician in Geriatric Medicine at the PA. As a clinical academic, she has always combined hospital practice with research and teaching. She completed an MSc in Medical Education in 2005 and an MD on pathophysiological changes in frail older people in 2008.

She was then awarded a grant from the Peel Research Trust, London to pursue her studies in frailty at Dalhousie University, Halifax, Nova Scotia (2007 – 2009) with Professor Ken Rockwood. Here, she was able to test hypotheses regarding the determinants and manifestations of frailty through the interrogation of large datasets. She has published widely on the inflammatory aetiology of frailty, the difficulties of measuring frailty in clinical practice and the relationships between frailty and obesity, smoking, socioeconomic status and exercise.



Associate Professor Warrick Inder

Dr Inder graduated from the University of Otago, NZ in 1988. He obtained his MD examining the effects of opioid peptides on ACTH secretion, before spending 2 years in the Neuroendocrine Unit of the Massachusetts General Hospital, Boston USA on a post-doctoral fellowship researching pituitary adenomas.

He has worked as consultant Endocrinologist at Christchurch Hospital, NZ and St Vincent's Hospital, Melbourne and is currently a senior staff specialist at Princess Alexandra Hospital, Brisbane and associate professor with the University of Queensland. He is the Treasurer of the Endocrine Society of Australia and a member of the Specialist Advisory Committee in

Endocrinology for the Royal Australasian College of Physicians. His major clinical and research interests are pituitary and adrenal disease.



Dr Katherine Irvine

Kate completed her PhD with at the University of Queensland Institute for Molecular Biosciences in 2004. She then held post-doctoral positions at the IMB and UQ Diamantina Institute, pursuing her interests in the role of macrophages in chronic inflammatory diseases, before joining the UQ Centre for Liver Disease Research as senior scientist in 2012. She was awarded the inaugural Pauline Hall Fellowship in 2012, supported by the Australian Liver Foundation and the PA Hospital Research Foundation.

PAH Health Symposium Speakers 2014



Ms Ruth Jebb

Ruth Jebb, RN, RM, MN (Emergency and Trauma) has been working as a Registered Nurse and Midwife for 17 years with experience in field, pre-hospital and tertiary hospital care settings. Ruth has worked as an Australian Red Cross Health Delegate since 2003, completing both long-term and short-term deployments (International Committee of the Red Cross and International Federation of the Red Cross) to Kenya, Darfur, Cambodia, Haiti, Chad, Zimbabwe and more recently to the Philippines. In 2011 she went to Christchurch where she worked as a member of the AusMAT team, supporting and providing medical care to those affected by the earthquake.

She currently works full-time as Clinical Nurse Consultant (CNC) in the Emergency Department and casually as a Birth Suite Midwife. She is about to embark on another mission to Tanzania with UQ/UniQuest where she will be Course Coordinator for a Maternal and Child Health short course as part of the AusAID funded Australia Awards.



Professor David Johnson

David Johnson is currently Director of the Metro South and Ipswich Nephrology and Transplant Service (MINTS) and Medical Director of the Queensland Renal Transplant Service at Princess Alexandra Hospital, Brisbane, Australia, Professor of Medicine and Professor of Population Health at University of Queensland, Chair of the CARI Guidelines Working Parties on Peritoneal Dialysis Adequacy, Evaluation of Renal Function and Management of Early CKD, Chair of the Kidney Check Australia Taskforce, Co-Chair of the Australasian Creatinine and eGFR Consensus Working Party, Co-Chair of the Australasian Proteinuria Consensus Working Party, Founding Member and Deputy Chair of the Australasian Kidney Trials Network (based at Princess Alexandra Hospital), Founding Member of the NHMRC-endorsed Cardiovascular and Renal Centre of Clinical Research Excellence (CCRE), Member of the ANZDATA Registry Peritoneal Dialysis

Working Group, International Society of Peritoneal Dialysis Councillor and International Society of Nephrology Councillor. He was Chair of the Queensland Statewide Renal Clinical Network from 2008 until 2013. He is the principal investigator on a number of large, multi-centre randomised controlled trials, including the balANZ, HERO, IDEAL, IMPENDIA, HONEYPOT and CKD-FIX trials, and is chair of the Data Safety and Monitoring Board for the FINESSE trial. He has published over 580 original manuscripts in peer-reviewed journals and presented over 360 abstracts at national and international scientific meetings. He has won numerous research awards for his clinical and basic science studies in the areas of peritoneal dialysis outcomes, cardiovascular risk factor modification in uraemia, renal transplantation, dialysis unit infection control, treatment of acute renal failure and mechanisms of progressive chronic kidney disease. In 2005, he was awarded the TJ Neale Award by the Australian and New Zealand Society of Nephrology for “outstanding contributions to nephrologic science.” He was a Queensland finalist in the Australian of the Year Awards for 2009. On Australia Day 2011, he was awarded a Public Service Medal by the Governor-General of Australia for outstanding public service, particularly research into the early detection and management of kidney disease. In 2014, he was awarded an International Distinguished Medal by the US National Kidney Foundation.



Dr Lizbeth Jordan

Dr Liz Jordan loved Brisbane and the Princess Alexandra Hospital so much she came here twice!

First as Deputy Director Medical Services in 2007 after several years as Medical Director of Argyll and Clyde Health Board in the West of Scotland. She left at the end of 2012 to look after elderly relatives but decided she had turned into a Queenslander and agreed to head back to take up the Executive Director Medical Services position in March 2014.

Dr Jordan has also worked as a Medical Director at the Scotland Executive Health Department and prior to that she ran a General Practice in a deprived part of Glasgow and also trained in Public Health Medicine.

An Edinburgh graduate she is a keen cyclist and runner as well as an enthusiastic cook.

PAH Health Symposium Speakers 2014



Dr Tony Kenna

Dr Tony Kenna undertook his PhD at University College Dublin, investigating the role of 'unconventional' T cells in healthy and cancer our liver. Dr Kenna then moved to Queensland and undertook post-doctoral training at The University of Queensland Diamantina Institute, using mouse models of autoimmunity to investigate novel ways to eliminate harmful T cells that cause several autoimmune diseases. Dr Kenna is a current research fellow at UQDI where his work focuses on understanding immune responses in autoimmunity. He has received project grant funding from the NHMRC and Arthritis Australia, and fellowship support from Arthritis Australia.



Professor Steve Kisely

Steve Kisely is a psychiatric epidemiologist at the University of Queensland. He is also Director of the Queensland Centre for Health Data Services (Health LinQ) and psychiatrist at Ipswich and Princess Alexandra Hospitals. Steve's research and clinical interests are in epidemiology/ pharmaco-epidemiology, chronic disease surveillance, health services research (HSR), and physical & psychiatric co-morbidity. He is the author of 143 full-length peer-reviewed papers on physical/psychiatric co-morbidity, psychiatric epidemiology and health services research. He was the winner of Special Judges Award in the category of Best Use of IT in Clinical Care in Great Britain as part of the 1998 National Health Care IT Effectiveness Awards, and the Canadian Psychiatric Association's R.O. Jones Award in 2008.



Dr Rathika Krishnasamy

Dr Rathika Krishnasamy is a part-time Nephrologist at Princess Alexandra Hospital. She is a final year PhD candidate with The University of University of Queensland and a proud recipient of PA Research Foundation Postgraduate Scholarship. Her major research effort focuses on novel strategies in cardiovascular risk assessment in patients with chronic kidney disease



Dr Graham Leggett

Dr Leggett was born and raised in Brisbane where he completed a Bachelor of Science with honours at the University of Queensland in 1989. He undertook Ph.D. studies on the immune response against parasitic worms at the Queensland Institute of Medical Research (QIMR), receiving his doctorate in 1993. Dr. Leggett then travelled overseas to the National Institutes of Health in Washington D.C. (USA) to begin a postdoctoral position studying killer T cell immune responses to the AIDS virus. After almost 4 years abroad, he then returned to the Princess Alexandra hospital campus in Brisbane to continue studies on the role of killer T cells in viral infection (and cancer). His current position as a Senior Lecturer/ Senior Research Fellow at the UQ Diamantina Institute involves studies on immunotherapy of non-melanoma skin cancers.

PAH Health Symposium Speakers 2014



Dr Jennifer Lethlean

Dr Jennifer Lethlean has been working in the Speech Pathology Department and the Geriatric and Rehabilitation Unit at the Princess Alexandra Hospital for more than 20 years and has particular expertise as an advanced clinician in the area of stroke rehabilitation. She is currently a Clinical Education Support Officer, guest lecturer at the University of Queensland and runs a Graduate Entry Masters Student aphasia clinic. Dr Lethlean chaired the inaugural Allied Health Research Committee in 1996 and more recently was involved in the working party to set up the Centre for Functioning and Health Research. She currently chairs the Metro South Health Practitioner Research Collaborative and is passionate about supporting clinical education and research in practice to maximize patient outcomes and health care experiences.



Dr David Lie

Dr David Lie is the Clinical Director for Metro South Older Persons Mental Health Services (OPMHS). Following general practice and specialist training, he set up the first public geriatric psychiatry service on the Gold Coast in 1999 and has had a role in developing psychogeriatric services elsewhere in Queensland.

His interests include mental health services in residential aged care and dementia care, telehealth and service development. Dr Lie contributes to a number of organisations/committees, including the national Expert Advisory Panel on Older Persons Mental Health Information Development. He is a Clinical Affiliate with the Centre for Research in Geriatric Medicine.



Dr Ben Light

Ben is Professor of Digital Media Studies, in the Creative Industries Faculty at the Queensland University of Technology, Australia. His research concerns critical interrogations of how digital media and users make arrangements work for them beyond the design room. Currently, he is leading the MMADM.org project which seeks to interrogate men's gendered experiences of a variety of digital media. He has also undertaken work for the UK National Health Service in the area of health education and evaluation through digital and social media. Visitor and audience engagement research with the Imperial War Museums and London Symphony Orchestra have also been a focus of his research through the UK's Digital R&D fund for the Arts.

He is a senior editor for the Journal of Information Technology and sits of the editorial board of New Media and Society. His monograph, Disconnecting with Social Networking Sites, is scheduled for release with Palgrave Macmillan during August 2014.

PAH Health Symposium Speakers 2014



Professor Melissa Little

Professor Little is an NHMRC Senior Principal Research Fellow & leads the Kidney Research Laboratory at the Institute for Molecular Bioscience, The University of Queensland, where she is Head of the Division of Molecular Genetics and Development. Throughout her career, Professor Little's achievements have been recognized by awards including the GlaxoSmithKline Award for Research Excellence (2005), the Australian Academy of Sciences Gottschalk Medal in Medical Sciences (2004) & an Eisenhower Fellowship (2006). From 2007-8 she was the Chief Scientific Officer of the Australian Stem Cell Centre. Professor Little was member of the Strategic Review of Health and Medical Research (McKeon) Review expert panel, which delivered its 10-year strategic health & medical research plan for the nation to the Australian Government in 2013.

Professor Little received her Bachelor of Science with Honours at the University of Queensland in 1984 and she completed her PhD, investigating the molecular aetiology of nephroblastoma and other childhood tumors, at the University of Queensland in 1989. Professor Little was initially a cancer geneticist, studying the genes and pathways that lead to the formation of Wilm's Tumor, first at the MRC Human Genetics Unit of Western General Hospital in Edinburgh, in Scotland from 1990-92 followed by her return to the University of Queensland in Brisbane in 1992. She became a Project leader in 1995, and since then, Professor Little's research has focused on the molecular basis of kidney development, renal disease and repair.

Professor Little has over 140 publications in high impact journals including Science, Nature Genetics, Nature Cell Biology, Cell Stem Cell, Cell Developmental Cell, PNAS, JASN and Development. She is internationally recognised both for her work on the systems biology of kidney development and for her pioneering studies into potential regenerative therapies in the kidney. Her work has encompassed the characterisation of adult stem cells in the kidney as well as analyses of the embryonic progenitor population. More recently, her work on the developing kidney has driven studies into the recreation of nephron stem cells via the transcriptional reprogramming of adult cells and the directed differentiation of human stem cells into kidney organoids.



Professor Stephen Lynch

Undergraduate training was completed at UNSW Sydney. Underwent basic and advanced surgical training at St Vincent's Hospital Sydney. Completed Transplantation Fellowship 1984/85 in Pittsburgh USA under the supervision of Prof. Tom Starzl. Admitted to Fellowship of the Royal Australasian College of Surgeons by examination 1985.

Since 1986 has held various positions including Director of Queensland Liver Transplant Service; Foundation Chair of Transplantation Biology Programme, Fellow of the Institute, and Member of the Board of the Queensland Institute of Medical Research; President of Transplantation Society of Australia and New Zealand; Council of Asian Transplantation Society; Council of The Transplantation Society; Member of Queensland Health Clinical Senate. Served as Associate

Editor/Co-Editor/Section Editor or on the Editorial Boards of "Liver Transplantation and Surgery", "Transplantation", "Graft", "Australian and New Zealand Journal of Surgery", "Hepatogastroenterology", "International Journal of Hepatology".

Published manuscripts: >150, book chapters: 4. Awarded the "Pro Sanitate Medal" by Republic of Hungary, shared in the Award for Excellence by the Royal Australasian College of Surgery, Best Manuscript of the Year in the Journal of Investigative Surgery, The 2012 Australia Day Queensland Health Medal for Surgical Leadership.

Currently Chair of Transplantation, Chairman of Division of Surgery Princess Alexandra Hospital Brisbane, Professor of Surgery University of Queensland, Surgical Stream Leader Brisbane Metro South Hospital and Health Service, Consultant Hepatobiliary Surgeon at Mater Private, Mater Children's Hospitals in Brisbane.



Associate Professor Paula Marlton

Associate Professor Paula Marlton is the Head of Leukaemia and Lymphoma Services at the Princess Alexandra Hospital where she is also Deputy Director of Haematology. Her previous appointments include three years at the MD Anderson Cancer Centre in Houston, Texas. She has extensive experience in clinical research including the role of principal investigator for national multi-centre trials and supervisor of molecular translational research associated with trials. She was the founding Chair of the Australasian Leukaemia and Lymphoma Group (ALLG) Laboratory Science Committee and has established and continues to direct the ALLG Tissue Bank. She serves on the QIMR Council, the Board of the Leukaemia Foundation of Queensland and is involved in a wide range of other academic and advisory services as well as maintaining a busy clinical practice.



Professor Alexandra McCarthy

Sandie was jointly-appointed as the Chair of Cancer Nursing, Division of Cancer Services and the School of Nursing, Queensland University of Technology, in January 2014. She is a member of the Translational Research Institute and the Institute of Biomedical Innovation, and active in key national cancer organisations. She leads a multidisciplinary research program, which investigates the prevention and management of the acute and long-term toxicities of cancer treatments, is firmly focused on producing quality cancer patient outcomes.



Dr Paul Millican

Dr Paul Millican MBBS FRACS FRCSE, a Queensland Plastic & Reconstructive Surgeon, was a VMO at Princess Alexandra Hospital for over a decade first beginning his residency at PAH in 1972. His major areas of interest have been burns and skin cancer. Over the last 10 years he has regularly visited HEAL Africa Hospital in Goma, eastern D.R.Congo teaching, operating and mentoring general surgical staff in plastic surgical applications. Together with Neil Wetzig they established AusHEAL, an Australian charity focussed on increasing clinical competency of the hospital through visiting medical teams, providing scholarships for its doctors for international specialist training & accreditation, and logistically resourcing hospital infrastructure to serve as a hub to its outside community of over 6 million people. There is no plastic surgeon in D.R.Congo, with a population of over 70 million people.



Associate Professor Marion Mitchell

Associate Professor Marion Mitchell holds a joint research appointment with the School of Nursing and Midwifery, Griffith University and the Intensive Care Unit at Princess Alexandra Hospital in Brisbane. The role involves both the support and conduct of clinical critical care research and post-graduate teaching. Supporting clinical staff in implementing evidence based practice and clinical projects are a key element of the role. Marion's research areas include the psychosocial care of the critically ill, family-centred care and research to improve educational outcomes. Her research involves multidisciplinary teams, patients, families and community representatives in the development and evaluation of interventions directed to improve the care of critically ill patients and families.

Marion is a previous President of the Australian College of Critical Care Nurses and was awarded in 2012, Life Membership in recognition of her contributions to ACCCN and critical care nursing. She is ACCCN's representative on the World Federation of Critical Care Nurses and the national Organ and Tissue Authority. Marion is on the editorial board for Australian Critical Care and reviews for a number of other journals. Marion is the Treasurer for Sigma Theta Tau International, Phi-Delta-at-Large Chapter in Queensland and Vice-President of Centaur Memorial Fund for Nurses which supports nursing scholarship.



Mr Tony Moore

Tony comes to Fairfax Media after working at The Queensland Times in Ipswich where he worked as a reporter, chief of staff and deputy editor over 14 years.

At Ipswich he started affairs with the Ipswich Motorway, southeast Queensland's population growth and how Brisbane and Ipswich needed to play nicely together.

They are affairs which continue to this day, though he is yet to tell his wife and two daughters, who are more interested in netball, basketball, circus and the rebuilding of the Brisbane Lions.

Tony is a cricket tragic who realised early in his career that being straight-driven for six was less than encouraging for a Brisbane swing bowler.

It took a ceremonial hip and shoulder bump to end his career as a young ruck-rover spreadeagled along the boundary fence at Wests at Chelmer.

He remembers The Strangers and Xero at Festival Hall, The Birthday Party at Souths Leagues Club and the Royal Exchange Hotel when it was a Triple Zed venue. Dimly.

Tony was born and still lives in Brisbane, went to Queensland University of Technology and Griffith University and is now addicted to Saturday mornings at netball courts with his two young daughters.



Professor Mark Morrison

Mark Morrison joined the University of Queensland Diamantina Institute in October 2013, as Chair and Group Leader in Microbial Biology and Metagenomics. Prior to that, he spent nearly 20 years working in US academia, before returning to Australia in 2006 as a Science Leader with CSIRO. In that capacity, he served as the leader of the "Gut Health" research stream for their Preventative Health Flagship Research Program, and also as one of the five CSIRO Capability Platform leaders (in Transformational Biology). My research group emphasizes the combined use of "omics" technologies with fundamental microbiological approaches to produce new insights into the microbiota that reside within the gastrointestinal tract. By doing so, we seek to better integrate characteristics of the gastrointestinal microbiome with established disease mechanisms (e.g. host genotype, immune activation, mucosal barrier function, and sensory function) to improve the diagnosis and treatment of gastrointestinal and related metabolic diseases.

PAH Health Symposium Speakers 2014



Associate Professor Julie Mundy

Associate Professor Julie Mundy trained in general surgery at the Princess Alexandra Hospital followed by cardiothoracic surgery training in Sydney at St.Vincent's Hospital in adult cardiothoracic surgery and heart-lung transplantation. Further training was obtained in thoracic surgery at The Royal Prince Alfred Hospital and paediatric cardiac surgery at the Royal Children's Hospital at Camperdown. After completing her cardiothoracic surgical training in Australia and gaining some overseas experience in Glasgow, Assoc Prof Mundy returned to St.Vincent's Hospital, Sydney in 1993 as a surgeon with the Dept of Cardiothoracic Surgery and Cardio-pulmonary Transplantation. In 1999 she commenced as the Director of Cardiothoracic Surgery at the Princess Alexandra Hospital and established this new unit.

She is actively involved with RACS activities as a Councillor and the Chair of Professional Standards. Her main interests are surgical education, blood usage minimisation and heart failure surgery. Her main hobbies are astronomy.



Mr Richard Nelson

Richard is the Chief Executive Officer of Queensland Alliance for Mental Health Inc, the peak body for the community mental health sector. He has an extensive career in executive leadership and management in the not for profit and public sector. Richard is committed to strengthening the community mental health sector and is passionate about working towards a mental health system that is focused on people's recovery in their own homes and communities. Richard previously held the position of Deputy CEO of the Aboriginal Health Council of South Australia and has executive management experience in Aboriginal and Torres Strait Islander health policy, planning, national reform and education.

He has also been a board member of the Health Consumers' Alliance of South Australia and has a proven track record of achievement in community sector planning, policy development, organisational development and workforce planning with State and Federal Governments and Aboriginal community organisations.



Dr John North

John North is the Clinical Director for the Queensland Audit of Surgical Mortality and the Northern Territory of Surgical Mortality and a practicing orthopaedic surgeon.

He continues as senior visiting orthopaedic surgeon at Princess Alexandra Hospital and has been a visiting orthopaedic surgeon to Beaudesert and Caloundra Hospital and practiced in each area for over two decades. He has, for the last three years been undertaking outreach through his fracture clinic to Mt Isa Hospital via telehealth.

He has also been involved in overseas outreach to Papua New Guinea, Samoa, Fiji and Solomon Islands and as training faculty for the Pacific Islands Orthopaedic Association.

He has, following specialist training, (in Australia UK and Canada) been heavily involved in teaching, training and assessment in surgery and was Part II examiner for the Royal Australasian College of Surgeons for ten years and Senior Examiner for three years. He continues to examine for the RACS Part I examination across Australia..

Dr North has served on the Human Research Ethics Committee Metro South for over a decade and now sits on the Clinical Ethics Committee.

Dr North is currently a clinical advisor to the Department of Health and Ageing, the Australian Commission for Safety and Quality in Health Care, AHPRA, Medical Panels, the Queensland Civil and Administrative Tribunal and QComp, the workers compensation regulator in Queensland.

His interests include family, grandchildren, medical student training, surgical education and training, training the trainers, non technical skills for surgeons and telehealth service development for consultant driven quality patient care to rural and remote communities.

PAH Health Symposium Speakers 2014



Professor Kenneth O'Byrne

Prof Kenneth O'Byrne is a Consultant Medical Oncologist at Princess Alexandra Hospital and Queensland University of Technology having recently arrived from St James's Hospital (SJH) and Trinity College, Dublin. He qualified from University College, Dublin (UCD) in 1984, completed his higher professional oncology training at the Churchill Hospital, Oxford 1997 and subsequently worked at the University Hospitals of Leicester NHS Trust and University of Leicester until returning to Dublin in November '03. He has a Doctorate Degree in Medicine from UCD and is a Fellow of the Royal College of Physicians, Ireland. . He was clinical director of the HOPE directorate at SJH until stepping down on 30th June 2012 after his appointment in Brisbane.

Prof O'Byrne is a founder member and president of the British thoracic oncology group (BTOG) and British mesothelioma interest group (BMIG). He is also a co-founder and board member of the European thoracic oncology platform (ETOP). He is past-chair and current member of the international association for the study of lung cancer (IASLC) fellowship committee and is a member of the CME committee. He is on the education committee for the IASLC world conference for lung cancer Sydney 2013 and is part of the ESMO chest tumours faculty and involved in developing the upcoming programs for the Amsterdam and ESMO meetings in Madrid. Prof O'Byrne was an active member of the Irish society of medical oncology (ISMO) and the Irish clinical oncology research group (ICORG) chairing the lung cancer disease specific sub-group. He is a member of the all Ireland lung cancer forum (AILCF), EORTC lung cancer group, American society of clinical oncology (ASCO) and the American association for cancer research (AACR). Prof O'Byrne retains an honorary chair at Trinity College and continues to supervise the thoracic oncology research group in the institute of molecular medicine on the SJH campus focusing on cancer cell survival and drug resistance mechanisms as novel biomarkers and targets for therapy. He and Dr Derek Richard are the directors of the cancer and aging research program (CARP) in the Translational Research Institute, Brisbane focused on DNA stability. Prof O'Byrne has protected intellectual property for a novel lung cancer diagnostic miRNA signature and Inhibitors of Apoptosis Protein (IAP) targeted novel small molecule SMAC mimetics.

Prof O'Byrne is a member of the editorial boards for the 'Journal of Thoracic Oncology', 'Lung Cancer', 'Lung Cancer Management' and 'Chinese Clinical Oncology', has edited 2 text books in thoracic oncology and published over 230 manuscripts in peer-reviewed books and journals



Ms Freyr Patterson

Freyr is an advanced Occupational Therapist working in the Brain Injury Rehabilitation Unit at the Princess Alexandra Hospital. She has recently commenced a research project and research higher degree exploring the use of group therapy interventions in inpatient rehabilitation post traumatic brain injury. She has a keen interest in clinical education, and providing holistic and client-centred rehabilitation post brain injury.

PAH Health Symposium Speakers 2014



Professor Andrew Perkins

Professor Andrew Perkins is a Co-Leader of the Blood and Bone Program at Mater Research in the Faculty of Medicine and Biomedical Sciences at the University of Queensland. He is also Head of the Blood Cancers Program of the Diamantina Health Partners and Metro South Health Care in Brisbane.

Professor Perkins is an expert in clinical and experimental genomics with a focus on how master control genes regulate normal blood cell production, and how they derail differentiation of blood cells when mutated in inherited or acquired genetic diseases. His research program is investigating the genetics and cell biology of haematopoietic stem cell (HSC) behavior during embryonic development and throughout adult life. His team hopes to use this knowledge to

develop new drugs to keep HSCs happy after chemotherapy, genetic insults or normal ageing.

In this presentation at PA Week he will discuss the genetics of myeloproliferative neoplasms (MPN) and how this knowledge is leading to development of effective personalized medicine.



Dr Edward Pink

Dr Edward Pink is the Deputy Director of the Emergency Department of QEII Jubilee Hospital, currently in the Acting Director role for most of 2014. His background of training has been split between Australia and the UK. Dr Pink has a particular interest in patient flow and having seen the effect the 4 hour target had on the UK system, he keen to make sure we learn from their mistakes.



Professor Elizabeth Powell

Elizabeth Powell is a graduate of The University of Queensland Medical School. After completing her early postgraduate training at the Royal Brisbane Hospital and a PhD at The University of Queensland, she won a Menzies Scholarship to study at Oxford University, UK. She returned in 1994 to take up the position of Director of Clinical Training and Hepatologist at the Princess Alexandra Hospital.

Dr Powell currently holds an NHMRC Practitioner Fellowship (third renewal) and has been awarded a Queensland Government Health Research Fellowship. She is a member of the Editorial Board of Hepatology (ranked as the number 1 Hepatology journal), the Clinical Research

Committee of the American Association for the Study of Liver Diseases and the abstract review committee for the Governing Board of the American Association for the Study of Liver Diseases.

Dr Powell is currently an Eminent Staff Specialist in Hepatology at the Princess Alexandra Hospital and Director of the Centre for Liver Disease Research, The University of Queensland.

PAH Health Symposium Speakers 2014



Dr Tarl Prow

Dr Tarl Prow is the Deputy Director of the Dermatology Research Centre within the School of Medicine and heads a group of 10 researchers focused on micromedical devices for dermatology and nanomedicine. In 2004, Dr. Prow earned his Ph.D. from the University of Texas in the field of Nanomedicine. He then completed his NIH-T32 funded fellowship at The Johns Hopkins Hospital and was faculty there until he relocated to the University of Queensland in Brisbane, Australia in 2007.

He is a multidisciplinary researcher with internationally recognized expertise in the fields of micro-medical device development, nanodermatology, topical drug delivery and non-invasive imaging. Since joining the University of Queensland, Dr. Prow has published more than 30 peer reviewed manuscripts in top journals with an average impact factor of 6.15. He more than 80 publications in top ranked journals including Advanced Drug Delivery Reviews, Hepatology, Nucleic Acids Research, Biomaterials, Advanced Functional Materials, Small, Nanomedicine and Journal of Controlled Release. Dr. Prow is an inventor on 6 patents and patent applications in the areas of nano- and micro-medical devices.



Dr Chamindie Punyadeera

Chamindie Punyadeera, Clinical Biochemist, graduated from the Department of Chemical Pathology, School of Medicine at the University of Witwatersrand, Johannesburg, South Africa in 2001. Her PhD research was aimed at investigating the pathogenesis and clinical manifestation of Type 2 Diabetes and obesity in two ethnically diverse South African population groups. She was awarded the Academic Excellence Scholarship from the University of Witwatersrand to pursue her PhD research. She did a 4-year postdoctoral fellowship at the University of Maastricht in the Netherlands in close collaboration with Merck Pharmaceuticals. The research was focused on endometrium physiology and oncology. She worked as Senior Scientist and a Project Leader at the Philips High Technology Research laboratories in the Netherlands till 2008. At Philips, she led a team of researchers in the development of novel, innovative diagnostic platforms.

She has published over 40 research papers, an inventor of 12 patent applications, 4 technical reports, 18 conference proceedings and has delivered key note lectures. She is an Associate Editor to the Journal of Dento Medical Science and part of the editorial board for three other Journals. She is also a recipient of the Smart State Senior Research Fellowship (2010-2013), The University of Queensland Foundation Research Excellence Award (2010) and the Queensland Government International Travel Fellowship (2012). Currently, she heads the saliva translational group and is also a research group leader at the University of Queensland Diamantina Institute. Her team focuses on unraveling the diagnostic potential of human saliva for detecting head and neck cancer and heart diseases.



Ms Amanda Purcell

Amanda Purcell is an occupational therapist working the cancer-related lymphoedema service at the PAH. Amanda has completed her PhD examining the effects of fatigue in people undergoing radiotherapy treatment. She now specialises her occupational therapy practice in lymphoedema management and has a particular interest in lymphoedema of the head and neck region.

PAH Health Symposium Speakers 2014



Associate Professor Gail Robinson

Director of Medical Services, Addiction and Mental Health Services Associate Professor Gail Robinson has worked extensively as a psychiatrist in adult mental health services and is a clinical supervisor for the Royal Australian and New Zealand College of Psychiatrists (RANZCP). Associate Professor Robinson has held leadership roles in Auckland, New Zealand and in Queensland Health Mental Health Services.

In her professional practice, she aims to support the implementation of evidence-based practices within the values of the consumer, family/carer and people in the wider community. She also has a number of research areas including: major psychiatric disorders, primarily schizophrenia and related psychoses, mood disorders and addictions health service research including the interface with primary health and hospital based services design and evaluation of programs focused on improving health from ethnic and cultural background suffering from mental illness.

Associate Professor Robinson contributes to a number of organisations including being an Associate Professor with Griffith University, and an active member of the RANZCP Committee for examinations.

Associate Professor Robinson's qualifications

- MBBCh (University of Witwatersrand)
- FC(Psych)SA (Colleges of Medicine, South Africa)
- Grad Dip Bus (New Ventures),(University of Auckland)
- FRANZCP
- FACHAM (RACP)
- RACMA.



Ms Julie-Ann Ross

Julie-Anne Ross is an Occupational Therapist who works in Allied Health Workforce Development at the PA Hospital. She has experience within the public sector in workforce development, clinical skills and management.

Professor Mark Ross

Professor Mark Ross graduated with a degree in Medicine and Surgery from the University of Queensland in 1987. He completed his FRACS in Orthopaedic Surgery in 1996 and undertook a fellowship in Hand and Upper Limb Surgery at the Princess Alexandra Hospital in 1997, before travelling to the USA to undertake a 12-month Fellowship at the Kleinert Institute for Hand and Microsurgery in Louisville, Kentucky.

Dr Ross was appointed as a full member of the Shoulder and Elbow Society of Australia in 2000 and the Australian Hand Surgery Society in 2001. In September 2004 he was also appointed an International Member of the American Society for Surgery of the Hand. He is currently the Director of the Upper Limb Surgery Fellowship Programme at Princess Alexandra Hospital and a founding member of the Upper Limb Research Group at the Institute of Health and Biomedical Innovation at Queensland University of Technology. He is also President of the Queensland Shoulder Society, and Secretary/Treasurer of the Queensland Hand Surgery Society. Dr Ross has lectured extensively both in Australia and overseas and has published numerous articles on hand and upper limb conditions. He has authored several book chapters. In September 2008, Dr Ross was confirmed as Associate Professor of Orthopaedic Surgery by the School of Medicine at The University of Queensland.

In 2005 Dr Ross was awarded the Shoulder and Elbow Society of Australia's International Travelling Fellowship for 2007 whereby he visited members of the European Society for Shoulder and Elbow Surgery. In 2006, Dr Ross was awarded the inaugural Australian Hand Surgery Society Travelling Fellowship to visit members of the American Society for Surgery of the Hand, which tour he also undertook in 2007.

PAH Health Symposium Speakers 2014



Ms Megan Rossi

Megan has a clinical dietetics background and currently works at Princess Alexandra Hospital part-time in conjunction with part-time private practice and is also undertaking her PhD at the University Of Queensland School of Medicine investigating synbiotic therapy in Chronic Kidney Disease management. Through her PhD work, Megan has received best presentation at the International Congress of Renal Nutrition and Metabolism in both 2012 and 2014 and at the International Science in Nutrition in Medicine Conference in 2013. Megan was also a finalist in this year's Diamantina Health Partners Research and Innovation Ideas Awards and in the 2012 Uniquist Trailblazer competition.

Megan is a member of the Dietetic Association of Australia (DAA) conference scientific committee, the Health Practitioner Research Collaborative working group and has previously consulted for DAA, specialising in International Dietetic and Nutrition Terminology education.

Her research is funded by the Princess Alexandra Research Foundation project grant and postgraduate scholarship.



Dr Jeff Rowland

Jeff Rowland is a Geriatrician working in General Medicine at The Prince Charles Hospital. He is currently

- Director of Physician Education
- Chair of the General Medicine Network including chairing the Qld Senate committee developing Advanced Care Planning
- Member of multiple projects (State and Local) looking at pt flow issues
- Member of Patient Safety committee

He has in the past been

- President of Australian and New Zealand Society for Geriatric Medicine (ANZSGM)
- Executive member of ANZSGM
- President NSW Branch of ANZSGM
- On multiple state and Commonwealth committees dealing with clinical matters of a wide variety
- Coordinator of pathway training for registrars across the Northern Region
- Developer of Palliative Care Pathways for both Residential and Community Care



Associate Professor Anthony Russell

Tony is an Endocrinologist and Director of the Department of Diabetes and Endocrinology at the Princess Alexandra Hospital, Brisbane. In partnership with Prof Claire Jackson, Tony was instrumental in developing the innovative model of care managing complex type 2 diabetes in the community with up-skilled GPs at Inala Primary Care. As a specialist in diabetes management, and with his experience at the interface of primary and specialist care, Tony has provided significant leadership for the diabetes component of an NHMRC Centre for Research Excellence looking at the interface between primary and secondary care. Tony is also CIB on a NHMRC partnership grant lead by Prof Brian Oldenburg implementing an Information and Communication Technology platform to improve the health of people with Type 2 diabetes.

Tony is the Co-Chair of the Qld Health Statewide Diabetes Clinical Network and has recently chaired the Steering Committee developing the Diabetes Services: Statewide Health Service Strategy 2013. Tony has participated on the Expert Advisory Panel for the NHMRC guidelines on management of Type 1 Diabetes. He was on the Expert Group for the "Therapeutic Guidelines: Endocrinology", 2009 and 2013.



Ms Cathie Schnitzerling

Cathie Schnitzerling is Senior Director of Media and Communications for Queensland's Department of Health. She took up the position in May 2013 after a 27 year career in television and radio. After starting as a cadet reporter with Nine News Brisbane she has worked in television news for two commercial networks, numerous national public affairs programs for the Nine network and presented and reported for the ABC's national rural program Landline.

She's reported and presented for ABC radio, produced independent documentaries and a short drama. In 15 years at the Ten Network she progressed from news producer in Melbourne, to news editor and then News Director firstly in Brisbane, then Sydney and back to Brisbane.

Cathie has won two awards recognizing her writing and producing skills.

She is a proud single mother of a 20 year old daughter and 14 year old son.



Professor Michael Schuetz

Prof Michael Schuetz was recruited from Humboldt University Berlin, Germany where he trained in Orthopaedics and Trauma and in 2001 became Associate Professor of Trauma. In 2004 he was jointly appointed the first Chair for Trauma in Queensland through QUT/Qld Health whilst commencing a clinical position at Princess Alexandra Hospital, becoming the Director of Trauma. Following participation on the Working Party to finalise a Trauma System concept for Queensland, and subsequent State government funding, he became the first Chair of the Queensland Statewide Trauma Clinical Network in 2007.

He is a Fellow of the Royal Australasian College of Surgeons and a Fellow of the Australian Orthopaedic Association with special clinical interest in Orthopaedic Trauma including complex joint reconstruction. He is the current theme co-ordinator for the Diamantina Health Partners flagship theme; Integrated Trauma Centre.

His research group is located at the Institute of Health and Biomedical Innovation, QUT and the Translational Research Institute on the Princess Alexandra Hospital campus. This research focuses on; fracture healing including mathematical modelling, CT/MRI Imaging and modelling, soft tissue trauma, and research that reviews and assess processes in trauma management. His research group currently holds several ARC grants along with further competitive research grants in these fields. In addition he is CI on a collaborative NHMRC grant on regeneration of large bone defects awarded \$450,000.



Associate Professor James Scott

A/ Professor James Scott is a child and adolescent psychiatrist whose main focus of research is broadly encapsulated under child and adolescent mental health and early psychosis. He is currently engaged in a programme of research examining psychotic-like experiences in otherwise healthy individuals, mental health outcomes of bullying in adolescents, the role of immune dysregulation in mental illness, and the outcomes of adolescents experiencing their first episode of psychosis. The programmes are a combination of clinical work with patient samples and epidemiological studies in collaboration with large mental health surveys and birth cohort studies.

PAH Health Symposium Speakers 2014



Dr Dan Siskind

Dr Siskind trained as a psychiatrist in Australia and the United States. He did his psychiatry training at Boston University and a Master of Public Health program at Harvard University. He spent two years undertaking research at the Harvard School of Public Health evaluating cost effective treatments for mental illness in developing countries. He returned to Brisbane in June 2008 to take a position as a clinical academic psychiatrist. He works with the PAH Mobile Intensive Rehabilitation Team at Metro South Addiction and Mental Health Services. He has completed his Ph.D. on “Supported Accommodation for People with Severe and Persistent Mental Illness” at the UQ Queensland Centre for Mental Health Research.

His research interests include supported accommodation, international and transcultural mental health, ECT, assertive community treatment and mental health services research.



Professor H. Peter Soyer

Professor Soyer is an academic dermatologist with over 30 years experience in the field. He was appointed as the inaugural Chair in Dermatology by The University of Queensland (UQ) in 2007 and as Director of the Princess Alexandra Hospital (PAH) Dermatology Department in 2008. He has a strong focus on translational skin cancer research in his dual role as the Director of the Dermatology Research Centre (DRC), part of UQ School of Medicine, and leadership of the Dermatology Department at the Princess Alexandra Hospital in Brisbane. He is also an Adjunct Professor within the UQ Diamantina Institute.

Professor Soyer is internationally recognised in the field of dermatology with particular expertise in the areas of clinical dermatology, dermatooncology, dermatopathology and dermatologic imaging (dermoscopy and reflectance confocal microscopy). Within the dermatology discipline he is a pioneer and world leader in the field of dermoscopy of pigmented skin lesions, a non-invasive diagnostic method. He has lead the development of the morphologic classification system currently used worldwide. In the last years one research focus of his has been to expand the concept and applications of teledermatology and teledermoscopy and he is CIE on a recently awarded NHMRC Centre for Research Excellence in Telehealth.

Professor Soyer has an extensive publication record with over 550 publications to date, with more than 500 citations per year (in the last 5 years) and an h-index of 41 (ResearcherID: E-6000-2010). Professor Soyer is the recipient of an NHMRC Practitioner Fellowship (2012-2016), and since his appointment with UQ, has been awarded 3 NHMRC project grants (2 as CIA), 1 NHMRC Centre for Research Excellence grant (as CIE), 1 ARC Discovery project grant (as CIB) and several other sources of competitive funding. In total, through his involvement as an investigator, he has achieved over \$9m in research funding for UQ.



Dr Lyndall Spencer

Dr Lyndall Spencer commenced her working life as a student nurse in Royal Perth Hospital. Over the intervening years she has occupied nursing roles in clinical, academic, and managerial positions in three Australian states, London, and Hong Kong. Immediately prior to joining the PAH team she held a joint appointment with the Western Australian Country Health Service and the University of Notre Dame Australia in the Kimberley. Her roles there included coordinating nursing research in the six hospitals in the Kimberley, and teaching in the undergraduate and postgraduate nursing programs delivered by the UNDA Broome campus.

PAH Health Symposium Speakers 2014



Professor Tony Stanton

Tony Stanton is a cardiologist with a special interest in non-invasive cardiovascular imaging. He has a particular interest in the interaction between multisystem disease and cardiovascular function. He practices at the Princess Alexandra Hospital and Ipswich Hospital. He is the Director of the Cardiovascular Imaging Research Group at the University of Queensland



Dr Michael R. Tallack

Michael has worked in the field of molecular genetics for 10 years with a particular focus on the molecular mechanisms responsible for red blood cell (erythroid) differentiation. He completed a BSc with honours in 2005 at the University of Queensland majoring in developmental biology. He subsequently completed his PhD in 2009 also at the University of Queensland under the supervision of Prof Andrew Perkins focused on the role of the erythroid specific transcription factor KLF1 in the differentiation and development of erythroid cells. He has since worked in the Perkins laboratory, formerly at the IMB, UQ and now at Mater Research to understand the genetic control of blood development and its application to human blood diseases with a focus on the myeloproliferative neoplasms. Michael has been awarded several prizes including the Post-

Doctoral Researcher Award at the 2012 Queensland Health and Medical Research Awards and a scholarship from the Royal College of Pathologists of Australasia in 2013.

In 2012 Michael began further study as a medical student, which he is now in his 3rd year at the University of Queensland. Michael hopes to combine his passion for emerging genomic technologies with significant unanswered clinical problems in order to further our understanding of blood diseases in the near future and to advance the possibility of patient specific therapies.



Dr David Theile (Snr)

Professor David Theile (Snr) has had a long career in clinical practice with progressive involvement in professional affairs and hospital administration, culminating in his appointment as District Chief Executive Officer of the Metro South Health Service District, which incorporates Princess Alexandra Hospital. Dr Theile graduated MBBS with honours from the University of Queensland in 1962, completed his postgraduate training as a resident and surgical registrar at Royal Brisbane Hospital and gained his fellowship to the Royal Australian College of Surgeons in 1967. After three years in the UK he returned to Brisbane and in 1974 was appointed to the Visiting Staff of PAH as a General Surgeon, a position he held until his appointment as CEO. Professor Theile committed himself extensively to the activities of the Royal Australasian College of Surgeons, serving as

national President and was awarded the College's highest award (the Sir Hugh Devine Medal). In 2000, Professor Theile was appointed Chairman of the Division of Surgery at PAH and he occupied this post until his appointment as PAH's Clinical CEO in 2006, and ultimately Metro South's District CEO in 2008. Dr Theile retired from this position in 2012.



Professor John Upham

John Upham is a clinical scientist and respiratory physician with a longstanding research interest in chronic lung diseases such as asthma, COPD and bronchiectasis. His research team examines why some people are susceptible to lung infections and allergies, and aims to develop novel ways to improve immune function.

After clinical training in Brisbane, John worked in Perth and at McMaster University in Canada, before returning to Brisbane in 2007. John runs a severe asthma clinic at Princess Alexandra Hospital, and leads the Lung & Allergy Research Group in the Translational Research Institute.

Michael Wagels

Michael is the Academic Staff Specialist Plastic and Reconstructive Surgeon for the Princess Alexandra Hospital and the University of Queensland. He graduated from the University of Queensland with an MBBS and BMedSci in 1999. After working in resident level jobs in regional, interstate and overseas centres, he was granted a RACS training position in Plastic and Reconstructive Surgery in 2006. His training was interrupted in 2008 to enrol in a research higher degree through the University of Queensland and was the recipient of the RACS-CONROD Trauma Fellowship in 2009. He was awarded FRACS in Plastic and Reconstructive Surgery in 2012 and PhD in 2013. His interests are in surgery of the hand and wrist, head and neck, melanoma and other cutaneous malignancies and lower limb trauma reconstruction



Ms Laurelie Wall

Laurelie Wall BSpPath(Hons) graduated with a university medal from The University of Queensland in 2012. She works part-time at the Princess Alexandra Hospital as a member of the acute speech pathology team. Laurelie has a keen interest in the delivery of speech pathology and broader multidisciplinary services to head and neck cancer patients receiving (chemo)radiotherapy. She is currently undertaking her PhD exploring the use of technology-assisted service-delivery models to enhance aspects of speech pathology assessment and management for the head and neck cancer population.



Associate Professor Euan Walpole

Euan Walpole has had an appointment as a specialist in medical oncology at PAH since 1990. Interests include clinical research particularly in Gastro-Intestinal, Breast, Melanoma/Sarcoma and Testicular Cancers. He has had multiple clinical trial involvement including Australasian PI on international studies. He has been Chairman of the Medical Oncology Group of Australia, Deputy Chairman of the Medical and Scientific Committee of the Queensland Cancer Fund and a member of the Medical and Scientific Committee of the Australian Cancer Society/Clinical Oncological Society of Australia.

Medical Oncology training and provision of cancer services in Australia have been a long interest and includes being the Chair of the Specialist Advisory Committee in Medical Oncology for the Royal Australasian College of Physicians. He is sponsor for the implementation of clinical information systems in cancer in Queensland with the radiation oncology information system and pharmacy oncology information system. He is also chair of the Queensland Cancer Control Safety and Quality Partnership and sponsor of the Queensland Cancer Control Analysis Team.

PAH Health Symposium Speakers 2014



Dr Timothy Warren

Dr Timothy Warren undertook a science degree in biomedicine, followed by honours in neonatology at UQ. Dr Warren completed his medical degree at the University of Sydney. After internship he returned to QLD and the PA hospital. He has done ENT PHO work at Greenslopes Private, Toowoomba and the PA.

In 2012, he was awarded a Clinical Research Fellowship by the PA Research Foundation to undertake a PhD through the UQ SOM. His PhD is titled Molecular and Epidemiological features of Cutaneous SCC with Perineural Invasion, and is under the supervision of Assoc Prof Ben Panizza. In 2013 he was awarded an NHMRC Postgraduate Scholarship to continue his research at PA and QIMR. Dr Warren is currently a SET 1 ENT Registrar in QLD working at Logan Hospital.



Associate Professor Jon Whitehead

After completing his PhD at the University of Liverpool (UK) in 1994, Dr Whitehead moved to the University of Cambridge (UK) where he began work in the area of insulin signalling, insulin resistance and obesity. In 1999 he secured an International Travelling Fellowship from the Wellcome Trust, taking up a position at the Institute for Molecular Bioscience at The University of Queensland (UQ), then the Diabetes & Obesity Research Program at the Garvan Institute of Medical Research in Sydney.

In 2002 he returned to UQ to take up an independent position as a Lions Senior Medical Research Fellow. In 2008 he was awarded an NHMRC Senior Research Fellowship and relocated to the Mater Research Institute in early 2010.



Dr Kerstin Wyssusek

Dr Kerstin Wyssusek is a Senior Staff Specialist Anaesthetist at the Princess Alexandra Hospital (PAH). Her anaesthesia interests include endocrine, hepatobiliary and transplant anaesthesia. Before moving to Australia Kerstin worked in Germany. She started her employment with QLD health at the Royal Brisbane and Women's Hospital and moved to the PAH in 2009. Dr Wyssusek has significant teaching and training responsibilities within the anaesthetic department at PAH and the Australian and New Zealand College of Anaesthetists.



Mr Dennis Young

Dennis Young is a consumer representative on the Metro South Health Clinical Ethics Committee and received a lifesaving liver transplant during 2006. Dennis currently is the Executive Director for Healthy Options Australia which incorporates Drug ARM Australasia, the Mental Health Association of Queensland and the Australian College of Community Services. Dennis holds a Doctorate in Health Services Management together with business and educational qualifications. Dennis served for approximately 17 years in the Queensland Police Service and is also a former member of the Queensland Parliament".



Professor Ross Young

Professor Ross Young was appointed Executive Dean, Faculty of Health in 2013. He was previously Executive Director, Institute of Health and Biomedical Innovation (IHBI), QUT, from 2006 -2012. He is also a Visiting Research Fellow at the Alcohol Research Center, University of California, Los Angeles and a Senior Clinical Psychologist at the Alcohol and Drug Assessment Unit, Princess Alexandra Hospital, Brisbane. Professor Young's previous roles include Director of the Behaviour Research and Therapy Centre (Psychiatry) at The University of Queensland where he also undertook his PhD studies at The University of Queensland in the School of Psychology. Professor Young completed undergraduate psychology and postgraduate clinical psychology studies at The University of Otago,

New Zealand.

Professor Young's research interests lie in the integration of psychological and biological risk factors in mental illness. His research includes work in substance misuse, schizophrenia, anxiety disorders and more broadly in behavioural medicine. This includes work in pharmacogenomics and the development of personalised medicine via the use of diagnostic gene chips. Professor Young is widely published and has over 190 published papers in genetic, medical, psychiatric and psychological journals.

Professor Young serves on a number of Boards including Cancer Council Queensland, Gallipoli Medical Research Foundation, Mantle (Pty) Ltd and is Patron of The Association of Relatives and Families of the Mentally Ill (ARAFMI) Queensland.

Information for Delegates and Presenters

Venue

Princess Alexandra Hospital
199 Ipswich Road
Woolloongabba
Queensland, Australia, 4102
Ph: 61 (0)7 3176 2111

The Translational Research Institute
199 Ipswich Road
Woolloongabba
Queensland, Australia, 4102
Ph: 61 (0)7 3443 7000

Registration

The registration desk will be attended 15 minutes prior each session. You will be requested to sign in for each session you attend.

Venue Layout

The registration desk is located in the Russell Strong Auditorium foyer. All breaks take place in The Russell Strong Auditorium foyer and the Russell Strong Auditorium courtyard. The Plenary and concurrent sessions are mainly held in the Russell Strong Auditorium excluding the Young Investigator Awards which will be held in the TRI auditorium. Please see Venue Map on the next page.

Poster Viewing

Delegates with posters can find the correct position for their poster by locating the presenters surname on the display panels. The panels are set up in the Princess Alexandra Hospital main foyer. Posters can remain on display from Tuesday morning and must be removed by morning tea Friday. During the formal Poster Expo (on Wednesday evening), the presenters should attend their poster to answer questions and meet colleagues with similar research interests. Refreshments will be served during this function.

Insurance

The hosts and organisers are not responsible for personal accidents, any travel costs, or the loss of private property and will not be liable for any claims. Delegates requiring insurance should make their own arrangements

Smoking

You cannot smoke anywhere on the Princess Alexandra Hospital campus. We are committed to a cleaner, healthier hospital. Your health is important to all of us. Fines of up to \$200 may apply for staff, patients and visitors who are in breach of our Smoking Management Policy.

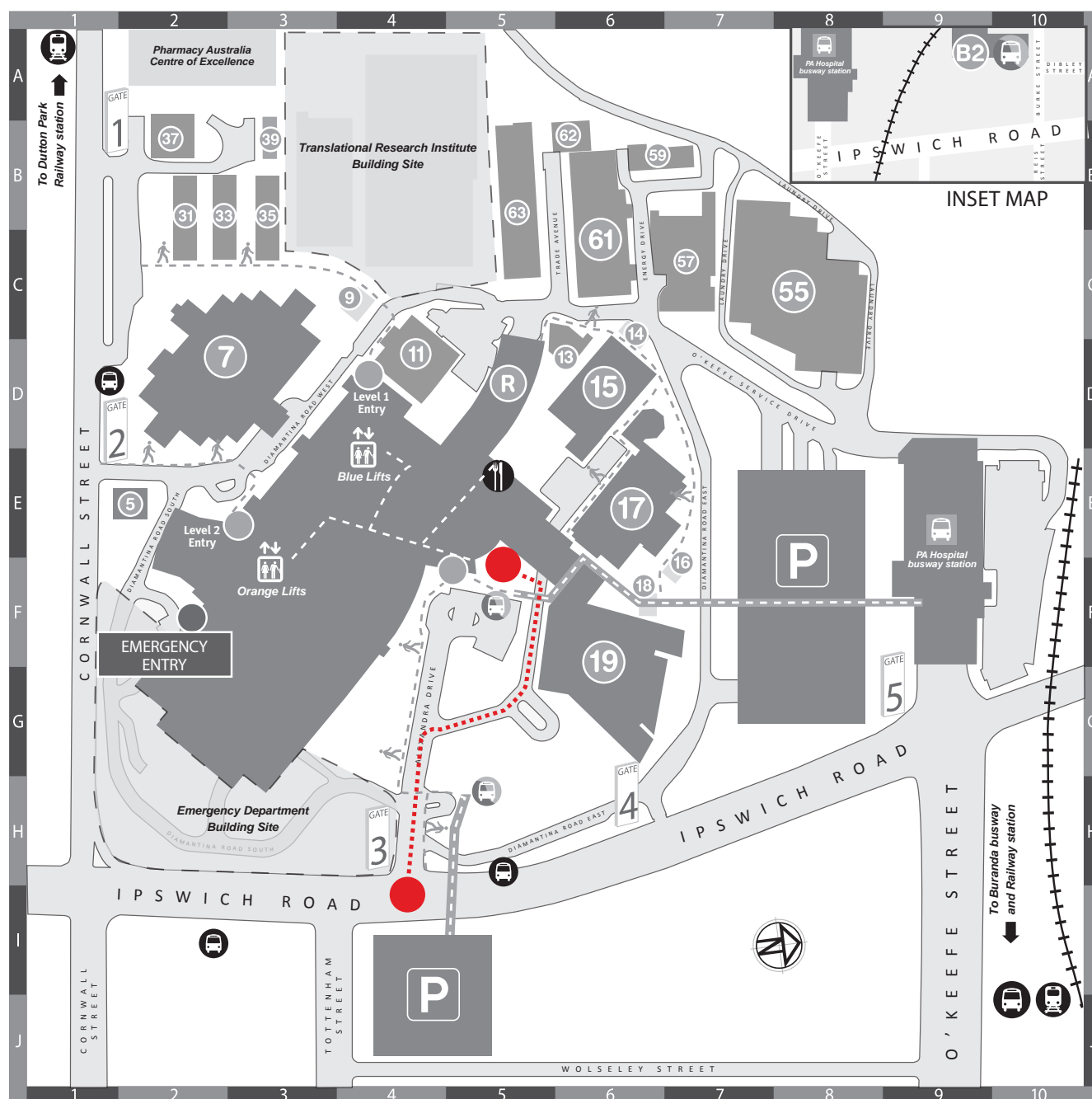
Mobile Phones

Please ensure they are turned off during any session you attend.

Disclaimer

The hosts, organisers and participating societies are not responsible for, or represented by, the opinions expressed by participants in either the sessions or their written abstracts.

Princess Alexandra Hospital Venue Map Layout



- | | | |
|---|---|--|
| ● main hospital entries D4, E3, F5 | 15 executive building D6 | 55 metropolitan linen services (mls) C8 |
| ● emergency entry F2 | 17 spinal injuries unit (siu) E6 | 57 central energy unit (ceu) C7 |
| i information desk E4 | 19 mental health services F6 | 61 general support services C6 |
| 公共厕所 E5, E5, F3 | R research wing D5 | 63 maintenance services B5 |
| 公共咖啡馆 E5 | 31 ambulatory and renal transplant services (arts) B2 | B2 burke street centre SEE INSET MAP |
| 5 diamantina health care museum E2 | 33 building 33 B3 | P parking |
| 7 geriatric and rehabilitation unit (garu) D3 | 35 building 35 B3 | ● train station |
| 13 aquatic physiotherapy pool D6 | 37 specialised health services (shs) B2 | ● bus stop |
| | | ● PA shuttle bus stops H4, F4, INSET A10 |

Monday, 4th August 2014

Department Research Showcase

1:00 PM - 2:25 PM

Co-chairs: Professor Ken Ho and Professor Michael Schuetz

Russell Strong
Auditorium

Professor Ken Ho

Welcome

Dr Goce Dimeski

Chemical Pathology, Princess Alexandra Hospital

Dr Chamindie Punyadeera

Head and Neck Surgery, Princess Alexandra Hospital

Dr David Evans

Genomic Medicine Program, UQ Diamantina Institute

Dr Michelle Hill

Cancer Program, UQ Diamantina Institute

A/Professor Marion Mitchell

Critical Care Nursing, Princess Alexandra Hospital

Dr Lyndall Spencer and Ms Kym Dalmaso

Emergency Nursing, Princess Alexandra Hospital

Professor Sandie McCarthy

Cancer Nursing, Princess Alexandra Hospital

Dr Michael Wagels

Plastic and Reconstructive Surgery, Princess Alexandra Hospital

Afternoon Tea

2:25 PM - 2:40 PM

Russell Strong
Auditorium Foyer

Department Research Showcase

2:40 PM - 4:00 PM

Co-chairs: Professor Matt Brown and Professor Gerald Holtmann

Russell Strong
Auditorium

Dr Mark Ross

Orthopaedic Surgery, Princess Alexandra Hospital

Ms Laurelie Wall

Speech Pathology, Princess Alexandra Hospital

Ms Amanda Purcell

Occupational Therapy, Princess Alexandra Hospital

Dr Helen Benham

Immunology Program, UQ Diamantina Institute

Professor John Upham

Respiratory Medicine, Princess Alexandra Hospital

Professor David Johnson

Nephrology, Princess Alexandra Hospital

A/Professor Anthony Russell

Diabetes and Endocrinology, Princess Alexandra Hospital

Networking Drinks Function

4:00 PM - 5:00 PM

Russell Strong
Auditorium Foyer

Trauma Grand Rounds <i>Trauma in Rural Places: how can the tertiary facility help?</i> 7:15 AM - 8:30 AM Chair: Professor Michael Schuetz Dr Sue Masel - Goondiwindi Hospital/President of Rural Doctors Association QLD Dr Matt Masel - Goondiwindi Hospital	Russell Strong Auditorium
Morning Tea 10:30 AM - 10:45 AM	Russell Strong Auditorium Foyer
Welcome and Official Opening 10:45 AM - 11:15 AM <i>Welcome</i> Dr Stephen Ayre - Executive Director, PAH-QEII Health Network <i>Official Opening</i> Dr Geoff Garrett AO - Chief Scientist to the State Government of Queensland	
Plenary 11:15 AM - 12:15 PM Chair: Professor Ken Ho Professor Boris Bastian - University of California, San Francisco Melanoma: a group of distinct diseases requiring different clinical management	Russell Strong Auditorium
Lunch 12:15 PM - 1:00 PM	Russell Strong Auditorium Foyer
Award Winners and Research Outcomes <i>The seeds we have sown</i> 1:00 PM - 2:30 PM Co-Chairs: Dr Liz Jordon and Mr Robert Bowen Dr Timothy Warren - Logan Hospital Molecular and epidemiological insight into cutaneous SCC with perineural spread Dr Rathika Krishnasamy - Princess Alexandra Hospital Myocardial Strain Assessment in CKD A/Professor Tony Stanton - University of Queensland Diabetic Cardiomyopathy: Predictors of progression and outcome after 10 years of follow up Ms Freyr Patterson - Princess Alexandra Hospital Group therapy interventions in traumatic brain injury rehabilitation: processes, perceptions and effectiveness Professor John Upham - University of Queensland Which people with asthma have impaired anti-viral immunity? Dr Katrina Campbell - Princess Alexandra Hospital SYNbiotics: Easing Renal failure by improving Gut microbiology (SYNERGY)	Russell Strong Auditorium

Afternoon Tea

2:30 PM - 2:45 PM

Russell Strong

Auditorium Foyer

Cancer

Tomorrow's cancer research today

2:45 PM - 4:15 PM

Co-Chairs: Professor Ken O'Byrne and A/Professor Devinder Gill

Russell Strong

Auditorium

A/Professor Euan Walpole - *Princess Alexandra Hospital*

Data collection and the implications for audit and research

A/Professor Paula Marlton - *Princess Alexandra Hospital*

Biobanking

Dr Andrew Barbour - *University of Queensland*

A novel target identification in upper GI medicines

Professor Andrew Perkins - *Mater Research*

Personalised treatment for blood cancers

Wednesday, 6th August 2014

Immunology and Inflammation

The microbiome in the regulation of disease and immune responses

9:00 AM - 10:30 AM

Co-Chairs: Dr Graham Leggatt and Professor Elizabeth Powell

Professor Mark Morrison - *University of Queensland*

Introduction to the microbiome, disease and immunity

Professor Matthew Brown and Dr Tony Kenna - *University of Queensland*

Ankylosing spondylitis (clinical introduction and basic research)

Professor David Johnson and Ms Megan Rossi - *Princess Alexandra Hospital*

SYNbiotics in kidney disease: Panacea or just another fad? (clinical introduction and basic research)

Professor Elizabeth Powell and Dr Kate Irvine - *University of Queensland*

Inflammation and altered immune function in decompensated cirrhosis: role of bacterial translocation (clinical introduction and basic research)

Russell Strong

Auditorium

Morning Tea

10:30 AM - 10:45 AM

Russell Strong

Auditorium Foyer

Mental Health

Continuity of care in mental health - a look at current research across the age span

10:45 AM - 12:15 PM

Co-Chairs: A/Professor Gail Robinson and Professor Steve Kisely

A/Professor James Scott - *University of Queensland*

Antibodies and schizophrenia

Dr Dan Siskind - *Metro South Addiction and Mental Health*

Impact and cost effectiveness of transitional housing/step up step down

Dr David Lie - *Metro South Addiction and Mental Health*

Dementia and difficulties of driving deterioration

Mr Richard Nelson - *Queensland Alliance*

Delivery of Mental Health care in the community

Russell Strong

Auditorium

Lunch

12:15 PM - 1:00 PM

Russell Strong

Auditorium Foyer

Chronic Disease

Russell Strong

Multi-disciplinary approaches to chronic disease

Auditorium

1:00 PM - 2:30 PM

Chair: A/Professor Warrick Inder

Dr David Gillis - *Princess Alexandra Hospital*

Monoclonal antibodies for dummies

A/Professor John Whitehead - *Mater Medical Research Institute*

Ten things you should really know about fat

A/Professor Tony Stanton - *University of Queensland*

Kidney disease and cardiac function: a new strain of thought

Ms Kate Bell - *Princess Alexandra Hospital*

Developing a nurse-led osteoporosis service

Dr Katrina Campbell - *Princess Alexandra Hospital*

A matter of (bad) taste: Complications in chronic disease

Afternoon Tea

Russell Strong

2:30 PM - 2:45 PM

Auditorium Foyer

Young Investigator Awards

TRI Auditorium

2:45 PM - 5:00 PM

Co-Chairs: Dr Michelle Hill, Dr Janet Davies, Professor Andrew Perkins, A/Professor Warrick Inder

Guest Adjudicators: Professor Boris Bastian Professor Matt Brown, Professor Lyn Griffiths,

Professor John Prins and Professor Ken Ho

2:45 PM - 3:45 PM Student Finalists

3:45 PM - 4:00 PM Break

4:00 PM - 5:00 PM Postdoctorate Finalists

Young Investigator Awards Poster Expo and Drinks Function

PA Hospital

5:00 PM - 7:00 PM

Main Foyer

Poster Judges: A/Professor Ingrid Winkler, Dr Patrick Ling, Dr Sally Mapp, Professor David Crompton and Dr Mark Taylor

Live entertainment - Empresarios

Covidien Surgical Prize

1.4L.2

7:30 AM

New Technology

Russell Strong

Emerging technologies

Auditorium

9:00 AM - 10:30 AM

Co-Chairs: Professor Andrew Perkins and Professor Peter Soyer

Dr Michael Tallack - *University of Queensland*

Genomics for clinicians

Dr Tarl Prow - *University of Queensland*

New technologies for skin cancer research

Professor Peter Gray - *Australian Institute for Bioengineering and Nanotechnology*

From biologics to stem cells – world leading Queensland bioengineering

Professor Melissa Little - *University of Queensland*

Teaching pluripotent cells to make kidney

Morning Tea

Russell Strong

10:30 AM - 10:45 AM

Auditorium Foyer

Trauma

Russell Strong

Trauma care in developing systems-what can a tertiary facility provide?

Auditorium

10:45 AM - 12:15 PM

Co-Chair: Professor Michael Schuetz and Dr Mark Elcock

Dr Patrick Honasia - *Central Hospital, Honiara Solomon Islands*

Trauma care in the Solomons - is there a role for Australia?

Dr Mark Elcock - *Retrieval Services Queensland*

Remote support for emergency departments in Queensland

Dr Paul Millican - *AusHeal*

Plastic surgery challenges in the Congo

Dr Devakar Epari - *Queensland University of Technology*

Finding affordable solutions for trauma care in developing systems -

QUT partnerships

Dr John North - *Princess Alexandra Hospital*

Telemedicine in Queensland-are there cost and time savings?

Lunch

Russell Strong

12:15 PM - 1:00 PM

Auditorium Foyer

St. George Bank Lunchtime Debate -

Mass media saves lives - an interactive debate

12:15 PM - 1.00 PM

Moderator: Ms Bernadette Thomson

Affirmative Team:

Ms Melissa Argent - Princess Alexandra Hospital

Ms Cathie Schnitzerling - Queensland Health

Dr Ben Light - Queensland University of Technology

Ms Naomi Ford - Princess Alexandra Hospital

Negative Team:

A/Professor Julie Mundy - Princess Alexandra Hospital

Mr Dennis Young - Drug Arm

Mr Tony Moore - Fairfax Media - Brisbane Times

Mr Patrick Condren - Fairfax Media - 4BC

Russell Strong

Auditorium

Education

What can I do to make a difference?

1:00 PM - 2:30 PM

Co-Chairs: Dr Georgina Cooke and Ms Julie-Ann Ross

Dr Mary Boyde - Princess Alexandra Hospital

Patient Education

Ms Delena Amsters - Princess Alexandra Hospital

Consumer involvement in research

Professor Amanda Henderson - Princess Alexandra Hospital

Students, Graduates, and Experienced Staff: Recipients of our Duty of Care

Ms Ruth Jebb - Princess Alexandra Hospital

"It's all about ME" Consumer Engagement in an International Context

Russell Strong

Auditorium

Afternoon Tea

2:30 PM - 2:45 PM

Russell Strong

Auditorium Foyer

Health System Innovation

Doing better with less: the real future of health care

2:45 PM - 4:15 PM

Co-Chairs: Dr Michael Daly and Dr Ruth Hubbard

Professor Nick Graves - Queensland University of Technology

Getting better care- how economics helps

Dr Jeff Rowland - Queensland Health

Getting out of my medical ward

Dr Edward Pink - QEII Hospital

Getting out of my Emergency Room

Dr Kerstin Wyssusek - Queensland Health

Getting waste out of my theatre

Professor Gerald Holtmann - Princess Alexandra Hospital/University of Queensland

Getting onto my endoscopy list

Russell Strong

Auditorium

Diamantina Health Partners -

Russell Strong

Princess Alexandra Hospital Health Odyssey - History Transforming Futures

Auditorium

8:45 AM - 10:45 AM

Co- Chairs: Dr David Theile (Snr) and Ms Sue Cumming

The ascending profile of Princess Alexandra Hospital

Professor Donald Cameron - Princess Alexandra Hospital

Research at Princess Alexandra Hospital - chain reaction?

Professor Stephen Lynch - Princess Alexandra Hospital

Where we are at - flashbacks to the past

Dr Judy Flores - Princess Alexandra Hospital

Medicine at PAH: out of the shadow and into the spotlight

Ms Veronica Casey - Princess Alexandra Hospital

The evolution of research in Nursing – past present and future

Dr Jenny Lethlean - Princess Alexandra Hospital

1996-2014: an allied health research odyssey

An epic drama of adventure and exploration

The Future PAH and Partnerships

Ms Areti Gavrilidis - Diamantina Health Partners

Realising the tripartite mission through partnerships

Panel Discussion - The ongoing quest for excellence, productivity and efficiency

Moderator: Professor Ross Young - Queensland University of Technology

Dr Richard Ashby - Metro South Health

Professor Matt Brown - University of Queensland

Professor David Crompton - Metro South Addiction and Mental Health

Professor Len Gray - Princess Alexandra Hospital/University of Queensland

Professor Ken Ho - Princess Alexandra Hospital/University of Queensland

Professor Gerald Holtmann - Princess Alexandra Hospital/University of Queensland

Morning Tea

Russell Strong

10:45 AM - 11:00 AM

Auditorium Foyer

Awards Ceremony and Kurt Aaron Oration

Russell Strong

11:00 AM - 12:25 AM

Auditorium

Dr Richard Ashby - Metro South Health

Chair: Dr Susanne Jeavons

Professor Boris Bastian - University of California, San Francisco

The promise of precision medicine

Closing Address

12:25 PM - 12:30 PM

Professor Ken Ho - Princess Alexandra Hospital

Author Index

Adams, M	52	Read, T	82
Ahmed, A	52	Reeves, P	83
Al-Kouba, J	53	Reiling, J	83
Amarathunga, J	53	Rossi, M	84
Ashton, N	54	Rudraraju, R	85
Baird, A	54	Shah, A	85
Barnett, C	55	Sharifi, B	86
Batra, J	56	Shorter, P	86
Bell, C	56	Sinnya, S	87
Benham, H	57	Small, D	88
Borg, D	58	Soong, S	89
Box, J	58	Srinivasan, S	89
Burgess, J	59	Tallack, M	90
Burke, M	59	Tang, K	91
Caragata, M	60	Thomas, J	91
Castillo, L	61	Thorling, C	92
Chacko, Y	61	Thuzar, M	92
Chai, R	62	Topkas, E	93
Cheng, M	63	Tran, L	94
Chikani, V	63	Tufekci, P	94
Dunn, L	64	Tullett, K	95
Gardiner, D	65	Victor, P	95
Gillinder, K	65	Wallace, N	96
Glatt, V	66	Zhuang, A	97
Hames, S	67		
Haynes, K	68		
Jaffary, S	68		
Kaur, S	69		
Keane, C	69		
Kemp, J	70		
Klenowski, P	71		
Krishnasamy, R	72		
Kulasinghe, A	72		
Lau, A	73		
Law, S	74		
Lenders, N	74		
Lim, Y	75		
Loechel, N	76		
Magor, G	76		
Maradana, M	77		
Mertens-Walker, I	78		
Minoda, Y	78		
Mok, W	79		
Nguyen, T	79		
Palamuthusinga, D	80		
Pavey, S	81		
Quirk N	81		

CDCA3 IS A NOVEL MARKER OF GENOMIC INSTABILITY IN CANCER

Mark Adams^{1,2}, Joshua Burgess^{1,2}, Desi Veleva^{1,2}, Ken O'Byrne^{1,2}, Derek Richard^{1,2}

1 Institute of Health and Biomedical Innovation, Queensland University of Technology, Kelvin Grove

2 Translational Research Institute, Woolloongabba

Progression through the mammalian cell cycle relies upon coordination of a complex network of proteins. Following genomic insult, checkpoints during each stage of the cell cycle are engaged to halt cell cycle progression to allow faithful DNA repair. Failure to arrest cell cycle may lead to genomic instability and cancer development. The focus of this project is on the normal cell cycle regulator cell division cycle associated protein 3 (CDCA3). CDCA3 modulates the cell cycle by promoting the degradation of the endogenous cell cycle inhibitor WEE1. However, a role for CDCA3 in disease is also emerging with upregulated expression noted in oral squamous cell carcinoma tissues and prostate cancer cells.

Herein we describe a novel function for CDCA3 in maintaining genomic stability. Cells depleted of CDCA3 (siRNA) exhibit genomic instability (neutral comet assay) and are sensitive to ionising radiation induced DNA breaks (clonogenic survival assay). Following induction of DNA breaks by ionising radiation, CDCA3 protein levels rapidly increase which is dependent on phosphorylation by one of the key DNA damage sensing kinases, ATM. Failure to phosphorylate CDCA3 yields cells that are unable to effectively arrest cell cycle following DNA damage (Flow cytometry). In addition, our tissue microarray analysis suggests that CDCA3 is overexpressed in non-small cell lung cancer and is associated with poor patient prognosis. Our data highlight a novel role for CDCA3 in maintenance of genome integrity by tightly regulating the cell cycle. Further work will establish whether CDCA3 is a valuable target for future therapy in cancer.

SEATED SALINE SUPPRESSION TESTING FOR THE DIAGNOSIS OF PRIMARY ALDOSTERONISM

Ashraf H. Ahmed, Diane Cowley, Martin Wolley, Richard D. Gordon, Shengxin Xu, Paul J. Taylor, Michael Stowasser

Endocrine Hypertension Research Centre, University of Queensland School of Medicine, Greenslopes and Princess Alexandra Hospitals, Brisbane, Australia

Background:

Failure of aldosterone suppression by sodium loading during fludrocortisone suppression testing (FST) or saline suppression testing (SST) confirms primary aldosteronism (PA). We previously found conventional recumbent SST (RSST) to lack sensitivity. Aldosterone levels can be higher upright (e.g. seated) than recumbent in PA patients and upright levels are used during FST. We therefore hypothesized that seated SST (SSST) is more sensitive than RSST, especially for posture-responsive PA.

Methods:

Of 66 patients who underwent FST (upright plasma aldosterone levels measured at 10am basally and after 4 days fludrocortisone 0.1mg 6 hourly and oral salt loading), 31 underwent SST (aldosterone measured basally at 8am and after infusion of 2L normal saline over 4h) both recumbent and seated in randomised order and at least 2 weeks apart.

Results:

FST confirmed PA in 23 of 31 patients (day 4 upright aldosterone $>165\text{pmol/L}$), excluded PA in 3 and was originally “inconclusive” in 5. However, one with “inconclusive” FST had PA confirmed by lateralizing adrenal venous sampling and was reclassified “unilateral PA”. Of 24 with confirmed PA (8 unilateral, 11 bilateral and 5 undetermined subtype), 23 (96%) tested positive by SSST (4h aldosterone $>165\text{pmol/L}$) compared to 8 (33%) by RSST (4h aldosterone $>140\text{pmol/L}$) (P

Conclusion:

SSST may be more sensitive than RSST for detecting PA, especially posture-responsive forms, and may represent a reliable alternative to FST.

THERAPEUTIC INDUCTION OF TOLERANCE TO REVERSE ALLERGEN-INDUCED AIRWAY INFLAMMATION

Jane AL-Kouba^a, Malcolm Starkey^c, Jay Horvat^c, Philip Hansbro^c, Janet Davies^b, Raymond J. Steptoe^a

a UQ Diamantina Institute, The University of Queensland, Brisbane, AUSTRALIA.

b School of Medicine, The University of Queensland, Brisbane, AUSTRALIA.

c Hunter Medical Research Institute, The University of Newcastle, Newcastle, AUSTRALIA.

Allergic asthma is a lower airways inflammatory disease often resulting from dysregulated T-cell responses to inhaled allergens. Complications are associated with chronic use of pharmacologic disease modifiers employed to control symptoms and current allergen-specific immunotherapies, are poorly efficacious or have other disadvantages. Previously, we have shown that antigen genetically targeted to dendritic cells (DC) inactivates CD4+ and CD8+ T cells. We propose this as the basis for a new approach to 'turn off' dysregulated T cells in asthma.

We first tested whether DC expression of ovalbumin (OVA) prevented sensitisation and airways inflammation that results from OVA₃₂₃₋₃₃₉/alum immunisation and intranasal (i.n.) OVA challenge. Production of IL-4, IL-5 and IL-13 was significantly decreased to baseline levels in OVA-expressing mice relative to non-Tg control and little or no inflammatory cell infiltrate was present in bronchoalveolar lavage fluid (BALF) in OVA-expressing mice. Next, we investigated whether pre-existing dysregulated (memory) T-cell responses could be inactivated in mice with established airways inflammation. Using non-myeloablative conditions, OVA-encoding or non-Tg BM was transferred to OVA₃₂₃₋₃₃₉/alum-immunised and OVA-intranasally challenged BALB/c mice. Production of IL-4, 5, 13 was dramatically reduced in recipients of OVA-encoding, but not non-Tg, BM. Eosinophil cell content in BALF and histological signs of mucus hypersecretion were also reduced indicating reversal of pathogenic processes associated with dysregulated T cell responses.

Therefore, expression of an allergen in DC prevents allergic sensitisation and subsequent respiratory immune responses to allergen challenge. Allergen-encoding BM transfer under non-myeloablative conditions terminates established allergic T-cell responses and reduces allergen-induced airway inflammation.

IS THERE A BONE SPECIFIC NAIL ENTRY POINT? - FIT QUANTIFICATION OF TIBIAL NAIL DESIGNS DURING THE INSERTION FOR SIX DIFFERENT ENTRY POINTS

J. Amarathunga^a, M.A Schuetz^{a,b}, KVD Yarlagadda^c, B. Schmutz^a

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^b Trauma Services, Princess Alexandra Hospital, Brisbane, Australia

^c School of Chemistry, Physics and Mechanical Engineering, Science and Engineering Faculty, Queensland University of Technology, Brisbane, Australia

Introduction:

Intramedullary nailing is the standard fixation method for displaced diaphyseal fractures of tibia. The standard entry point (SEP) may not always optimise the bone-nail fit due to geometric variations of bones. This study aimed to investigate the optimal entry for a given bone-nail pair using the fit quantification software tool, developed by the authors.

Methodology:

3D models of Expert Tibial Nail (ETN) and ETN-Proximal-Bend (Synthes) and twenty 3D cortex models of Japanese tibiae were used. In addition to the SEP, three new entry points were established at 5mm medially, laterally and anteriorly from the SEP and another two at 10mm medially and laterally, respectively.

The software automatically inserted the nail into the inner cortex surface at each entry point. The sums of nail protrusions from the cortex surface (surface area, maximum distance) were used to quantify the overall fitting for each entry point.

Results:

The SEP was the optimal entry point for 50% of the bones used. For the remaining 50%, the optimal entry point was located 5mm away from the SEP. For the latter, shifting the entry point 5mm from the SEP improved the overall fit by 40% on average. However, the entry points 10mm away from the SEP doubled the misfit.

Conclusion:

The optimised bone-nail fit can be achieved through the SEP and within the range of a 5mm radius, except posteriorly. Entry points beyond the 5mm range are not recommended. The developed software tool can potentially be utilised as teaching and/or pre-operative planning tool for surgeons.

HUMAN SINGLE-STRANDED DNA-BINDING PROTEIN 1 (hSSB1) FUNCTIONS AT SITES OF STALLED REPLICATIVE FORKS

Nicholas W. Ashton¹, Nicolas Paquet¹, Emma Bolderson¹, Kenneth J. O'DByrne^{1,2}, Derek J. Richard¹.

¹ Cancer and Ageing Research Program, Queensland University of Technology at the Translational Research Institute, Brisbane, QLD 4102.

² Medical Oncology Department at the Princess Alexandra Hospital, Brisbane, QLD 4102

Human single-stranded DNA-binding protein 1 (hSSB1) is an essential protein of the homologous recombination (HR) pathway of double-strand DNA-break (DSB) repair. By binding short single-stranded DNA stretches at sites of DSBs, hSSB1 is able to recruit and stimulate the endonuclease activity of the Mre11-Rad50-Nbs1 (MRN) complex, initiating a cascade of reactions which result in the activation of downstream targets involved in cell cycle checkpoint activation and directly in DSB repair. Here, hSSB1 is required for full activation of the ataxia telangiectasia mutated (ATM) kinase, initiating a positive feedback loop in which hSSB1 is phosphorylated at threonine 117 (T117); this stimulates further ATM activation.

Recently we have found that hSSB1 also localises to sites of stalled replicative forks, where it functions in the recruitment and activation of the ataxia telangiectasia- and Rad3-related (ATR) kinase. The functional importance of hSSB1 in this process is highlighted by the failure of hSSB1-depleted cells to re-start stalled replication forks, ultimately resulting in elevated sensitivity to replicative stress. In the current study we present data relating to the mechanism of hSSB1 function in this process.

TARGETING NF- κ B IN CISPLATIN RESISTANT NON-SMALL LUNG CANCER

Anne-Marie Baird^{1,2}, Peter Godwin², Susan Heavey², Kazuo Umezawa³, Martin Barr², Derek Richard¹, Kathy Gately², Kenneth J. O'DByrne^{1,4}

¹Thoracic Oncology Research Group, Institute of Molecular Medicine, St. James's Hospital/Trinity College Dublin, Dublin, Ireland

²Cancer and Ageing Research Programme, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia

³Dept. of Molecular Target Medicine Screening, Aichi Medical University, Aichi, Japan

⁴Oncology Department, Princess Alexandra Hospital, Woolloongabba, Australia

Background:

Cisplatin based doublet-chemotherapy is the mainstay of non-small cell lung cancer (NSCLC) treatment with an initial objective response rate of 40-50%. However, intrinsic and acquired chemo-resistance constitutes a major clinical obstacle in lung cancer management and has yet to be fully understood. We have previously demonstrated that NF- κ B levels are elevated in cisplatin resistant cells. The goal of this project is to elucidate the mechanistic links between NF- κ B regulated pathways and the development of cisplatin resistant NSCLC.

Methods:

The expression of NF- κ B downstream targets and signalling mediators were assessed in an isogenic NSCLC cell line model of cisplatin resistance using qPCR arrays (168 genes). The data was analysed using Ingenuity® iReport™. A number of targets were identified and validated using PCR. The effect of a specific NF- κ B inhibitor, DHMEQ, was examined using apoptosis (FACS) and proliferation (BrdU) assays. The effect of drug combinations (Cisplatin and DHMEQ) was also determined.

Results:

NF- κ B mediators such as *TLR4*, *CASP1*, *TNF*, *TNFRSF1A*, *CCL2* and *CCL5* were significantly elevated in cisplatin resistant (CisR) cells compared with cisplatin sensitive (PT) ($p < 0.05$). Conversely, decreased levels of *IL1B* and *IL1R1* were observed in the CisR cell line ($p < 0.05$). Treatment with DHMEQ resulted in decreased cellular proliferation in both CisR and PT cells, however CisR cells demonstrated increased sensitivity to the drug. In addition, DHMEQ enhanced the cytotoxic effect of cisplatin in both cell lines ($p < 0.05$). An animal study will commence shortly.

Conclusions:

DHMEQ may be a viable option in addressing inflammatory associated acquired and intrinsic NSCLC chemoresistance.

EBC-46: A NOVEL TREATMENT FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA

Catherine Barnett, Ryan Adams, Glen Boyle, Paul Reddell, Ben Panizza, Peter Parsons

Princess Alexandra Hospital

University of Queensland

Queensland Institute of Medical Research

Qbiotics Pty Ltd

Purpose

The five-year survival rate for patients with head and neck squamous cell carcinoma (HNSCC) has remained at ~50% for the past 30 years despite advances in surgical technique, chemotherapy agents and radiation therapy technology. EBC-46 is a novel diterpene ester developed by Qbiotics Pty Ltd that induces HNSCC cell senescence in vitro. The purpose of this study was to confirm the efficacy and safety of intratumoural treatment of HNSCC with EBC-46 in mouse models.

Methods

Subcutaneous xenografts of different HNSCC cell lines were grown in Balb/c (*FoxN1*^{-/-}) mice and treated with intratumoural injection of 30 μ g EBC-46 or a control solution.

Results

Treatment with EBC-46 completely ablated the HNSCC xenografts via haemorrhagic necrosis and stimulation of the innate immune response. The control solution had no effect on tumour growth. No significant adverse effects were identified.

Conclusions

EBC-46 effectively and safely ablated HNSCC in a mouse model. These significant results provide the foundation required for progression to human clinical trials.

GENOME-WIDE ASSOCIATION STUDIES OF miRSNPs IDENTIFY NOVEL PROSTATE CANCER RISK LOCI

Jyotsna Batra¹, Shane Stegeman¹, Kerenaftali Klein, Leire Moya¹, PRACTICAL Consortium, Amanda B. Spurdle³, Judith A. Clements¹

1. Australian Prostate Cancer Research Centre-Qld, Institute of Health and Biomedical Innovation and School of Biomedical Science, Translational Research Institute, Queensland University of Technology, Brisbane, Australia

2. Molecular Cancer Epidemiology Laboratory, Genetics and Computational Biology Division, QIMR Berghofer Medical Research Institute, Brisbane, Australia

Background:

Single nucleotide polymorphisms (SNPs) within microRNA (miRNA) binding sites of its target gene, referred to as miRSNPs, are known to have functional consequences for cancer risk.

Methods: We investigated the association between 2,169 putative miRSNPs and prostate cancer risk in a large population including 22,301 cases and 22,320 controls of European ancestry from 23 participating studies within the largest prostate cancer (PRACTICAL) Consortium. We validated the functional role of *KLK3* rs1058205 (T>C) and *MDM4* rs4245739 SNP (A>G) SNPs.

Results:

We identified 22 miRSNPs to be associated with risk of prostate cancer, seven of which has not been previously reported by GWAS studies. We compared the expression levels of the 16 genes harbouring 22 significant miRSNPs and found the expression of 7 genes to be deregulated in prostate cancer in a previously published dataset of 59 tumour and 28 non-tumour samples. We showed that miR-3162-5p has specific affinity for the *KLK3* rs1058205 SNP T-allele. We also found miR-191-5p and miR-887 downregulated *MDM4* protein expression in C-allele containing PC3 cells but not in LNCaP cells homozygous for the A-allele, thus validated two of the functional effects of the two of the miRSNPs.

Conclusions:

Findings from this large study provide evidence that an association study using comprehensive functional SNP approach such as miRSNP can identify additional novel functional risk loci. Further fine-mapping and functional studies on the novel risk loci identified in our study is warranted in the future.

EVX1AS LNCRNA IS REQUIRED FOR VISCERAL ENDODERM AND MESODERM FORMATION

Charles Bell¹, Lorena di Lisio¹, Mathieu Lajois^{1,2}, Seth Cheetham^{1,2}, Kevin Gillinder¹, Graham Magor¹, Pierre Tangermann³, Paulo Amaral³, Anton Karlsbeek³, Jessica Frith^{3,4}, Michael Tallack^{1,3}, Ke-Lin Ru³, Joanna Crawford³, Brooke Gardiner², Jill McMahon⁴, Andrew McMahon⁴, John Mattick^{3,5}, Marcel Dinger^{2,5}, and Andrew Perkins^{1,3,7}

¹ Mater Research-UQ, Translational Research Institute, University of Queensland, Woolloongabba

² Diamantina Institute; Translational Research Institute, University of Queensland; Woolloongabba

³ Institute for Molecular Bioscience, University of Queensland, St Lucia

⁴ The Australian Institute for Bioengineering and Nanotechnology, University of Queensland; St Lucia

⁵ The Garvan Institute, University of New South Wales, Sydney

⁶ Department of Molecular and Cellular Biology, Harvard University, USA

⁷ The Princess Alexandra Hospital; Brisbane, Woollongabba

Long non-coding RNAs (lncRNAs) are dynamically expressed during development and differentiation. There is increasing evidence to suggest they play important roles in organogenesis and differentiation even though they do not encode a protein product. We performed a screen for lncRNAs that are dynamically expressed during ES cell differentiation into embryoid bodies (EBs). We identified many important lncRNAs including *Evx1as*, which is expressed in an antisense direction with respect to *Evx1*, a Hox gene at the 3' end of the *HoxA* cluster. Like *Evx1*, *Mixl1*, and *T*, expression of *Evx1as* is limited to the murine primitive streak from E6.5 to E8.5 *in vivo*. Knockdown of *Evx1as* results in complete failure of the primitive streak wave of differentiation from day 3 of EB differentiation from ES cells. We also generated precise loss of function ES cell lines using CRISPR/Cas9 recombineering to

confirm *Evx1as* lncRNA is essential for gastrulation whereas the lined *Evx1* gene, is not. We performed RNA-seq to determine the transcriptome alterations upon loss of *Evx1as*. *Evx1*, *Mixl1*, *T*, other primitive streak genes are poorly expressed in the absence of *Evx1as*. Surprisingly, there is also loss of expression of visceral endoderm (VE) genes such as BMPs, Wnts, *Cer1* and *Dkk1*. In contrast, ES cell and epiblast (pre-streak) specific gene programs are up-regulated suggesting a specific role for *Evx1as* in primitive streak and VE derivation from epiblast.

We also engineered a conditional *Evx1as* expression construct into the ROSA26 locus. Activation of *Evx1as* with taxmoxifen results in enhanced and persistent expression of VE and primitive streak programs as determined by RT-PCR and RNA-seq. ChIP-seq in *Evx1as*-knockdown EBs shows loss of occupancy of H3K4me3 'marks' at certain gene promoters and a spread of occupancy at other promoters. Thus, we suggest *Evx1as* normally functions to limit the activity of MLL or similar histone methyl-transferases during development. In short, *Evx1as* is necessary and sufficient (in *trans*) for regulation of primitive streak and VE gene expression programs and differentiation of the second (VE) and third (mesoderm) germ layers from epiblast. We will discuss our attempts to further address the molecular mechanisms by which this lncRNA works as a master regulator of gastrulation. This work will revolutionize our understanding of mesoderm formation which is fundamental for development of all of the internal organs.

IL-23 MEDIATES PSORIASIS-LIKE INFLAMMATION IN THE SKG MOUSE MODEL OF SPONDYLOARTHROPATHY

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Psoriasis (Ps) is a common immune-mediated inflammatory skin disease and is a well-recognised extra-articular manifestation of the spondyloarthropathies (SpA). Genetic studies implicate IL-23 signalling in the pathogenesis of both Ps and SpA. Spondyloarthritis and psoriasis-like disease develop in an IL-23-dependent fashion in ZAP70-mutant SKG mice. We characterized curdlan (1,3-D α -glucan) induced psoriasis-like inflammation in SKG mice, investigating the role of IL-23, IL-22/IL-17, regulatory T cells (Tregs) and microbiota.

SKG, IL-17A-deficient, Germ Free (GF) and Foxp3-DTR SKG mice were injected i.p. with curdlan. Anti-IL-22, anti-IL-23 or isotype antibodies were given before curdlan and weekly until sacrifice. Recombinant IL-23 or PBS was administered intra-dermally into ear skin. Outcomes were measured by histological scoring; cytokines by qRT-PCR and in supernatants of cultured explants by ELISA.

Curdlan induced psoriasis-like inflammation in addition to SpA in 100% of SKG mice. Skin lesions showed a histological phenotype similar to human Ps with elevated *IL-23a(p19)* and increased secretion of IL-17 and IL-22. Neutralisation of IL-23 and IL-22 suppressed development of skin inflammation, IL-17A-deficient mice were partially spared. GF SKG mice failed to develop significant skin inflammation, however colonization with a limited microbiota induced mild psoriasis-like inflammation. Tregs modulated severity through suppression of IL-23. Intradermal injection of IL-23 induced IL-22 mediated, microbiota dependent psoriasis-like inflammation.

In curdlan-treated SKG mice IL-23-driven psoriasis-like inflammation is induced in the setting of spondyloarthritis. The skin inflammation recapitulates several features of human Ps and is dependent on the relative contributions of IL-17, IL-22, microbiota and the balance of Tregs and T effector cells.

REDUCING ADVANCED GLYCATION END PRODUCTS IN EXPERIMENTAL DIABETES MODERATES ISLET INFLAMMATION THROUGH ISLET LOCALISED EFFECTS

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Background: Advanced glycation end products (AGEs) are independent predictors of type 1 diabetes progression in islet autoantibody positive children. We aimed to study the immune effect of two AGE lowering therapies administered short term, prediabetes.

Methods: Female NOD mice (n=10/group) received (i) no treatment (ii) a diet 4-fold lower in AGE content or (iii) the drug, alagebrium chloride (ALT; 1mg/kg/day sc) from day 50 - 100 of life and were followed until diabetes diagnosis or day 200. For functional studies, NOD mice were treated from day 50-80 of life.

Results: ALT treatment (50 days) significantly reduced diabetes incidence of NOD mice by day 200 compared to control mice (80% vs 20%, p=0.005). Conversely, mice fed a low AGE diet for 50 days and then returned to standard chow were not protected from diabetes compared to control (80% vs 60%, p=0.35). Therapy from day 50-80, showed little variation in CD4+, CD8+ or regulatory T cell, or antigen presenting cell numbers in pancreatic lymph nodes or spleen, however reduced islet infiltration was observed in mice treated with ALT (p<0.05) or a low AGE diet (p<0.01), with fewer CD4+ T cell numbers within pancreata compared to controls (20 vs 80 vs 650 cells/nm², respectively). Despite this, splenocytes from ALT, but not low AGE fed mice, transferred diabetes to NODscid recipients compared to control cell transfer (69% vs 100% vs 62%, respectively).

Conclusions: This suggests that AGE-lowering therapies may reduce diabetes incidence by modulating anti-islet immunity locally at the pancreatic islet or via direct immune-suppression.

NESTOR GUILLERMO PROGERIA SYNDROME: A BIOCHEMICAL INSIGHT INTO BANF1 A12T MUTATION.

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Premature aging syndromes recapitulate many aspects of natural aging and as such provide an interesting insight into this phenomenon at a molecular and cellular level. Recently, a coding mutation (c.34G>A [p.A12T]) in the Barrier to Autointegration Factor 1 (BANF1) gene was identified as the genetic basis of Nestor-Guillermo Progeria syndrome (NGPS). To explore this in greater depth, we used biochemical and cellular techniques to characterize the mutant BANF1 protein in order to determine how expression of this protein may contribute to the Nestor-Guillermo Progeria syndrome cellular phenotype. In doing so, we have demonstrated that while A12T BANF1 is similarly folded to the wild type (WT), the mutant was impaired for DNA-binding when compared to WT BANF1. In addition, we investigated a previous observation of reduced BANF1 detection in NGPS patient cells, which may be due to a reduction in BANF1 protein levels. Interestingly however, while we were unable to detect a reduction in A12T BANF1 half-life, we did note a decreased antigenicity of the mutant protein, which offers a potential explanation for these findings. We further demonstrate that while overexpression of A12T BANF1 mimics the nuclear phenotype seen in NGPS patient cells, the mutant protein still interacts with nuclear envelope scaffold protein and histones. Suggesting that this phenotype may be solely due to the DNA-binding deficiency. Our study clarifies the role of the A12T mutation in NGPS patients, which will likely be of importance for therapeutic targeting in these patients.

ZINC FINGER PROTEIN 801 ROLE IN DNA DAMAGE REPAIR.

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Zinc finger protein 801 (ZNF801) has been linked to human single stranded DNA binding protein 1 (hSSB1) by a connectivity screen where ZNF801 levels were positively correlated with hSSB1. ZNF801 is over expressed in a number of cancers and functions as a transcription factor. ChIP seq screening has identified a number of ZNF801 binding sites including on the p53, NFkB, PPAR1/2 and P300 promoters. Interestingly these proteins all participate in DNA damage repair. Furthermore, the ZNF801 protein contains an XPA domain, with the XPA protein being involved in nucleotide excision repair of UV induced damage.

In this study we report that ZNF801 is required for the normal cellular response to DNA damage. ZNF801 is rapidly stabilised following DNA damage from ionising radiation, with ZNF801 depleted cells showing sensitivity to DNA damage causing drugs cisplatin and hydroxyurea and this sensitivity is likely due to a cell signalling defect. Interestingly we observed that ZNF801 is cleaved after DNA damage to form a smaller peptide. In light of the defects observed in ZNF801 depleted cells, we suggest ZNF801 has a crucial role in regulating DNA repair signalling pathways and maintaining genomic stability.

EXPRESSION OF BCL-XL AND MCL-1 IN THE NON-MELANOMA SKIN CANCERS OF RENAL TRANSPLANT RECIPIENTS

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Background and Aims:

Renal transplant recipients (RTRs) treated with immunosuppressive medications have an increased risk of non-melanoma skin cancer (NMSC) compared with the general population. Dysregulation of the Bcl-2 protein family and failure of malignant cells to undergo apoptosis is a common pathway in cancer development. This study aims to investigate how immunosuppression influences the protein expression of anti-apoptotic members of the Bcl-2 family, namely Bcl-xL and Mcl-1, in the neoplastic and peri-tumoral epidermis of RTRs.

Methods:

NMSC and peri-tumoral epidermis were assessed by immunohistochemistry in 11 RTRs receiving tacrolimus; 10 RTRs receiving sirolimus and 10 patients from the general population not receiving immunosuppression. Protein expression of Bcl-xL and Mcl-1, apoptosis and mitosis were compared between peri-tumoral epidermis and NMSC.

Results:

NMSC from RTRs compared with patients not receiving immunosuppressant medications had a reduced Bcl-xL expression intensity ($p=0.042$) but no difference in Mcl-1 expression intensity ($p=0.277$) or number of Mcl-

1 positive cells ($p=1.00$). Mcl-1 expression intensity in NMSC was decreased in tacrolimus-treated patients compared with sirolimus treated patients and the non immunosuppressed population ($p=0.024$). Bcl-xL expression intensity was increased in peri-tumoral epidermis compared with NMSC ($p=0.002$). NMSC compared with peri-tumoral epidermis had increased rates of mitosis ($p=0.029$) and apoptosis ($p<.001$)

Conclusions:

Bcl-xL and Mcl-1 expression are widespread in the peri-tumoral epidermis and non-melanoma skin cancers of renal transplant recipients. Sirolimus does not reduce the expression of Bcl-xL and Mcl-1 in peri-tumoral epidermis or NMSC. The development of novel therapeutics that target the Bcl-2 family may advance the prevention and treatment of NMSC in RTRs.

NOVEL SALIVARY PROTEIN BIOMARKERS TO DETECT HEART FAILURE

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Heart Failure (HF) is the second killer in the world and in Australia alone one person dies of cardiovascular disease complications. Currently, there are no detection methods. Saliva has recently gained attention as a diagnostic fluid for detecting biomarkers in systemic diseases such as HF. Human saliva is an ideal diagnostic fluid because of its non-invasive nature and ease of sampling. Therefore, we aimed to develop a robust method to detect biomarkers of HF in saliva, depleting the high abundant proteins and validating these markers using a mass spectrometry (MS) method called SWATH-MS.

Saliva samples were collected from controls ($n=9$) and HF patients ($n=8$). ProteoMiner® beads were used to deplete the high abundant proteins in saliva followed by trypsin digestion and information dependent acquisition LC-ESI-MS/MS to identify proteins. Proteins were then validated with SWATH-MS.

Validation using SWATH-MS identified a panel of four proteins which, when combined in a ratio abundance comparing controls to HF patients, display significant discrimination for HF patients over controls, *i.e.* Protein C:Protein D ($p<0.0005$, AUC= 1, sensitivity 100%, specificity 88.89%), Protein B:Protein D ($p<0.0021$, AUC= 0.9444, sensitivity 87.5%, specificity 88.89%), Protein A:Protein D ($p<0.0015$, AUC=0.9583 sensitivity 87.5%, specificity 88.89%). These four salivary biomarkers should therefore be considered as a powerful panel to detect HF.

ENDOCARDITIS AFTER DOG BITE

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Capnocytophaga canimorsus is a commensal, Gram-negative bacillus living in the oral cavities of dogs and cats. It has been implicated in severe human infections, mainly septicaemia and more rarely, infective endocarditis with only 19 cases in the published literature since its identification in 1976.

We are presenting a case of a 57-year-old man with bicuspid aortic valve endocarditis complicated by aortic root abscess caused by *C. canimorsus* secondary to a dog bite. The patient underwent cardiac surgery for aortic valve replacement and patch repair of the abscess. The excised aortic tissue along with multiple blood cultures were submitted for culture. All specimens grew *Capnocytophaga sp.* which was identified phenotypically. The patient was post-operatively treated with intravenous ceftriaxone for six weeks. Three weeks after the completion of antibiotics, the patient presented with decompensated cardiac failure. The patient underwent surgery for replacement of the bioprosthetic aortic valve and patch repair of the abscess. All blood cultures collected thereafter, including the bioprosthetic aortic valve & root abscess were all culture-negative. 16S rRNA gene sequencing on the subsequent aortic root abscess detected the presence of *Capnocytophaga canimorsus*. Initial attempts to secure the valve and repeated patch repair were successful but ongoing bleeding, and subsequent repeated attempts to repair the defect resulted in cardiopulmonary failure not consistent with survival and the patient was declared deceased ten hours into the operation.

This case illustrates the possibility of a relapse of *Capnocytophaga canimorsus* endocarditis leading to a fatal outcome which has never been documented in the literature.

COMPARISON OF INVASIVE HAEMODYNAMICS, BRAIN NATRIURETIC PEPTIDE AND HIGH SENSITIVITY TROPONIN T LEVELS WITH RIGHT VENTRICULAR APICAL AND RIGHT VENTRICULAR OUTFLOW TRACT PACING IN NORMAL HEARTS

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Background:

Right ventricular apical (RVA) based pacing is the main stay of ventricular pacing, however it has been associated with deleterious effects and increased morbidity. The mechanism and duration required is unknown. Alternative pacing strategies including right ventricular outflow tract (RVOT) pacing are being investigated.

Aim: To determine the acute haemodynamic, biochemical and hormonal response to right ventricular pacing; comparing RVOT and RVA pacing in structurally normal hearts.

Methods:

In 21 patients with structurally normal hearts undergoing electrophysiology studies, the acute invasive cardiac hemodynamic response, levels of Brain Natriuretic Peptide (BNP), N-Terminal Brain Natriuretic Peptide (NT-proBNP) and high sensitivity Troponin T (hs-TnT) to 10 minutes of either RVOT or RVA asynchronous pacing was assessed in a randomised crossover fashion and compared to baseline and each other.

Results:

Compared to baseline (BL), both pacing sites showed a significant rise in pulmonary capillary wedge pressure

(BL 9mmHg, RVA 13 mmHg, RVOT 12 mmHg, $p < 0.001$), increase in QRS width and time to peak systolic blood pressure. Compared to baseline, RVA and RVOT pacing demonstrated significant increases in arterial BNP, venous NT pro-BNP and arterial hs-TnT. There was no significant difference between RVA and RVOT pacing in hemodynamic, hormonal and biochemical responses.

Conclusions:

Right ventricular based pacing strategies demonstrated increases in filling pressures and elevated serum levels of BNP, NT pro-BNP and hs-TnT above baseline with very short durations of pacing (10 minutes). There was no difference in response between RVOT and RVA sites. These findings imply asynchronous right ventricular pacing is potentially deleterious.

A SALIVA-BASED TEST FOR THE DETECTION OF HPV-ASSOCIATED HEAD AND NECK CANCERS

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Background:

Human papilloma virus (HPV) infection is a major risk factor for a distinct subset of head and neck squamous cell carcinoma (HNSCC). The incidence of HPV-associated HNSCC is increasing and there are no early detection methods with most cases at an advanced stage upon diagnosis. The current study aims to develop a saliva-based assay for the detection of oncogenic HPVs in patients with HNSCC.

Methods:

Salivary rinse was collected from HNSCC patients recruited from the Head and Neck clinic at Princess Alexandra Hospital (PAH). Briefly, genomic DNA and RNA were extracted from rinse samples using a commercial kit and phenol-chloroform method respectively. PCR amplification was performed using MY11/MY09 primers that target >25 HPV strains as well as primers specific to oncogenic HPV16 and HPV18. HPV16-related transcripts (p16, E6 and E7) were detected using reverse transcription PCR (RT-PCR).

Results:

Oncogenic HPV-16 DNA was detected in the salivary rinse of 23/26 (88.5%) patients diagnosed with HPV-positive HNSCC and none in the salivary rinse of patients with HPV-negative tumour (0/19). In addition, the presence of HPV-related mRNA was correlated with high viral load in patient rinse samples.

Conclusions:

Salivary rinse is a promising diagnostic medium for the detection of oncogenic HPV in the oral cavity. The current study will aid in the detection of HPV infection in people at a high risk of developing HPV-associated HNSCC in a non-invasive and cost effective way. Early detection and intervention will significantly reduce the mortality and morbidity associated with HNSCC.

OBESITY A RISK FACTOR FOR CHEMOTHERAPY DOSE REDUCTION IN BREAST CANCER: A MULTI-CENTERED APPROACH

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Introduction.

Obese women with breast cancer have 30% worse survival than non-obese women. The cause of this survival disadvantage is currently not well understood. We postulated that this was due to relative under-dosing for body size in obese compared to non-obese women.

Aims.

To compare body size-adjusted chemotherapy dose between obese and non-obese women undergoing adjuvant treatment of breast cancer.

Methods.

We conducted a multi-centered retrospective audit of 712 women treated since 2000 with adjuvant chemotherapy for breast cancer. Cases were identified from the hospitals' chemotherapy database. Subject, tumour and chemotherapy data was extracted from patient charts. Dosing was analysed by comparing expected dose based on patient body surface area to actual dose received. A multivariate analysis was performed examining dose reductions across patient and tumour characteristics.

Results.

482 women had complete data available and were eligible for inclusion. In this population 30.9% (n=149) were obese with a body mass index greater than 30kg/m². An initial dose reduction was independently associated with obesity (OR=5.08; 95% CI 1.96 to 13.14; p=0.001) Overall in the first cycle, obese women were dosed significantly less for their body size with a median 97.9% of expected dose based on actual body size, compared to 99.6% in non-obese women (p

Discussion.

Obese women now account for a large proportion of breast cancer patients. These women are relatively under-dosed for body size compared to non-obese woman. The results confirm altered treatment of obese women with doses being reduced from the initiation of treatment. This may be a contributing factor to the survival disadvantage observed in obese women, compared to non-obese women with breast cancer. Further work needs to be undertaken to ascertain the relationship between individualised dose for particular body size using concentration-outcome data.

EFFECTS OF GROWTH HORMONE ON ANAEROBIC EXERCISE CAPACITY IN ADULTS WITH GROWTH HORMONE DEFICIENCY: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background

Anaerobic exercise capacity is reduced in GH-deficient (GHD) adults (1). Short-term GH therapy improves anaerobic exercise capacity in recreational athletes without a change in muscle strength (2).

Aim

To investigate whether short-term GH improves anaerobic capacity and physical function in GHD adults.

Method

17 hypopituitary adults, aged 47 ± 2.4 years were randomized into a 2-month double-blind placebo-controlled GH replacement (0.5mg/day) study with crossover at 1-month. Anaerobic capacity (watts) was assessed by the Wingate test and aerobic capacity by the VO_2max (L/min) test. Physical function was assessed by the stair-climb test, chair-stand test and 7-day pedometry. Lean body mass (LBM) was quantified by DEXA. Data were analyzed by repeated-measures ANOVA and tested for carry-over effects. Results are expressed as mean \pm SE.

Results

There were no statistically significant changes in body composition, anaerobic capacity, aerobic capacity and measures of physical function between placebo and GH treatments for one month.

	Baseline	Placebo	GH
LBM (kg)	43.9 \pm 1.6	43.0 \pm 1.7	44.3 \pm 1.5
Anaerobic power (W/kg.LBM)	5.9 \pm 0.3	6.0 \pm 0.3	5.7 \pm 0.3
VO_2max (mL/kg.LBM/min)	36.8 \pm 5.4	38.7 \pm 6.9	37.6 \pm 5.5
Stair climb test (secs)	19.5 \pm 0.7	19.1 \pm 0.7	19.1 \pm 0.8
Chair stand test (number/30 sec)	19.1 \pm 1.0	21.7 \pm 1.1	21.4 \pm 0.9
Pedometry (Steps/day)	7029 \pm 567	6652 \pm 455	6594 \pm 566

Summary

One month of GH replacement did not increase LBM, anaerobic power, VO_2max or measures of physical function.

Conclusion

Short-term GH replacement does not improve anaerobic exercise capacity. Longer term studies are required to ascertain whether GH improves anaerobic capacity in GHD adults.

1. Chikani V, et al. ASM of the Endocrine Society of Australia, Sydney 2013;Abstract 117
2. Meinhardt U, et al. Ann Intern Med.2010;152(9):568-77.

GENDER SPECIFIC INTRAPARTUM AND NEONATAL OUTCOMES IN TERM BABIES

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Background:

More male than female babies are born although the population ratio of boys to girls is substantially reduced. Adverse perinatal outcomes for male babies contribute to this phenomenon. This paper documents the gender specific intrapartum and neonatal outcomes in term, singleton, appropriately grown babies.

Methods:

De-identified, routinely collected data of all women meeting inclusion criteria between 2001 and 2011 was examined (n=9,223). Inclusion criteria were public (non insured), primiparous women who had delivered singleton, appropriately grown babies at term. In this retrospective cohort study, we estimated 95% confidence intervals. Maternal demographics, mode of delivery and neonatal outcomes, as measured by birthweight, APGAR score, cord blood acidemia, respiratory distress, any resuscitation requirement, nursery admission and stillbirth rates, were assessed.

Results:

The sex ratio of male babies was 1.05:1 (4,718 males; 4,505 females, p=0.85). Male babies were more likely

to be born by instrumental ($p=0.004$) or cesarean delivery ($p<0.001$). Despite having greater birthweights ($p<0.001$), male babies were more likely to have lower APGAR scores at 5 minutes ($p=0.004$), require neonatal resuscitation ($p<0.001$), develop respiratory distress ($p=0.005$) and require nursery admission ($p<0.001$). No statistical difference between male and female babies was found for cord blood acidemia ($p=0.58$) or stillbirth ($p=0.49$).

Conclusion:

This large cohort study demonstrates that term, appropriately grown male babies in primiparous pregnancies fare more poorly in the intrapartum and neonatal periods than female babies, though the underlying contributing physiology is not thoroughly established. The gender of the baby perhaps should be considered when counselling parents in the antepartum period.

PERINEURAL SPREAD OF CUTANEOUS MALIGNANCY IN A LIVE MOUSE AND GANGLION TUMOUR CO-CULTURE MODEL

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Perineural invasion (PNI) is a relatively uncommon but important method of metastatic spread in cutaneous squamous cell carcinoma of the head and neck. Squamous cell carcinoma is our second most common malignancy and the head and neck is the most common site to be diagnosed with a squamous cell carcinoma. The head and neck is an important site for perineural invasion due to the high density of both sensory and motor innervation, close proximity to the central nervous system once perineural invasion is established and large number of sensitive surrounding structures making treatment with surgery and or radiotherapy more challenging. Cutaneous squamous cell carcinoma of the head and neck with perineural invasion is associated with poorer outcomes in terms of local control, regional and distant metastasis and survival when compared to lesions without PNI. Little is known about the molecular mechanisms that drive this neurotrophic behavior and much of the work to date has focused on other tumours with a predilection for PNI such as pancreatic, prostate and adenoid cystic carcinoma. In our own microarray data comparing gene expression from tissue specimens with clinical perineural invasion with specimens without perineural invasion the expression of transglutaminase 3 was significantly down regulated in tumours with clinical perineural invasion. We are studying the role of transglutaminase 3 in perineural invasion using an in vitro mouse dorsal root ganglia co-culture assay and live mouse xenograft model.

MUTATIONS IN THE ZINC FINGER DOMAIN OF HUMAN AND MOUSE KLF1 CAUSE CONGENITAL DYSERYTHROPOIETIC ANEMIA (CDA) VIA PROMISCUOUS DNA BINDING AND ECTOPIC TARGET GENE EXPRESSION

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Küppel-like factor-1 (KLF1) is an essential erythroid-specific transcription factor [1, 2]. A number of studies have shown up to ~700 genes are poorly expressed when KLF1 is absent [3-6]. This global loss of expression is responsible for failure of effective red blood cell production in KLF1 knockout mice, and partly responsible

for congenital dyserythropoietic anemia type IV (CDA-IV) observed in humans with dominant mutations in the DNA-binding domain of KLF1 [7]. Recently an ENU-generated mouse model of neonatal anemia, 'nan', was also reported to harbour a mutation in the second zinc-finger of KLF1 [8]. Remarkably, the 'nan' mutation (E339D) resides at exactly the same amino acid which results in human CDA IV (= E325 in humans). Unlike loss of function point mutations in KLF1, this mutation leads to a more severe phenotype than the KLF1 null allele, suggesting it is an unusual dominant mutation [9].

To investigate how this mutation might cause disease, we introduced tamoxifen-inducible versions of KLF1 and KLF1^{nan} into an erythroid cell line derived from *Klf1*^{-/-} fetal liver cells [10]. We performed ChIP-seq to determine differences in genome occupancy *in vivo*, and identified novel sites occupied by EKLF-E339D but not by wild type KLF1. Using de novo motif discovery [11], we find KLF1^{nan} binds a slightly degenerate CACC box element (CCMNGCCC) in comparison with wild type KLF1 (CCMCRCCT). This specificity is novel with respect to any known TFs, so we think it represents a sequence specificity not normally encoded in mammals. Ectopic binding to non-erythroid gene promoters is accompanied by aberrant gene expression as determined by 4sU labelling and deep sequencing of primary nuclear RNAs. The degenerate motif is consistent with structural models of how the second zinc finger of KLF1 specifically interacts with its 9bp binding site [12, 13]. Together RNA-seq and ChIP-seq studies have provided a novel explanation for how mutations in KLF1 result in dominant anaemia in mice and man. To our knowledge this mechanism, whereby a transcription factor DNA-binding domain mutation leads to promiscuous binding, activation of an aberrant transcriptional program and subsequent derailing of co-ordinated differentiation, is novel.

References:

- 1.Perkins, A.C., A.H. Sharpe, and S.H. Orkin. Nature, 1995. 375(6529): p. 318-22.
- 2.Nuez, B., et al., Nature, 1995. 375(6529): p. 316-8.
- 3.Pilon, A.M., et al., Mol Cell Biol, 2006. 26(11): p. 4368-77.
- 4.Drissen, R., et al., Mol Cell Biol, 2005. 25(12): p. 5205-14.
- 5.Hodge, D., et al., Blood, 2006. 107(8): p. 3359-70.
- 6.Tallack, M.R., et al., Genome Res, 2012. 22(12):2385-98
- 7.Arnaud, L., et al., Am J Hum Genet. 87(5): p. 721-7.
- 8.Siatecka, M., et al., Proc Natl Acad Sci U S A. 2010. 107(34):15151-6
- 9.Heruth, D.P., et al., Genomics, 2010. 96(5): p. 303-7.
- 10.Coghill, E., et al., Blood, 2001. 97(6): p. 1861-1868.
- 11.Bailey, T.L., et al., Nucleic Acids Res, 2009. 37(Web Server issue): p. W202-8.
- 12.Schuetz, A., et al., Cell Mol Life Sci, 2011. 68(18): p. 3121-31.
- 13.Oka, S., et al., Biochemistry, 2004. 43(51): p. 16027-35.

THE EFFECT OF FIXATION STABILITY ON THE BMP-2 DOSE RESPONSE HEALING OF LARGE BONE DEFECTS

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Introduction:

Large bone defects fail to heal and remain a clinical problem. Our studies demonstrated the influence of the local mechanical environment on these defects with BMP-2(11µg)Glatt,JBJSAm,2012. This study's aim is to determine if the BMP-2 dose can be reduced through the manipulation of the mechanical environment.

Materials and Methods:

Rat, 5mm defects stabilized using different stiffnesses were treated with 11, 5.5 or 1.1µg BMP-2 delivered via

collagen sponge. A dose-response was established using external fixators of low, medium and high stiffnesses with various doses of BMP-2. Defect healing was monitored by weekly X-ray, and evaluated by μ CT at 8-weeks.

Results:

The lowest dose deposited small amounts of bone under constant stiffness, which failed to fill the defect despite the stiffness of fixator used. Conversely, defects treated with higher doses of BMP-2 showed evidence of intra-lesional mineralization by 3-weeks. However, defects treated with a 5.5 μ g dose had less uniformity, smaller callus size, delayed healing by one week compared to 11 μ g dose, and a presence of radiopaque line, except with the highest stiffness fixator. This confirmed our previous findings that lower stiffness fixators formed a bigger callus compared to rigid fixators. These results suggest that 5.5 μ g doses enabled the healing of defects, but the healing was delayed and had inferior quality of bone to BMP-2(11 μ g).

Conclusion:

Defect healing was influenced by the dose of BMP-2 and the fixation stability. If true, these findings will have significant consequences on the fixation stability used to maximise the regenerative capacity of bone healing while minimising the dose of BMP-2 required clinically.

AUTOMATED INTERPRETATION OF THE PHYSIOLOGICAL STRATA OF THE SKIN IN REFLECTANCE CONFOCAL MICROSCOPY DEPTH STACKS

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Background:

Reflectance confocal microscopy is an emerging tool for in-vivo imaging of human skin. Clinical use of reflectance confocal microscopy is limited by the need for an expert to interpret and assess the acquired images. The aim of this study is to automatically and objectively interpret the physiological strata of human skin in reflectance confocal imagery.

Methods:

312 depth stacks were acquired on the dorsal and volar forearm from 50 volunteers with varying degrees of photo- and chrono-aging. Cross sections covered 1mm² and were acquired at 2 μ m depth spacing to a depth of at least 100 μ m. An expert labelled the junctions between the distinct strata of human skin: the stratum corneum, viable epidermis, papillary dermis and dermis.

A bag of features approach was used to represent each cross-section from normalized and whitened image patches. Random forests were used for strata classification. Accuracy was tested using five-fold cross validation.

Results:

The automated assessment correctly classified the strata of the skin in a cross section in 74.9 \pm 1.5% of cases. The stack with the worst classification error still had 30 of the 50 cross sections correctly identified.

Conclusions:

Machine assessment of reflectance confocal microscopy leads to an automated understanding of the strata of the human skin that is physically reasonable and compares well to human assessment.

OASIS IN A GENE DESERT

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Background:

Ankylosing spondylitis (AS) is a severely debilitating inflammatory arthritis of unknown aetiology which primarily affects the joints of the spine and pelvis. Large-scale international genome-wide association studies lead by our group have identified a number of loci strongly associated with AS including the “gene desert” at 21q22.

Methods:

In order to fully characterise transcriptional activity from this locus, we have designed an RNA-Seq capture array (CaptureSeq) which enables ultra-deep targeted sequencing to identify very rare transcripts around 21q22. We have investigated expression from this area in peripheral blood mononuclear cells from five AS patients and five healthy controls.

Results:

There is evidence of bi-directional transcription from the 21q22 locus, indicative of enhancer RNAs (eRNAs). The presence of these eRNAs was confirmed in a large RNA-Seq study on AS patients, and in a third cohort using qPCR. Quantitation of data from CaptureSeq, RNA-Seq and qPCR shows higher expression of these transcripts in AS patients compared to healthy controls, implying higher enhancer activity in AS patients. In data recently released by the FANTOM5 consortium, the 21q22 eRNAs were identified to be exclusively expressed in monocytes, which we have confirmed using magnetic cell sorting. 21q22 eRNA expression was further enhanced on microbial stimulus.

Conclusions:

We have identified eRNAs produced from a genetic locus associated with AS risk, expressed exclusively by monocytes and with enhanced transcription in AS patients. Our future work will examine the effects of perturbing expression levels of 21q22 eRNAs on nearby candidate genes, and on monocyte functions.

DECIPHERING THE ROLE OF HSSB2 IN GENOME STABILITY

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Genome instability is the driver of all cancers. Further, genome instability causes genetic heterogeneity, allowing rapid tumor adaptation, metastasis, invasion and drug resistance.

The single-stranded DNA binding (SSB) family of proteins are ubiquitous to life. They function in many cellular processes including DNA replication, repair and transcription. In DNA repair, the human SSB proteins have been demonstrated as essential for the repair of cytotoxic double strand DNA breaks. Human SSB1 and SSB2 are newly discovered members of the SSB protein family. A number of recent studies have observed that hSSB1 is required for the detection, signalling, and repair of double strand DNA breaks by homologous recombination. Unlike hSSB1 however, a role for hSSB2 in genomic stability maintenance has not been investigated. In this study we will analyse the function of hSSB2 in DNA damage repair by employing in vivo and in vitro techniques. Depletion of hSSB2 and other members of the DNA repair pathways will be performed in order to identify how hSSB2 functions at the molecular level. Moreover, a biochemical approach will be utilised to unravel how hSSB2 interplays with the damaged genome.

ROLE OF MACROPHAGES IN BONE MARROW TRANSPLANTATION

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Background:

Resident bone-marrow macrophages (BM-Macs) support haematopoietic stem cell (HSC) niches and their depletion induces HSC mobilization. BM-Macs are the first cells to repopulate the HSC niche-rich endosteal environment following cessation of treatment with the HSC mobilizing agent, granulocyte-colony stimulating factor. We hypothesize that macrophages play an integral role in assembling the cells required for HSC niche homeostasis, including re-establishment of niches after HSC transplantation.

Methods:

To determine if recipient BM-Macs are resistant to myeloablation and persist long-term post transplantation, Macgreen mice (myeloid cells express eGFP) were conditioned using lethal total body irradiation (11Gy split dose) and transplanted with C57BL/6 bone-marrow (BM) or HSC. BM and spleen cells were isolated at day (D) 13, D27 and 8 weeks post-transplantation and analysed by flow cytometry (normalized as cells/femur). Distribution of cells was examined in situ using immunohistochemistry.

Results:

2% of eGFP⁺F4/80⁺CD11b⁺Ly6G^{neg}CD169⁺ recipient classical BM-Macs were irradiation resistant and persisted at D13 and D27 post-transplant. At 8 week post transplantation these recipient BM-Macs expanded 10 fold to 21% of this population in controls. All BM monocytes and granulocytes were donor-derived confirming efficient recipient HSC ablation. The expansion of recipient BM-Macs coincided with increased BM residence of donor HSC and progenitor cells. Immunohistochemistry in 8 week post-transplant serial sections supported that persisting GFP⁺ recipient cells were F4/80⁺ macrophages. Prominent perivascular and endosteal location supported contribution to active and quiescent HSC niche function.

Conclusions:

BM contains myeloablation-resistant resident macrophages that can self-repopulate independent of classical haematopoiesis and may participate in autologous HSC transplantation mechanisms.

THE IMMUNOBIOLOGICAL SCORE: A ROBUST 3-GENE ASSAY THAT SEGREGATES THE INTERNATIONAL PROGNOSTIC INDEX INTO DISPARATE SURVIVAL CATEGORIES IN AGGRESSIVE B-CELL LYMPHOMA

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Background:

Diffuse large B-cell lymphoma (DLBCL) is a common and aggressive lymphoma with approximately 30% mortality. Risk-stratification requires prognosticators to identify poor outcome patients in whom investigational therapeutic intervention is justified. Circulating lymphocyte:monocyte ratios are prognostic, implicating them as surrogate immune-effectors and monocyte/macrophage-checkpoints within the tumor microenvironment.

Methods:

Blood from 140 'R-CHOP' chemo-immunotherapy treated DLBCL patients from an Australasian Leukaemia and Lymphoma Group trial was analysed. Detailed functional and quantitative assessment enabled identification of the optimal immune-effector and monocyte/macrophage-checkpoint molecules to interrogate within the tissue.

Results:

CD163 identified a highly immunosuppressive subset of CD14+HLA-DRlo monocytoïd-myeloid-derived-suppressor cells 'moMDSC'. Ratios of various immune-effectors to CD163himoMDSC were used as a measure of total anti-tumoral immunity: i.e. the net balance between the antagonistic forces of immune-effectors and monocyte/macrophage-checkpoints. All ratios were higher in early R-CHOP responders compared to delayed responders, with CD8:CD163himoMDSC the most discriminatory. To test for intratumoral applicability, genes were quantified by digital hybridization in an independent cohort of 128 R-CHOP treated DLBCL patients. Co-clustering of CD8 with CD163 was observed, consistent with an adaptive immune-checkpoint response to immune-effector activation. CD8:CD163 ratios were prognostic independent of cell-of-origin and international prognostic index (IPI). An immunobiological score combining CD8:CD163 to the germinal-centre marker LMO2 strengthened the predictive ability, identifying 24% at risk of very poor outcome. It separated low-risk IPI into 91% and 44%, and high-risk IPI into 76% and 26% 4-year survivals. Results were externally validated in 233 patients.

Conclusions

The immunobiological score is a powerful new 3-gene assay that segregates IPI into markedly disparate survival categories.

PHENOTYPIC DISSECTION OF BONE MINERAL DENSITY REVEALS SKELETAL SITE SPECIFICITY AND FACILITATES THE IDENTIFICATION OF NOVEL LOCI IN THE GENETIC REGULATION OF BONE MASS ATTAINMENT

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Heritability of bone mineral density (BMD) varies across the skeleton, reflecting different contributions of genetic and environmental influences. To quantify the degree to which genetic variants tag and environmental factors influence BMD, we estimated the genetic (r_g) and residual (r_e) correlations between BMD measured at upper limbs

(UL-BMD), lower limbs (LL-BMD) and skull (SK-BMD) using ~4,890 participants of the Avon Longitudinal Study of Parents and their Children (ALSPAC). Point estimates of r_g indicated that appendicular sites have a greater proportion of shared genetic architecture (LL-/UL-BMD $r_g=0.78$) than with the skull (UL-/SK-BMD $r_g=0.58$ and LL-/SK-BMD $r_g=0.43$). Likewise, residual correlation between BMD at appendicular sites ($r_e=0.55$) was higher than between SK-BMD and BMD at appendicular sites ($r_e=0.20-0.24$). To further investigate these differences, genome-wide association (GWA) meta-analyses were performed, combining data ($n\sim9,395$) from ALSPAC and the Generation R Study. Thirteen loci reached genome-wide significance at one or more skeletal sites and two displayed site-specific effects (i.e. differ in the strength of their association and magnitude of effect across different sites). Specifically, variants at *CPED1* exerted larger influences on SK-BMD and UL-BMD when compared to LL-BMD ($P=2.01\times10^{-37}$), whilst variants at *WNT16* influenced UL-BMD to a greater degree than SK- and LL-BMD ($P=2.31\times10^{-14}$). We further observed novel associations between variants near *RIN3* (previously associated with Paget's disease) and LL-BMD ($P=1.4\times10^{-10}$). In conclusion, BMD at different skeletal sites may be under a mixture of shared and specific genetic and environmental influences. Allowing for these differences may help uncover new genetic influences on BMD.

INSIGHTS INTO THE PROCESSING OF EMOTIONAL ANXIETY AND STRESS: LOCAL CONNECTIVITY AND MORPHOLOGY OF THE BASOLATERAL AMYGDALA.

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The basolateral amygdala (BLA) is a complex brain region associated with processing emotional states such as anxiety and stress. To understand how BLA morphology drives neuroplasticity and behavioural responses during states of high emotion and arousal, we have used a technique that allows morphology, physiology and the distribution of neurochemical synapses in a three-dimensional neuronal arbor to be determined in single BLA neurons.

We used brain slices from Wistar rats and targeted intact neurons using patch-electrodes filled with the fluorescent tracer neurobiotin. An electrode tip was maneuvered against the neuronal soma and electroporation was performed causing the membrane to breakdown and allowing diffusion of neurobiotin into the cell. In this configuration, the physiological properties of each cell could also be determined by recording synaptic currents. Slices containing filled neurons were fixed and labelled with antibodies for pre and post synaptic components of GABAergic synapses. We then used confocal imaging and analysis software to examine morphology and GABAergic inputs in 3D and correlated this with the recorded electrophysiology.

Our morphology data revealed two distinct cell types within the BLA. Furthermore, we have mapped the distribution of GABAergic synapses within the entire dendritic arbor of both cell types and show that these inputs contribute to distinct synaptic physiology and neuroplasticity.

Our work provides a powerful tool that allows morphology and physiology analysis to be determined in the same neuron. This technique will allow us to investigate how changes in BLA morphology cause the brain to rewire during emotional disorders caused by chronic anxiety and stress.

VOLUMETRIC BONE MINERAL DENSITY (vBMD) AND FUNCTIONAL BONE-MUSCLE UNIT ASSESSMENT WITH PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (pQCT) IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD) STAGE 4 AND 5

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Background:

Bone disease and muscle wasting are common complications in CKD. PQCT is an emerging technique that distinguishes cortical and trabecular vBMD and quantifies muscle mass. This study aimed to 1) assess the effect of CKD on vBMD, bone strength and muscle mass 2) identify associations between bone-muscle parameters and bone mineral metabolism (BMM), arterial stiffness and functional status

Methods:

Cross sectional study in CKD Stage 4/ 5 [n= 47, age 63 ±10 years, male 70%, estimated glomerular filtration rate (eGFR) 19±7mL/min/1.73m²] compared with 45 age-, sex-, body mass index-matched controls. PQCT at non-dominant radius and tibia, markers of BMM, pulse wave velocity (PWV) and functional status [grip strength, 6-minute walk test (6MWT)] was collected.

Results:

CKD patients had reduced cortical radial vBMD compared with controls, 1075±52mg/cm³ versus (vs.) 1097±50mg/cm³ (p=0.04). Lower cortical vBMD was associated with diabetes(r=-0.34,p=0.001), increasing age(r=-0.39, p=0.001) and lower eGFR(r=0.31,p=0.003). Cortical vBMD was also associated with BMM [parathyroid hormone (PTH)(r=-0.34, p<0.001), phosphate r=-0.24, p=0.01], PWV (r=-0.32, p=0.002)] and functional status [6MWT (r=0.31, p=0.005)].

CKD patients had reduced muscle cross sectional area (CSA) (7224±1502 mm² vs. 7931 ± 1415mm²,p=0.02) compared with controls. Muscle CSA was strongly associated with cortical thickness(r=0.61, p<0.001), bone strength(r=0.56, p=0.001), PTH(r=-0.22, p=0.03), eGFR(r=0.25, p=0.01), phosphate(r=-0.37, p<0.001), 6MWT(r=0.26, p=0.02) and grip strength(r=0.59, p<0.001).

Conclusions:

Cortical bone was abnormal in this CKD cohort and associated with BMM, arterial stiffness and poorer functional status. PQCT may be a promising tool to examine bone disease and muscle wasting in CKD.

DETECTING CIRCULATING TUMOUR CELLS IN METASTATIC HEAD AND NECK CANCER

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Head and neck squamous cell carcinoma (HNSCC) is the 6th most common cancer globally with less than 40% survival beyond 5 years. Locoregional and distant metastatic disease is responsible for 88% of patient deaths within 12 months of diagnosis. The ability to identify high risk patients with disseminated disease prior to presenting with clinically detectable metastases holds remarkable potential. Circulating tumour cells (CTCs) are

a hallmark of invasive cancer cells expressing epithelial cell adhesion molecule (EpCAM) and key to metastasis. CTCs have been used as surrogate markers of overall survival and progression free survival for breast, prostate and colorectal cancers using the CellSearch® system. The aim of this study is to use CellSearch® (FDA-approved) and ScreenCell® to detect and compare CTCs in HNSCC. In a cohort of 24 HNSCC patients from the Princess Alexandra Hospital (PAH), CTCs were detected in 6 patients. To increase the number of CTCs, we are looking at a broader range of epithelial and mesenchymal markers which are not selected for by the CellSearch®. Preliminary data displays some degree of mesenchymal nature is present, suggesting of an epithelial to mesenchymal transition.

UTILITY OF POST-PROCEDURE CHEST X-RAY IN THE ERA OF ULTRASOUND GUIDED THORACENTESIS: EXPERIENCE FROM A TERTIARY QUEENSLAND HOSPITAL.

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Background:

Chest X-ray is commonly performed post thoracentesis to rule out pneumothorax despite paucity of evidence based guideline. Current literature, however, suggests to avoid this in asymptomatic patients due to low yield, and recent adoption of ultrasound guidance has further reduced this risk. This study aims to evaluate local practice and safety outcome at Princess Alexandra Hospital.

Methods:

Retrospective audit on thoracentesis performed in Department of Respiratory Medicine, from June 2011 to June 2013. Data collected include patient demographics, characteristics of pleural effusion, pattern of procedure, peri-procedural imaging results and analysis of pneumothorax.

Results:

75 thoracentesis were performed on 64 patients. Mean age was 65 and 67% male. Procedures were mostly done on inpatients (75%) and during hours (96%) by senior staff (65%). Etiology of effusion were mainly pulmonary malignancy (47%) and other malignancy (19%). Most cases had moderate pleural effusion (25-50% lung field) and mean volume drained was 1076ml. 90% had routine post-thoracentesis chest X-ray while incidence of pneumothorax was 5/75 (6.6%), 4 due to trapped lung and 1 due to other mechanism, none required treatment. Rapid re-accumulation of effusion was common in patients with malignant effusion and most required repeated procedures.

Conclusions:

Pneumothorax rate was low in ultrasound guided, physician supervised thoracentesis. Most were due to trapped lung and did not require treatment. Role of routine post-thoracentesis chest x-ray is limited for detection of pneumothorax, however it can help to identify trapped lung and therefore patient selection for further treatment (e.g. Pleurodesis), especially in patients with malignant effusion.

DETECTION AND CHARACTERISATION OF SELF-REACTIVE T CELLS IN PERIPHERAL BLOOD OF RA PATIENTS AND HEALTHY INDIVIDUALS

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Background:

Rheumatoid arthritis (RA) is characterized by chronic joint inflammation, resulting in functional disability and premature death. RA is strongly associated with the shared epitope (SE)+ *HLA-DRB1* alleles including *HLA-DRB1*0401* and development of autoantibodies specific for citrullinated-self-antigens. HLA-SE preferentially binds citrullinated-peptides. Citrullination occurs during antigen processing and is augmented by stress, including inflammation and smoking. The preferential binding of citrullinated-peptides by SE suggest its role in selection and expansion of citrullinated-peptide-specific T-cells in SE+ individuals at risk of RA. This study investigated the role, frequency and phenotype of citrullinated-peptide-specific T-cells in SE+ RA patients. Methods: Fluorescent tetramers, a complex of four *HLA-DRB1*0401* molecules, loaded with citrullinated-aggreCAN⁸⁹⁻¹⁰³ cit-93,95, vimentin⁵⁹⁻⁷¹ cit-64 peptides or influenza hemagglutinin (HA)³⁰⁶⁻³¹⁸ were constructed to identify antigen-specific CD4+T-cells in the peripheral blood of RA patients and healthy controls.

Results:

Citrullinated-peptide-specific T-cells were present in similar numbers in RA patients and controls, the proportion of citrullinated-peptide-specific CD4+FoxP3+ resting and activated regulatory T-cells (Tregs) were significantly reduced in RA patients compared to controls. Strikingly, the number of citrullinated-peptide-specific T-cells correlated with RA disease activity score. Interestingly, citrullinated-peptide-specific T-cells in RA contained higher proportions of recently-activated CD69+ cells and ICOS+CXCR5+FoxP3- follicular-helper T-cells which activate autoreactive B-cells compared to controls and HA³⁰⁶⁻³⁸¹-specific T-cells in RA.

Conclusions:

RA patients have fewer citrullinated-peptide-specific Tregs to control inflammation and the generation of autoantibodies triggered by citrullinated-antigens presented in the context of SE. We propose that citrullinated-peptide-specific autoreactivity is present in all individuals bearing HLA-SE risk alleles but that deficient antigen-specific regulation promotes the development of RA.

THE NATURAL HISTORY OF NON-FUNCTIONING PITUITARY ADENOMAS: A LONGITUDINAL VOLUMETRIC EVALUATION

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Background:

Non-functioning pituitary adenomas may present without any symptomatic mass effect and minimal hormonal dysfunction. Data on optimal management and follow-up of these tumours are sparse.

Methods:

Non-functioning pituitary adenomas where the initial plan was for observation with serial MRIs over at least 6 months between 2003 and 2013 were identified. Longitudinal data were collected for hormonal function and pituitary tumour volume, with measurements undertaken by a single viewer (NL).

Results:

53 non-functioning pituitary adenomas (24 macroadenomas and 29 microadenomas) were identified. Mean follow up was 35.2 months (range 6-73), and age was 49 years (range 17-85). Those with macroadenomas were older – 59.1 ± 3.9 vs 40.8 ± 2.7 years, $P < 0.001$. There was a significant increase in tumour volume over the follow up period ($P=0.026$), with the mean percent increase in size being $9.9 \pm 5.5\%$. A significant increase in size occurred in macroadenomas (1647 ± 221 to 1984 ± 336 mm³, $P = 0.026$) but not microadenomas (169 ± 25 to 178 ± 35 mm³, $P=0.75$). A $>20\%$ increase in size occurred in 6/24 macros compared with 2/29 micros. Hormonal dysfunction was present in 11/53 (21%) at baseline. New hormone deficiency developed in only 2 macroadenoma patients during follow-up. Seven macroadenoma patients proceeded to surgery after a mean of 3.1 years (range 1-6).

Conclusions:

Non-functioning pituitary macroadenomas have a greater tendency to grow and require surgical intervention than microadenomas. Microadenomas rarely progress and could be safely reimaged at an interval of 3 years for the first follow-up scan

HEAD AND NECK CANCER DETECTION IS A SPITTING DISTANCE AWAY

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Background

Head and neck squamous cell carcinoma (HNSCC) encompasses a diverse group of aggressive tumours. HNSCC patients, particularly those with a history of smoking, often develop secondary tumours. Currently, there are no diagnostic tests to detect these cancers at an early stage; as such, most patients present with metastatic disease at the time of diagnosis.

Objective

With an increasing recognition of the link between oral and systemic disease, attention has turned to saliva as an alternative diagnostic medium for a diverse array of health conditions. Compared with blood, saliva collection is non-invasive, easy sampling with multiple sampling opportunities, does not need pre-processing and is ideal for 3rd world countries. It is well established that tumour cells secrete biomolecules into the saliva.

Methods

We collected saliva from HNSCC patients and healthy controls and interrogated hypermethylation events in tumour suppressor genes using a sensitive methylation-specific PCR (MSP) assay.

Results

RASSF1a, DAPK1 and p16, showed an overall specificity of 87% and sensitivity of 80%. The test panel performed extremely well in the detection of the early stages of HNSCCs, with a sensitivity of 94% and specificity of 87%, and a high κ value of 0.8, with an excellent overall agreement between the presence of HNSCC and a positive MSP panel result.

Conclusion

In conclusion, we demonstrate that salivary DNA methylation biomarkers are clinically useful in detecting HNSCC in a non-invasive manner.

REVERSE DYNAMIZATION IMPROVES BONE HEALING IN A RAT MODEL

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Background:

Healing of fractures is influenced by the mechanical environment, which plays a major role in the rate and success of the healing process. We hypothesize that the healing of bone fractures can be accelerated by the implementation of an appropriate mechanical environment that is purposefully modulated as healing progresses. This study aims to investigate the modulation of fixation conditions, from flexible to stiff, termed Reverse Dynamization, on the healing outcome.

Methods:

One millimetre osteotomies were created in rat femurs between the two inner pins of unilateral external fixators. Reverse dynamization (RD) was performed at 21 days postoperatively and compared to control groups, with either flexible or stiff fixation for the entire healing period. After five weeks the rats were euthanized and healing was analysed using biomechanical testing, microcomputed tomography (μ CT) and histology.

Results:

The RD and stiff groups had significantly higher flexural rigidity compared to the flexible group, indicating a superior healing outcome. This was confirmed by the μ CT and histological evaluation, where the RD and the stiff groups resulted in significantly smaller callus volume (129 mm³ and 120 mm³, respectively) compared to the flexible group (179 mm³). There were larger amounts of un-mineralised tissue and cartilage (1.65 mm²) within the osteotomy in the flexible group compared with the RD (0.64 mm²) and stiff (0.27 mm²) groups.

Conclusions:

Reverse dynamization at 21 days produced a superior healing outcome compared to flexible fixation. This presents a potential clinical strategy to improve the healing outcome of unstable fractures, particularly for non-unions through increased stabilization

KLF1 NULL NEONATES DISPLAY HYDROPS FETALIS AND A DERANGED ERYTHROID TRANSCRIPTOME

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KLF1 is a master regulator of erythroid gene expression. Knockout mice die *in utero* from severe anemia. We describe the first case of severe neonatal anaemia with kernicterus due to compound heterozygosity for null mutations in human KLF1, each inherited from asymptomatic parents. One of the mutations is novel. This is the first described case of a KLF1 null human. The phenotype of severe DAT-negative non-spherocytic haemolytic anaemia (NSHA), jaundice, hepatosplenomegaly, and marked erythroblastosis is more severe than that present in CDA type IV due to heterozygous dominant mutations in the second zinc finger of KLF1. There was very high levels of HbF expression into childhood (>70%), consistent with a key role for KLF1 in human hemoglobin switching.

We performed RNA-seq on circulating erythroblasts and found human KLF1 acts like mouse Klf1 to coordinate expression of many genes required to build a red cell including those encoding globins, cytoskeleton components, AHSP, heme synthesis enzymes, cell cycle regulators, and blood group antigens. We identify many

novel KLF1 target genes including KIF23 and KIF11 which are required for proper cytokinesis of erythroblasts. We also identify roles for KLF1 in autophagy, stress erythropoiesis, transcription and RNA splicing. We identify many new genes which are likely to be important for building a red blood cell. We suggest loss of KLF1 should be considered in otherwise unexplained cases of severe neonatal NSHA or *hydrops fetalis*.

TARGETED DELIVERY OF CURCUMIN TO LIVER MYELOID CELLS PROTECTED MICE FROM MCD DIET INDUCED STEATOHEPATITIS

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Background:

Non-alcoholic steatohepatitis (NASH) is characterized by an increase in the number of hepatic macrophages with a pro-inflammatory phenotype, which augment disease progression by secreting inflammatory mediators. To preserve macrophage integrity but reduce inflammatory activation in NASH we have developed liposomes with anti-inflammatory drug curcumin entrapped and injected these nanoparticles into mice fed methionine and choline deficient (MCD) diet and tested their capacity to target inflammatory macrophages, reduce inflammation and treat disease.

Methods:

C57BL/6 mice were fed MCD diet for 2 weeks and then intravenously injected with 100uL of Dil-labelled curcumin liposomes. Serum and livers were harvested 1 week post treatment, immune cells were isolated and stained for leukocyte markers and analysed for Dil positive cells using flow cytometry. Stage of disease and severity was assessed by measuring serum ALT levels, cellular inflammation by H&E and steatosis by Oil-Red O staining. RNA was also extracted from liver and expression of genes associated with macrophage function determined by qPCR.

Results:

Mice fed MCD diet for 3 weeks developed severe steatohepatitis with cellular recruitment of CD11b⁺F4/80⁺ pro-inflammatory macrophages compared to mice on control diet. Curcumin liposomes targeted antigen presenting cells (APC) including macrophages and dendritic cells. The outcome on targeting APC with curcumin liposomes was reduced liver damage as measured by serum ALT and NAFLD assessing score of H&E stained liver sections. Furthermore, curcumin liposomes treatment increased anti-inflammatory gene expression including TGF β and Arginase-1 in the liver.

Conclusion:

Targeting curcumin to hepatic myeloid cells is a novel approach to prevent NASH progression.

THE TUMOUR-PROMOTING RECEPTOR TYROSINE KINASE, EPHB4, REGULATES EXPRESSION OF INTEGRIN $\alpha 8$ IN PROSTATE CANCER CELLS

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The objective of this study was to define the molecular networks that the EphB4 receptor is involved to promote prostate cancer.

Background:

EphB4 is a receptor tyrosine kinase that is overexpressed in 66% of prostate cancers playing essential roles in tumour promotion. We identified integrin $\alpha 8$ (ITGB8) as one of the genes regulated by EphB4. The integrin receptors are essential in the communication between the cell and the extracellular matrix, influencing migratory aspects of cancer cells.

Methods:

We employed transient knockdown of EphB4 in LNCaP cells followed by cDNA microarray analysis, coupled with bioinformatic approaches. Validation experiments were done using real-time PCR and western blotting. Examination of migration and invasion was carried out using transwell assays after ITGB8 knockdown.

Results:

The microarray analysis revealed that 260 genes were up- and 300 were downregulated upon EphB4 knockdown. Several integrins appeared to be deregulated, but ITGB8 was the top (29-fold downregulation). Overexpression of EphB4 led to a simultaneous increase in ITGB8. Datamining using the Oncomine database revealed that ITGB8 and EphB4 are both highly expressed in prostatic intraepithelial neoplasms (PIN) with decreasing expression in prostate carcinomas and basal expression in metastases. Upon ITGB8 knockdown, migration and invasion of prostate cancer cells was diminished.

Conclusions:

We have discovered that EphB4 regulates ITGB8 expression and that both are highly expressed in PIN. Furthermore, ITGB8 alters cell migratory behavior, a prerequisite for metastases. This suggests that both proteins could be involved in prostate cancer onset and progression and combined targeting may hamper the advance of this disease

DEVELOPMENT OF A HUMANISED MOUSE MODEL TO EVALUATE HUMAN VACCINES

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Dendritic cells (DC) are the key initiators of adaptive immune responses and comprise multiple subtypes with specific functions. In mice, CD8⁺ DC subtypes is specialised in the induction of cytotoxic T cells that are critical for the induction of anti-viral and anti-tumor immune responses. Delivering antigen to the CD8⁺ DC subset in vivo using antibodies (Ab) specific for CD8⁺ DC receptors, such as Clec9A, is an effective vaccine strategy in mice. However, translating this to humans has been confounded by their rarity and lack of models to study the human CD141⁺ DC equivalent of mouse CD8⁺ DC. To overcome this limitation, we developed a model of human haematopoietic stem cell (HSC) engraftment in NOD/SCID/IL2r^gnull/HLA-A2 (NSG-A2) mouse strain.

We demonstrated robust multilineage differentiation of human CD34⁺ cord blood HSC after transplantation into NSG A2 neonatal mice via intrahepatic injection. Human B cells, T cells, monocytes and all dendritic cells subsets, including CD141⁺ DC, develop in the peripheral blood, bone marrow, spleen, liver and lung by 10-14wk post transplantation. As few as 2×10^4 human HSC facilitate engraftment of up to 30% of human cells in peripheral blood. Human CD141⁺ DC in the mice specifically take up anti-human Clec9A Ab in vivo and effectively prime naive CD8⁺ T cells in vitro. Our data suggests this humanised mice model will be a powerful model to understand human DC function and evaluate new human vaccine strategies in vivo.

HUMAN CD1C⁺ DENDRITIC CELLS ARE MAJOR PRODUCERS OF INTERLEUKIN-23 AND INTERLEUKIN-12p70 IN RESPONSE TO TOLL-LIKE RECEPTOR AGONISTS

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Dendritic cells (DC) are professional antigen presenting cells that play a crucial role in mounting immune responses. Human blood DC comprise plasmacytoid DC (pDC), CD1c⁺ DC and CD141⁺ DC. pDC excel in anti-viral defence *via* production of Type I interferons. CD141⁺ DC promote anti-tumour and CD8⁺ T cell responses. Whilst the function of CD1c⁺ DC is unknown, its putative mouse equivalent is specialised at inducing CD4⁺ T cell responses in particular Th17 responses *via* IL-23. We hypothesise that human CD1c⁺ DC are capable at inducing CD4⁺ T cell responses. IL-23 is a heterodimeric cytokine sharing a common subunit with Th1-polarising cytokine, IL-12p70 and plays an important role in driving autoimmune diseases. Cytokine production by DC is induced by recognition of pathogens and damaged host cells by specific pattern recognition receptors (PRR) expressed by DCs such as the toll-like receptors (TLR). TLR8 binds single stranded RNA and has been recently linked to autoimmune diseases such as Still's disease and systemic lupus erythematosus due to the increased levels of IL-23. We demonstrated that CD1c⁺ DCs produced significant levels of IL-23 and IL-12p70 in response to the TLR7/8 agonist, R848 alone, which was further enhanced by the addition of agonists for TLR3 (poly I:C) or TLR4 (LPS). Furthermore, direct comparisons with monocytes, CD141⁺ DC and pDC demonstrated that CD1c⁺ DC were the main producers of IL-23 and IL-12p70 under these conditions. Our results suggest that human CD1c⁺ DC are the major producers of IL-23 and may therefore play an important role in driving autoimmune responses upon TLR8 ligation.

LINE-1, A NOVEL BIOMARKER FOR HIGH-GRADE SEROUS OVARIAN CARCINOMA

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High-grade serous ovarian carcinoma (HGS OvCa) is the most common and most deadly type of ovarian cancer. Poor screening and ineffective chemotherapies contribute to a poor 5-year survival rate, which has remained at 31% in the last 30 years. LINE-1 (Long Interspersed Nuclear Element 1) retrotransposons mobilise autonomously in mammalian genomes using a "copy-and-paste" mechanism disrupting normal cellular regulation leading to genome instability, and potentially cancer. Our aim is to investigate LINE-1 activity in HGS OvCa.

We have demonstrated that LINE-1 is active in HGS OvCa. We found a significant number of malignant tumours (5/7, $\chi^2 = 6.17$, $p < 0.05$) expressed LINE-1 mRNAs and ORF1 protein required for LINE-1 mobilisation. For the first time, using Retrotransposon-Capture sequencing (RC-seq), we showed active endogenous LINE-1 mobilisation in 14 primary HGS human tumours. We discovered that ~1 in 3 (43/128) de novo LINE-1 insertions affected exons and introns of known genes. Of particular interest, ADCY8, STC1 and CA10 were previously implicated in OvCa, the functional consequences of which will be investigated. Additionally, we demonstrated

the potential for OvCa cell lines ($n = 8$) to support LINE-1 mobilisation in vitro using an engineered LINE-1 reporter. Epigenetic regulation of LINE-1 promoter as indicated by bisulphite sequencing also revealed that HGS OvCa cell lines (SKOV3 and OVCA420) were significantly ($p < 0.0001$) hypomethylated compared to control and other OvCa cell lines.

Together, this study demonstrates LINE-1 as a promising novel biomarker for HGS OvCa and provides a viable target for adjuvant chemotherapy for ovarian cancer.

BLOOD PRESSURE MEASUREMENTS AND LEFT VENTRICULAR GLOBAL LONGITUDINAL STRAIN IN CHRONIC KIDNEY DISEASE PATIENTS

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Background:

We aimed to determine which method of blood pressure (BP) measurement best correlated with Global Longitudinal Strain (GLS), a subtle marker of left ventricular dysfunction, in the CKD population. In addition, we examined the relationship between nocturnal dipping status and GLS.

Methods:

A cross sectional study of patients with moderate CKD stages 3 and 4 ($n=136$). Clinical characteristics, 24 hour ABPM, office BP measurement (average of 3 seated readings), pulse-wave analysis for Central Blood Pressure (CBP) and a transthoracic echocardiogram were performed. GLS was determined from 3 standard apical views using 2-dimensional speckle tracking. Multivariate models were used to explore the relationship between GLS and BP measuring modality, as well as the association with dipping status (Non-dippers defined as failure in the BP to fall by 10% during sleep).

Results:

Patient characteristics for this study population include age 59 ± 9.8 years, 58% male, estimated Glomerular Filtration Rate (eGFR) 44.4 ± 10 ml/min/ 1.73m^2 , GLS $-18.3 \pm 3.6\%$. Average systolic office BP and ABPM systolic BP were similar, 138 ± 21 mmHg and 134 ± 15 mmHg, respectively. The central systolic BP was 117 ± 17 mmHg. Following adjustment for demographics and baseline morbidities, office systolic BP and central systolic BP was independently associated with GLS ($R^2 = 0.2$, $p=0.001$).

Non-dippers had poorer strain compared to dippers ($-18.1 \pm 3.6\%$ v $-19.6 \pm 2.8\%$, $p=0.02$).

Conclusions:

Both office BP and central BP measurements closely correlated with GLS when compared to 24hour ABPM. However, the added benefit of performing 24hr ABPM, is that it provides additional information about the dipping status of the patients. Nocturnal non-dippers may have early cardiac dysfunction.

CHARACTERISATION OF A CELL CYCLE CHECKPOINT AND REPAIR RESPONSE TO LOW-DOSE UVB EXPOSURE THAT IS COMMONLY DEFECTIVE IN MELANOMA

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Background:

The high load of UV signature DNA mutations found in melanomas is evidence of not only the role of UV in melanomagenesis but also of a defect in repair of UV-induced lesions. We have previously identified a G2 phase cell cycle checkpoint and repair response to low-dose UVB that is commonly defective in melanoma cell lines. Here we aim to identify the components of the checkpoint and repair pathways involved in this UV-induced response.

Methods:

We have investigated the global alterations in: transcription; translation; protein abundance; and microRNAs associated with the UV response. We have used two model systems previously characterised for the UV-induced G2 delay, an A2058 melanoma cell line model and a whole skin organ culture model. Total mRNA and polysome mRNA were analysed using Illumina whole genome microarrays, microRNAs were analysed by RNA-seq, and protein changes were analysed by SILAC proteomics.

Results:

Data was combined from these analyses to identify a set of 45 high probability candidates, and 11 UV-responsive microRNAs potentially contributing to this response. Candidates are being further examined using high-throughput functional analyses, to determine their involvement in the normal UV response. A summary of ongoing work characterising the UV response will be presented.

Conclusions:

Once the mechanisms of the normal UV response have been characterised, we can identify defects in the normal surveillance, checkpoint and/or repair mechanisms which allow escape of UV-induced mutations. This may offer opportunities to expand diagnostic (and potentially therapeutic) options for melanoma patients.

POSSIBILITIES FOR MUSCULOSKELETAL MODELLING; PRELIMINARY INVESTIGATION OF LOWER LIMBS IN NETBALL MOTIONS AND EXTRA-STEP UPON LANDING EFFECT ON KNEE JOINT CONTACT FORCES

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Introduction:

Musculoskeletal modelling software allows for muscular-contraction force calculation (and subsequent joint loading) of subject musculoskeletal system during recorded motion. This tool can be used in numerous situations such as patient specific rehabilitation assessment. To demonstrate possibilities; musculoskeletal modelling was used to quantify the joint loading conditions of Netball motions during landings, the effects of an extra step upon landing and whether this could reduce joint loading in the knee (previously reported as a negligible solution to decreasing knee joint contact forces).

Methodology:

A musculoskeletal model was developed for preliminary investigation into common netball maneuvers. Musculoskeletal model was driven by motion capture data obtained from participants performing a standard netball jump-landing motion and then a replica motion with extra step allowance on landing (maneuvers performed across force plate setup).

Results:

Consistent decreases in force components of knee joint were reported through addition of an extra step on landing. Forces calculated and trends exhibited remain consistent across all subjects. Higher than expected anterior-posterior knee force component (defined by tibial plateau) was reported however after consideration was deemed acceptable due to constraints of the musculoskeletal model used.

Conclusion:

Through application of musculoskeletal modeling, greater understanding of patient specific musculoskeletal system can be achieved. System improvement is continuously on-going and will only improve in validity and operation ease. The potential for use in both clinical and research settings are vast. Demonstration of such analysis on Netball motions has resulted in a new observation pertaining to lower limb injury prevalence that has been reported previously as negligible.

PHYLLODES TUMOURS: AN INSTITUTIONAL REVIEW AND ASSESSMENT OF DIAGNOSTIC METHODS

Tavis READ, Vanketa Seelamanthula, Chuan Tan, Ian Bennett.

BACKGROUND

Phyllodes tumours are rare fibro-epithelial malignancies of the breasts primarily affecting women between the ages of 40 - 60 years. Currently, reported disease characteristics vary significantly between patient cohorts and existing literature indicates there is poor correlation between histopathologic findings and treatment outcomes.

STUDY PURPOSE

To provide a structured analysis of the clinical, pathological, diagnostic and treatment factors influencing outcomes of patients receiving surgical treatment for phyllodes tumours.

METHODS

The medical records of 43 patients who received surgical treatment between 2002-2014 in the Breast and Endocrine Surgery Unit, PA Hospital were retrospectively assessed. 40 patients met inclusion criteria, 35 with confirmed phyllodes disease, 5 with benign pathology.

RESULTS

The mean age at diagnosis was 42.8 years and average follow-up duration 23.9 months. 88.6% of patients presented with clinically palpable disease, there was a predominance of right-sided breast pathology (54.3%), 62.9% were benign lesions, 20.0% borderline and 17.1% malignant. Core biopsy had greater diagnostic accuracy (sensitivity 81.8%, specificity 66.7%) compared to FNA (sensitivity 28.6%, specificity 66.7%). Thirty-two patients (91.4%) initially underwent breast-conserving surgery and 17.1% were eventually treated with total mastectomy.

CONCLUSIONS

The clinicopathological results and patient characteristics described approximated those reported for phyllodes tumours within existing literature. Core biopsy was superior to FNA for pre-operative diagnosis. A conservative treatment algorithm favours localised excision with clear surgical margins (>10mm) for benign pathology, WLE for borderline tumours and total mastectomy reserved for malignant or recurrent disease. This treatment strategy appeared effective and produced low recurrence rates.

TRANSGENIC EXPRESSION OF PROINSULIN OVERCOMES TOLERANCE DEFECTS IN NOD MICE

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Type 1 diabetes (T1D) results from autoimmune destruction of pancreatic β cells. CD8⁺ and CD4⁺ T-cells are critical to T1D progression and pathogenic T-cell responses are well established at disease diagnosis. In mouse models, CD8⁺ T-cells directly destroy β cells. For effective immunotherapy, diabetogenic CD8⁺ T-cells must be inactivated. Targeting antigen expression to antigen-presenting cells (APC) induces antigen-specific tolerance in CD8⁺ T-cells. To investigate therapeutic potential, we want to determine whether expressing insulin in APC is tolerogenic in a spontaneous diabetes model. Transferred insulin-specific CD8⁺ (G9) T-cells proliferated only in pancreatic lymph nodes (LN) of non-transgenic (non-Tg) mice, where insulin is normally presented as an antigen. In transgenic mice, G9 cells proliferated in spleen, skin-draining LN and pancreatic LN indicating widespread expression of potentially tolerogenic proinsulin. G9 cells persisted in non-Tg pancreatic LN and, at that site, predominantly exhibited an effector phenotype. Despite extensive proliferation in proinsulin-expressing recipients, the number of G9 cells recovered was low relative to non-Tg recipients and decreased over time. The few G9 cells remaining in proinsulin-transgenic recipients had reduced T-cell receptor expression and displayed a phenotype consistent with tolerance. These data suggest G9 cells undergo deletion in proinsulin-transgenic recipients and remaining G9 cells are tolerised and likely unresponsive to further antigen challenge. Overall, an important observation here is that insulin-specific CD8⁺ T-cells are amenable to peripheral tolerance induction when antigen is over-expressed despite previously demonstrated tolerance defects in NOD mice. This has potential implications in developing immunotherapeutic approaches to T1D and other autoimmune diseases.

SUCCESSFUL EX-VIVO NORMOTHERMIC OXYGENATED MACHINE PERFUSION OF HUMAN DONOR LIVERS

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Background:

Currently, empirical criteria determine the viability of donor livers but they have a low predictive value. We have assessed viability of livers, considered unusable by existing criteria, by studying them in a normothermic machine perfusion (NMP) protocol.

Methods:

The perfusion circuit consisted of a centrifugal pump which receives blood from the inferior vena cava, passes it through an oxygenator/heat-exchanger, then splits the output into a pressure-controlled hepatic artery supply and gravity fed portal venous supply via a reservoir. During a perfusion period of up to twenty-four hours there was continuous monitoring of haemodynamic parameters and perfusate, bile, liver and bile duct tissue samples were collected.

Results:

Three livers donated after cardiac death (DCD) and one donated after brain death (DBD) have been studied to date. All were metabolically active throughout the perfusion period reflected by lactate clearance (mean peak lactate 6.41 ± 2.66 mmol/L to 1.21 ± 0.98 mmol/L at 4h), urea production (mean increase 7.93 ± 3.84 mmol/L after 4h) and bile production. Histology at the end of the perfusion period showed extensive biliary damage in DCD versus DBD livers as reflected by epithelial cell loss and mural necrosis.

Conclusion:

This study shows that NMP is feasible from a technical perspective. This continuing study is comparing the results of both DCD and DBD donor livers. The extensive degree of biliary damage in the DCD liver may underline the need to consider biliary tract integrity when assessing graft viability.

SYNBIOTICS EASING RENAL FAILURE BY IMPROVING GUT MICROBIOLOGY (SYNERGY): A PLACEBO-CONTROLLED RANDOMISED CROSS-OVER TRIAL

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Background:

Synbiotic (pre- and probiotics) administration to patients with chronic kidney disease (CKD) represents a promising and cost effective strategy for modifying the gut microbiota and thereby the production of key uremic nephrovascular toxins, indoxyl sulphate (IS) and p-cresyl sulphate (PCS). To date, translation of this intervention into widespread clinical practice has been impeded because of inconsistent findings derived from poorly designed trials.

Methods:

Participants who were pre-dialysis, stage 4/5 CKD were randomised to synbiotic therapy or placebo for 6 weeks, with a 4 week washout period between cross-over. The primary outcome was serum IS and PCS. Secondary outcomes included quality of life (QOL), gastro-intestinal symptoms and serious adverse events (SAE).

Results:

Overall, synbiotic administration resulted in a significant change in serum concentrations of PCS for the 31 patients that completed the study (mean difference, $-14 \mu\text{mol/L}$; 95% CI range -27 to $-2 \mu\text{mol/L}$ [$p=0.025$]). This benefit was more pronounced in participants who did not receive antibiotics during the study ($n=21$), with significant reductions in both PCS (mean reduction, $-25 \mu\text{mol/L}$; 95% CI range -38 to $-12 \mu\text{mol/L}$ [$p=0.001$]) and IS (mean reduction $-5 \mu\text{mol/L}$; 95% CI range -8 to $-1 \mu\text{mol/L}$ [$p=0.025$]). The intervention did not affect participants' QOL or gastro-intestinal symptoms (both $p>0.05$) and was not associated with any SAEs.

Conclusions:

Synbiotics are a safe and effective nutritional intervention for decreasing key uremic toxins in CKD patients, particularly in the absence of antibiotic treatment. The impact of synbiotic administration on markers of cardiovascular risk, further kidney damage and gut microbiota are currently underway.

TARGETING MULTIPLE ISLET AUTO-ANTIGENS FOR TOLERANCE INDUCTION

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Background:

Type 1 diabetes is an autoimmune disease characterized by CD4+ and CD8+ T-cell mediated destruction of insulin-secreting pancreatic beta cells. Insulin-specific T cells appear early in the disease process and transferring hematopoietic progenitor cells (HPCs) encoding proinsulin prevents diabetes in young mice by inducing immunological tolerance to proinsulin. However, T cells specific to the other islet antigens appear later in the disease process and tolerization of these T cells may be required to prevent progression of disease in symptomatic individuals.

The aim of this study is to evaluate whether targeting the presentation of multiple islet autoantigens to resting antigen presenting cells (APCs) can effectively tolerize autoreactive T cells with multiple specificities.

Methods:

To facilitate this, lentivirus vectors were generated containing tandem sequences encoding islet antigenic determinants from proinsulin, IGRP, AI4 (mimotope) and Chromogranin A.

Results:

Here, we demonstrate that these lentivirus vectors transduce murine HPCs efficiently leading to expression of the polytope and the reporter GFP.

Conclusions & Future directions:

HPCs transduced with the lentivirus vectors encoding the polytope will be transferred into NOD mice to achieve long-term polytope expression in resting APCs. Subsequently, the capacity for tolerization of autoreactive T cells will be evaluated by transferring TCR transgenic T cells specific for each individual epitope. Then to determine whether tolerance can be induced simultaneously to multiple determinants, mixed populations of T cells with specificity for the encoded antigenic determinants will be transferred together. These studies could lead to the development of effective cell-based therapies even in individuals with symptoms of type 1 diabetes.

SERUM GLYCOPROTEIN BIOMARKERS FOR DIAGNOSIS OF BARRETT'S OESOPHAGUS AND OESOPHAGEAL ADENOCARCINOMA

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Oesophageal adenocarcinoma (EAC) is the most rapidly increasing cancers globally. The patients suffering from pre-cancerous asymptomatic metaplastic condition Barrett's oesophagus (BE) are monitored by upper gastro-oesophageal endoscopy-biopsy for early neoplastic changes. This procedure requires patient hospitalisation and specialist appointment hence not suitable for population screening. Altogether, majority of EAC cases are diagnosed at very late stages hence <15% of the patients survive 5 year post-diagnosis. The aim of this project is to identify serum diagnostic biomarkers for BE/EAC.

We focused on alterations in circulatory protein glycosylation, using a panel of 20 lectins to isolate different glycan structures on serum glycoproteins. Serum samples from healthy, BE and EAC patients (n=29) were analyzed by lectin magnetic bead array (LeMBA)-coupled mass spectrometry. Data analysis was performed using a customized database and analysis package "GlycoSelect" incorporating sparse Partial Least Squares-

Discriminant Analysis.

We identified a ranked list of glycoprotein biomarkers that distinguish a) EAC from BE b) BE from healthy and c) EAC from healthy group. Overall, glycoproteins bound several lectins and specific glycan structure changes were observed as loss/gain of binding to a single lectin. Top two candidate biomarkers were validated using orthogonal validation technique LeMBA-immunoblotting in an independent patient cohort (n=80) which showed Area under Receiver Operating Characteristic curve (AUROC) of >0.70. Future work will validate all candidate lectin-glycoprotein pairs using LeMBA-triple quadrupole mass spectrometry in an independent patient cohort. The specificity and sensitivity of panels of glycoprotein biomarkers will be determined for developing future screening test for BE/EAC.

REAL-TIME 3D MAPPING OF BIOPSY FIDUCIAL POINTS USING TWO INFRARED CAMERAS

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Background:

A CT-guided biopsy is a specialized surgical procedure where a needle is used to withdraw a tissue or fluid specimen from a lesion of interest. The needle is guided while being viewed by the surgeon on a computed tomography (CT) scan. CT guided biopsies expose patients to high dosage of radiation, they are lengthy and costly procedures and the lack of spatial reference while guiding the needle down the predicted path are some of the difficulties currently encountered. Currently the operator advances the needle in a stepwise fashion, re-imaging

the patient at each step to determine any required corrections in trajectory

Methods:

To explore possible approaches to this problem, I investigate the use of two infrared cameras capable of imaging the biopsy needle area. These are then mapped using custom software into scaled 3D co-ordinate space using an extension of a known approach. The system is able to read, in real-time, infrared data from two cameras and import the data. The result is a scaled 3D estimate of the needle endpoints.

Results:

The results indicated that the real-time data acquisition is able to translate to the estimated 3D position as the IR sources are moved.

Conclusions:

Inserting the biopsy needle at a predicted angle and advancing it along a desired path is a challenging task that requires much practice and experience as well as sound judgement in spatial reference. This system is designed to help improve the spatial reference of the biopsy operator.

SENSORINEURAL HEARING LOSS: WHO IS MOST AT RISK AND WHAT CAN WE DO ABOUT IT?

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Background:

Patients with virally-mediated head and neck cancer (HNC) are often long term cancer survivors. Therefore, research is being directed towards minimising side effects and improving patient quality of life. Ototoxicity is a known complication for patients receiving Cisplatin-based chemoradiation therapy (CbCRT). This study sought to identify potential risk profiles for patients at risk of sensorineural hearing loss (SNHL).

Methods:

One hundred and fifty patients with HNC, who received CbCRT, were retrospectively reviewed. The impact of diagnosis, chemotherapy regimen, radiation dose, inner ear delineation accuracy and dose to inner ear structures, were evaluated. Sensorineural hearing function was assessed using pure tone audiometry. SNHL was diagnosed if the bone conduction threshold test showed a clinical significant change of >10 dB.

Results:

Only fifty-two (34.7%) patients received baseline and follow-up audiograms during treatment. Seven (13.5%) patients had pre-existing SNHL. Following CbCRT, forty-two (80.8%) patients were diagnosed with or had worsening SNHL, four (7.7%) had mixed hearing loss and six (11.5%) patients hearing was unaffected. Primary sites included: oropharynx (61.9%); larynx (14.3%), hypopharynx (9.5%); oral cavity (7.1%), nasopharynx (4.8%) and paranasal sinus (2.4%). Chemotherapy regimen, radiation dose and nodal involvement were correlated with SNHL diagnosis. There was high variation in the accuracy of inner ear contouring among clinicians, including average volume, position and structures.

Conclusions:

In this study, a significant proportion of patients developed SNHL following CbCRT for HNC. The proportion of patients with SNHL may be under-reported without routine audiometry. These findings will be considered in a future prospective radiotherapy study.

KERATINOCYTE CANCERS AND ACTINIC KERATOSIS IN THE LIVER TRANSPLANT RECIPIENTS IN QUEENSLAND - RESULTS FROM A PROSPECTIVE CROSS-SECTIONAL STUDY.

Sudipta Sinnya, Marcia Davis, Michelle Iannaconne, Lisa Ferguson, Sharan Burton, Nirmala Pandeya, Jonathan Fawcett, H. Peter Soyer, Adele Green

Introduction

Keratinocyte Cancer rates in the transplant population in Australia are among the highest in the world, leading to significant morbidity and associated costs to the health care system. While skin disease have been studied quite extensively in kidney and heart transplant patients, data pertaining to liver transplant recipients remain sparse. This study aims to review the prevalence of keratinocyte cancers and actinic keratosis in the Queensland.

Methods

183 liver transplant patients were prospectively reviewed at the Princess Alexandra Hospital in Queensland, Australia. Prevalence of keratinocyte cancers and actinic keratoses were reviewed relative to personal and phenotypic characteristics such as age, sex, skin type and previous skin cancers; ultraviolet exposure characteristics and transplant specific characteristics such as reason and length of transplantation.

Results

A total of 49 of the 183 study participants (27%) had 102 histopathologically proven keratinocyte cancers. 89% also had clinical diagnosis of actinic keratosis, the prevalence in females being 28% and in males 61%. The mean AK count in our study population was 26 (SD 44). Age, sex, previous skin cancer as well as length of immunosuppressive therapy were associated with increased risk of these conditions.

Conclusions

This prospective study suggests that the prevalence of keratinocyte cancers and actinic keratoses in liver transplant recipients despite being lower than heart and lung transplantation recipients remains an inherent problem. Regular skin surveillance especially in the older age groups and those with history of previous skin cancers, coupled with careful optimisation of immunosuppressive medication in this high-risk population.

METABOLIC ALTERATIONS TO KIDNEY TUBULAR CELLS FOLLOWING ACUTE KIDNEY INJURY DRIVES PROGRESSION TO CHRONIC KIDNEY DISEASE

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Acute kidney injury (AKI) often progresses to chronic kidney disease (CKD). Oxidative stress and mitochondrial dysfunction exacerbate AKI but their role in progression to CKD remains unclear.

Aim:

To determine whether the metabolic changes associated with oxidative stress during AKI contribute to progression to CKD.

Methods:

Male C57Bl6 mice underwent kidney ischaemia (20min) followed by reperfusion (IR). Chronic changes developed over 21 days (21d). Intravital multiphoton microscopy (MPM) was used to assess endogenous nicotinamide adenine dinucleotide (NADH) in kidneys: without IR (controls); during ischaemia; at IR; and at 21d (n=4/group). Fluorescence lifetime imaging microscopy (FLIM) measured free/bound NADH (ϕ_1/ϕ_2 ratio), and the average weighted lifetime (ϕ_m) of NADH in cortex and medulla. Perfusion with a mitochondrial dye (TMRM) coupled with MPM assessed mitochondrial health. Matched molecular and histological assessments were performed post-MPM and FLIM.

Results:

NADH fluorescence intensity (EFI) significantly decreased during ischaemia ($p < 0.05$ v control). 21d post-IR showed tubular atrophy, with significantly-increased NADH EFI in structurally-normal tubules. Tubular epithelial TMRM decreased, the ϕ_1/ϕ_2 ratio increased, and the ϕ_m of NADH/FAD decreased in the cortex ($p < 0.05$). Protein analyses showed: nuclear factor-like-2 expression increased at reperfusion ($p < 0.001$) but decreased at 21d ($p < 0.05$); increased apoptosis, collagen, heme-oxygenase-1, transforming growth factor- α 1, proliferating cell nuclear antigen, and 8-hydroxy-2'-deoxyguanosine ($p < 0.05$ at 21d); and decreased superoxide dismutase-2 ($p < 0.05$ at 21d).

Conclusions:

This is the first demonstration that dynamic changes in NADH utilisation by kidney tubular cells promote oxidative stress in progressive CKD. This presents mitochondrial preservation as a crucial target to halt progression of CKD.

VAGINAL DELIVERY OF DICHORIONIC DIAMNIOTIC (DCDA) TWINS AFTER 32 WEEKS IS ASSOCIATED WITH POORER NEONATAL OUTCOMES COMPARED TO TWINS DELIVERED BY ELECTIVE CAESAREAN SECTION

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Background:

To explore the perinatal outcomes associated with different modes of delivery in DCDA twins delivered after 32 weeks gestation at a major maternity centre in Australia.

Methods: Retrospective study of DCDA twins delivered at the Mater Mothers' Hospital from January 1997 to November 2013.

Results:

A total of 1261 sets of twin pregnancies were identified, of which 2088 babies were delivered >32 weeks. Elective caesarean section (CS) was the commonest delivery route (837, 40.1%), followed by 654 (31.3%) emergency CS, 418 (20.0%) spontaneous vaginal delivery (SVD) and 179 (8.6%) instrumental vaginal delivery (ID). Of the 245 pregnancies where Twin 1 was delivered via SVD, 88 (35.9%) Twin 2 required ID or an emergency CS. APGAR scores <7, at 1 minute, were 44 (24.6%) in ID, 128 (19.6%) in emergency CS, 57 (13.6%) in SVD and 96 (11.5%) in elective CS ($p<0.05$). The highest rate of NICU admission resulted from emergency CS (290, 44.3%), followed by ID (65, 36.3%), SVD (123, 29.4%), and elective CS (230, 27.5%), ($p<0.05$). Composite outcome scores, calculated from APGAR scores, neonatal resuscitation, deaths and NICU admissions data, were 1.26 in SVD, 1.77 in ID, 2.00 in emergency CS, and 1.50 in elective CS ($p<0.05$).

Conclusion:

Our study has demonstrated significantly poorer neonatal outcomes in twins >32 weeks requiring ID or emergency CS, when SVD has failed, compared to elective CS. This is in contrast to the recent publication in NEJM by Barrett et al. In our series, as only 20% of women successfully deliver either one or both twins via SVD, they should be counselled about local outcome rates before attempting labour.

FUNCTIONAL VALIDATION OF A KLK3 VARIANT, RS17632542, ASSOCIATED WITH PROSTATE CANCER RISK

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Background:

KLK3 or PSA is the current biomarker for prostate cancer and has a significant role in the proteolytic cascades involved in seminal clot dissolution and prostate tumor biology. Fine-mapping studies identified a missense single nucleotide polymorphism (SNP) rs17632542 (Ile178Thr) in exon-4 of KLK3 to be associated with prostate cancer risk. We aim to delineate the molecular consequences of this missense rs17632542 SNP.

Methods:

In-silico tools were employed to analyze the effect of the SNP on splicing, protein stability and glycosylation. Mini-gene assays verifying the differential splicing effect for the SNP were performed in LNCaP and PC3 cell lines. Recombinant KLK3 (261 aa) protein harbouring the variant (Thr) and wild-type (Ile) at amino-acid position 179,

were made in insect cell lines. Protein stability analysis by differential scanning fluorimetry (DSF) and substrate activity assays using a fluorescent peptide were performed.

Results and conclusions:

In-silico analysis for the rs17632542 SNP suggests an alteration in a KLK3 splice site, KLK3 protein stability and glycosylation for the risk allele. Mini-gene assay herein provide evidence for differential allele specific splicing. DSF and activity assays using peptide substrates suggested the SNP affects the stability and activity of the KLK3 protease. These results indicate the missense rs17632542 SNP to have biological effect on the expression and/or function of the KLK3 protein, which has role in prostate cancer prognosis.

RAPID MOLECULAR DIAGNOSIS OF JAK2V617F NEGATIVE MPN BY TARGETED DEEP SEQUENCING USING THE ION TORRENT PGM

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Myeloproliferative neoplasms (MPN) are a heterogeneous group of blood disorders characterized by excess production of mature blood cells, increased risk of thrombotic complications and slow progression to myelofibrosis or, less often, leukemia. Activation of the JAK-STAT signaling pathway is a common underlying feature of these diseases and JAK kinase inhibitors are efficacious in the more advanced forms of disease. Most cases of polycythemia vera (PV) and approximately 60% of essential thrombocythemia (ET) and primary myelofibrosis (MF) harbor a point mutation in JAK2 (V617F) which leads to constitutive JAK-STAT signaling and factor independent cell growth. The remaining 40% of cases of MF and ET harbor a broad range of mutations in many genes including those involved in cytokine receptor signaling, other components or the JAK-STAT pathway or epigenetic regulators. This poses a challenge for rapid molecular diagnosis. Also, since ET is essentially a diagnosis of exclusion of reactive causes of thrombocytosis, many cases of chronic 'ET' may not be clonal hematological neoplasms but reactive conditions.

We have developed a rapid deep sequencing pipeline to detect mutations in 65 genes which have been implicated in MPN through previous reports of human mutations, mouse models of MPN, or other known components of hematopoietic cytokine receptor signaling. We used 10ng of DNA from blood to amplify and sequence all the exons of these 65 genes using Ampliseq and Ion Torrent PGM. Using 318 PGM chips and 8-fold multiplexing we achieved on average 200 fold coverage of the target exome. The bioinformatics of SNP validation and rapid generation of reports will be presented. From a pilot study of 30 cases referred for molecular diagnosis, we have detected the likely causative mutation in approximately 80% of ET and MF where JAK2 is wild type. Many of these mutations are known to be causative in MPN, including those in MPL, ASXL1, SET2, SH2B3 (LNK), EZH2, CBL, DNMT3A, CALR and other genes. We have identified a novel inherited mutation in a family with MPN and validated it in BAF3 factor-independency assays. We have identified further novel mutations in JAK3, EED, DNMT3A, APC and two phosphatases involved in silencing activated JAK-STAT pathway components. The biological significance of these is under investigation. In many cases we find evidence for clonal evolution involving secondary mutations in epigenetic modifying proteins on top of driver mutations in the JAK-STAT pathway.

In short, targeted exome re-sequencing using Ampliseq and Ion Torrent PGM provides a rapid and relatively cheap method for molecular diagnosis and characterization of most cases of MPN.

TIE-2 REGULATES STEMNESS AND METASTASIS OF PROSTATE CANCER CELLS.

Tang KD and Ling MT

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Prostate cancer (PCa) is the most commonly diagnosed male cancer in Western countries. Currently, the major treatment challenge for PCa patients is the development of tumor metastasis. Ample evidence supports the idea that tumor metastasis originates from a rare population of cancer cells known as cancer stem cells (CSCs). Unfortunately, little is known about the identity of these cells, making it difficult to target prostate tumor metastasis. Here we reported the identification of a rare population of PCa cells which express the Tie-2 protein, a tyrosine kinase receptor required for the bone marrow homing and colonization of hematopoietic stem cells. Notably, this Tie-2+ population exists exclusively in highly metastatic and aggressive PCa cell lines. Data from our study revealed that prostate CSC markers were upregulated in Tie-2+ cells express higher level of prostate CSC markers when compared to the Tie-2- population. Meanwhile, Tie-2+ cells are highly adhesive to both osteoblast and endothelial cells, a characteristic necessary for tumor metastasis. We also found that Tie-2+ cells are more quiescent and resistant to the chemotherapeutic drug cabazitaxel, further support that these cells possess CSC-like characteristics. More importantly, we found that Tie-2+ cells, but not the Tie-2- cells population, developed metastatic tumor in vivo. Our data suggested that Tie-2 plays an importantly role in the development of drug resistance and prostate tumor metastasis. Thus, Tie-2 might be a novel therapeutic target for the treatment of advanced PCa patients.

NON-INVASIVE BIOMARKERS ARE SUPERIOR TO CLINICAL MEASURES IN PREDICTING HEPATIC DECOMPENSATION AFTER LIVER RESECTION

James A Thomas, Ashok Raj, Uthayanam Chelvaratnam, Marianne Black, Linda Fletcher, Caroline Tallis, Jonathan Fawcett, Gerald Holtmann, Katherine A Stuart

Background/Aim: Novel, non-invasive biomarkers to assess liver function and predict clinical outcomes are urgently needed. Hepatocellular carcinoma (HCC) is the fifth commonest malignancy worldwide. Potentially curative surgical resection of HCC can cause hepatic decompensation. No single test currently in clinical use offers reliable risk stratification. This study aims to assess the clinical utility of 13C methacetin breath test (13CMBT, measure of hepatocyte microsomal function), transient elastography using FibroScan and indocyanine green (ICG) clearance (measure of liver perfusion and excretory function) in predicting hepatic decompensation in patients undergoing liver resection.

Methods: 13CMBT, FibroScan and ICG clearance were measured prospectively in 105 patients being assessed for liver resection. Clinical and laboratory data were recorded. 23 patients underwent surgery; post-operative hepatic decompensation was determined by biochemical and clinical parameters.

*=p

Results: There was significant correlation of 13CMBT, FibroScan and ICG clearance with serum bilirubin ($R=-0.43^{**}, 0.21^*, 0.42^{**}$) and albumin levels ($R=0.37^{**}, -0.41^{**}, -0.72^{**}$), respectively. Both Child-Pugh (C-P) ($R=-0.44^{**}, 0.46^{**}, 0.68^{**}$) and MELD scores ($R=-0.2$ [$p=0.08$], $0.28^*, 0.38^{**}$) correlated with these biomarkers. Receiver operating characteristic curve plots assessed the performance of these tests in predicting post-operative decompensation. The areas under the curve for C-P (0.46) and MELD (0.55) offered limited clinical utility compared to ICG (0.78). Multivariate analysis was used to control for duration of surgery and weight of resected liver; 13CMBT was strongly associated with post-operative decompensation ($R=0.68^*$).

Conclusions: ICG and 13CMBT were superior to routine blood tests, MELD and C-P scores in predicting hepatic decompensation after liver resection. This result justifies further evaluation in other cohorts and settings.

ASSESSING STEATOTIC LIVER FUNCTION AFTER ISCHEMIA-REPERFUSION INJURY BY IN VIVO MULTIPHOTON IMAGING OF FLUORESC EIN DISTRIBUTION

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Background:

The liver is important for metabolism of various drugs, and liver disease could result in increased systemic concentrations. Ischemia-reperfusion injury is a common complication during liver surgery, where steatotic livers are more prone to the injury and are more prevalent in the growing obese population. This study aimed to characterize liver morphology and understanding changes in function in steatotic livers exposed to ischemia-reperfusion injury through quantitative description of fluorescein distribution obtained by multiphoton microscopy using a physiological pharmacokinetic model.

Methods:

Rats developed liver steatosis using a high fat diet for 7 days. Ischemia was induced, following reperfusion for 4 hours, where-after fluorescein was injected. Liver was imaged, bile and blood were collected until 180 min. Blood and liver tissue were collected for liver function assessment and histology.

Results:

Ischemia-reperfusion injury was associated with an increase in alanine transaminase levels and apoptosis. In addition, steatosis also had the presence of lipid droplets and an increase in fluorescein associated fluorescence observed in the hepatocytes by multiphoton imaging. Analysis of the hepatic concentration-time profiles

STANDARDISED COOLING IMPROVES THE DETECTION OF BROWN ADIPOSE TISSUE BY 18FDG-PET WITHOUT SIGNIFICANT SEASONAL VARIATION

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Background:

Detection of human brown adipose tissue (BAT) by 18FDG-PET-CT is low in non-temperate regions and is markedly affected by seasonal temperature.

Aim:

To determine whether a standardised cooling protocol improves detection of BAT.

Methods:

18 (12 men, 6 women) volunteers were placed in an air-conditioned room cooled to 19°C for 3 hours before undergoing 18FDG-PET-CT. 11 subjects were studied twice to ascertain reproducibility, giving a total of 29 scans. The 18FDG dose was 75 MBq, four times lower than that for diagnostic scanning. The data were compared to 450 scans of patients who underwent diagnostic 18FDG-PET-CT for various medical indications at room temperature. BAT-positivity was defined by SUV_{max} ≥ 2 in supraclavicular and cervical areas localising to fat attenuation on CT. The detection rates were analysed for summer, spring and winter.

Results:

Under standardised cooling, BAT was detected in 76% (22 of 29). Among those studied twice, the scans were concordant in 82%. In diagnostic scans, BAT was detected in 2% (9 of 450) and the prevalence was significantly greater ($p=0.01$) in winter (4.7%) than summer (0.66%) or spring (0.66%). With standardised cooling, the seasonal differences were not significant ($p=0.34$) between winter (85.7% of 14), spring (80% of 5) and summer (60% of 10).

Summary:

BAT prevalence under standardised cooling was 35 fold higher than the background prevalence despite employing a much lower FDG dose. Standardised cooling confers high reproducibility with detection rates that do not vary significantly between seasons.

Conclusion:

Standardised cooling markedly improves BAT detection without significant seasonal variation.

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Identification and validation of two novel metastatic markers in Osteosarcoma

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Background:

Osteosarcoma (OS) accounts for 56% of malignant bone cancers in children and adolescents. Pulmonary metastasis occurs in approximately 50% of patients and leads to a 5-year survival rate of only 20%. It is crucial to identify genes and pathways that drive the metastatic behavior of OS for effective therapeutic targets.

Methods:

To identify markers that define metastatic behaviour in OS, we conducted a comparative transcriptomic analysis of two highly metastatic (C1 and C6) and two poorly metastatic clonal variants (C4 and C5) isolated from an inherently metastatic cell line, KHOS. Two novel markers were therapeutically targeted in vitro and in vivo.

Results:

DCBLD2 and TXNRD2 were identified as potential markers for OS metastasis with 2-4 fold increased expression in highly metastatic clonal variants. Gene expression of DCBLD2 and TXNRD2 was validated in a transcriptomic screen of non-malignant bone (NB), OS patient biopsies who developed metastatic disease (M-OS) and patients with localized disease (NM-OS). These markers were found to be highly expressed in 29-42% of M-OS with little to no expression seen in NB and NM-OS. Knockdown of DCBLD2 using shRNA reduced colony forming ability in vitro and significantly decreased pulmonary metastasis in vivo. Targeting TXNRD2 with auranofin increased ROS in KHOS cells and induced mitochondrial dysfunction resulting in apoptosis in vitro. Auranofin treatment in vivo significantly decreased pulmonary metastasis in a mouse model of spontaneous OS lung metastasis.

Conclusions:

This transcriptomic screen identified TXNRD2 and DCBLD2 as promising targets for the prevention and treatment of metastatic OS.

IL-17/ARGINASE-1 MEDIATES ACUTE CUTANEOUS INFLAMMATORY RESPONSE TO 2,4-DINITROCHLOROBENZENE IN HUMAN PAPILLOMAVIRUS E7 ONCOPROTEIN TRANSGENIC MICE

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We have shown that the expression of human papillomavirus type 16 E7 (HPV16.E7) protein within epithelial cells results in local immune suppression and a weak and ineffective immune response to E7 similar to that occurring in HPV-associated premalignancy and cancers. However, a robust acute inflammatory stimulus can overcome this to enable immune elimination of HPV16.E7 transformed epithelial cells. 2,4-Dinitrochlorobenzene (DNCB) can elicit acute inflammation and has been shown to initiate the regression of HPV-associated genital warts. Although clinical use of DNCB is discouraged due to its mutagenic potential, understanding how DNCB induced acute inflammation alters local HPV16.E7 mediated-immune suppression might lead to better treatments. Here, we show that topical DNCB application to skin expressing HPV16.E7 induces a hyperinflammatory response, not seen in non-transgenic control animals. The E7 associated-inflammatory response is characterized by enhanced expression of Th2 cytokines and increased infiltration of CD11b+Gr1^{int}F4/80+Ly6ChiLy6G^{low} myeloid cells, producing arginase-1. Inhibition of arginase with an arginase specific inhibitor, N(omega)-hydroxy-nor-L-arginine, ameliorates the DNCB-induced inflammatory response. Moreover, HPV16.E7 expressing skins lacking IL-17A but not Th2 cytokines fail to induce arginase activity and develop alleviated inflammatory response to DNCB. Our results suggest that HPV16.E7 protein enhances DNCB associated-production of IL-17A which mediates arginase-1 production by myeloid cells and consequent inflammatory cellular infiltration of skin. These findings imply a potential immune-based therapy strategy for breaking the tolerance to HPV persistent infection by modulating IL-17A/arginase-1 axis.

ESTABLISHMENT OF A NOVEL EXPERIMENTAL MODEL TO STUDY MECHANOBIOLOGY OF BONE HEALING

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Introduction:

Bone healing depends on the mechanical environment. Understanding mechanobiology is crucial to optimize treatment for fractures and improving bone regeneration. Studying the mechanobiology of bone healing is challenging as current experimental models have incompletely defined loading conditions. In this study we present a novel model that eliminates functional loading and allows for the application of defined loading and *in vivo* monitoring on the progression of healing of an experimental fracture.

Methods:

In a sheep tibia a novel defect configuration of a double osteotomy and a mobile segment in between was created. The proximal osteotomy represents the experimental fracture (3mm) separated from a segmental defect in the distal third by a mobile segment. A preliminary defect validation study was completed to analyze the healing capabilities of the bone healing model under different fixation configurations (unilateral and dual fixation).

Results:

3D microCT analysis demonstrated that the dual fixation group had produced as expected an understimulation with minimal external callus formation after 9 weeks. In contrast external callus formation and healing was seen in the unilateral fixation group.

Conclusions:

This model provides an opportunity to apply defined loads to a healing fracture during different phases of

healing to understand the mechano-regulation of callus formation. Future work involves the incorporation of an active instrumented fixator. This fixation device drives the mobile segment with a precision motor to create defined loading within the fracture gap, whilst simultaneously monitoring the *in vivo* progression of healing through measurement of the resistance of the tissues to motion.

Targeting antigen to human CD141+ DC via CLEC9A results in superior cross-presentation to CD8+ T cells compared with targeting DEC-205.

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Cytotoxic T lymphocyte (CTL) responses are initiated by dendritic cells (DC) and are required for immune-mediated clearance of tumours and many pathogens for which there are currently no effective vaccines. Targeting antigen (Ag) to DC *in vivo* is an attractive strategy for vaccine development and clinical trials are currently underway using antibodies (Ab) specific for the DEC-205 receptor to deliver tumour Ag to DC in patients with solid malignancies. However, DEC-205 is widely expressed on all human DC subsets and other cell types, which may compromise targeting efficiency. Human CD141+ DC have been identified as the main subtype involved in Ag cross-presentation and are considered the most effective subset to target for CTL induction. The C-type lectin-like receptor CLEC9A is specifically expressed on CD141+ DC, binds actin filaments exposed by dead cells and facilitates cross-presentation of dead cell Ag, making it an attractive candidate for specifically targeting this DC subset. We have produced and validated recombinant human chimeric IgG4 Ab specific for human CLEC9A, DEC-205 and an isotype control. We fused a fragment of the human CMV pp65 Ag, including the HLA-A2-restricted NLVPMVATV epitope, to the Ab heavy chains to create Ab-Ag fusion proteins. These fusion proteins retain binding specificity for their target receptor, are internalised at equivalent rates by CD141+DCs, and accumulate within DCs. We investigated the ability of CD141+ and CD1c+ DCs to cross-present the NLVPMVATV epitope to Ag-specific CTL lines following uptake of the fusion proteins in the presence and absence of adjuvant. Our data demonstrate that anti-CLEC9A Ab are more effective at delivering Ag for cross-presentation by CD141+ DCs compared to anti-DEC-205 Ab, while CD1c+ DCs did not cross-present Ag from either Ab. Thus, targeting of human CD141+ DC via CLEC9A is a strategy that warrants development as an immunotherapeutic for cancer or infectious disease.

STABILITY INDICATING RP-HPLC METHOD FOR VANCOMYCIN EYE DROPS.

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Vancomycin is bactericidal against many Gram-positive and works by weakening the bacterial cell wall. Formulated in an eye drop, Vancomycin is used principally for the treatment of serious external ocular infections caused by gram-positive bacteria that are resistant to beta-lactams and anti-infectives such as methicillin-resistant *Staphylococcus aureus* (MRSA) or methicillin-resistant *Staphylococcus epidermidis* (MRSE). Crystalline degradation products of Vancomycin (CDP) are antibiotically inactive [1], but are responsible for falsely elevating results of some immunoassays due to their cross reactivity. This study aims an assay which is specific in the presence of Vancomycin breakdown products.

As there are no commercial Vancomycin eye drop products in the Australian market, a compounded eye drop has been prepared by Central Pharmacy. An Acetonitrile-based HPLC method with short run time, symmetrical peak shape and good resolution from the excipients has been developed and validated. Three stress conditions (Acid,

alkali, and heat) were applied in the degradation study. Degraded vancomycin samples were analysed to control the separation of the antibiotics from its degraded products.

The current method is able to identify the changes that occur during forced degradation of Vancomycin with no degradation peaks co-eluted at the same retention time of the active thereby achieving the measure of true Vancomycin content in the formulation.

[1] C.M.Harris, H.Kopecka, T.M. Harris. J.Am.Chem.Soc.(1983) 105 ,6915-6922

THE ROLE OF FKBP52 IN THE DNA DAMAGE RESPONSE PATHWAY.

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Damage to genetic material represents a constant threat to genomic stability, with tens of thousands of DNA lesions occurring every day in every cell, if these are not repaired correctly it can lead to disease states such as cancer and neurodegenerative disorders. To protect the integrity of the DNA, cells have evolved a global signalling network known as the DNA damage response. This DNA damage response pathway, detects, signals and then repairs the lesion. Human single strand DNA binding protein 1 (hSSB1) is central to the repair of DNA double strand breaks, functioning in both the detection of these breaks and their repair^{1,2}.

To increase our understanding of the DNA damage response pathway, we utilised a bioinformatics screen called “connectivity mapping”. Using hSSB1 as our focus we identified a number of co-regulated genes, including FKBP52. FKBP52 is a peptidyl-prolyl isomerases, that has already been implicated in cancer biology and to interact with DNA damage signalling proteins ^{3,4}. The aim of this project is to determine if FKBP52 is a central mediator in the DNA damage response pathway.

We have determined that depletion of FKBP52 increases genomic instability and cells display increased sensitivity to ionising radiation. Furthermore, we have demonstrated that FKBP52 interacts with hSSB1 following DNA damage. Thus suggesting that FKBP52 is a crucial member of the DNA damage response pathway.

By elucidating the novel role of FKBP52 in DNA damage signalling and repair, it will potentially lead to the identification of new therapeutic options in diseases such as cancer.

1. Richard, D., Bolderson, E. & Khanna, K. K. Multiple human single-stranded DNA binding proteins function in genome maintenance: structural, biochemical and functional analysis. *Critical Revs. in Biochem. & Mol. Biol.* 1–19 (2009). doi:10.1080/10409230902849180
2. Richard, D. J. *et al.* hSSB1 rapidly binds at the sites of DNA double-strand breaks and is required for the efficient recruitment of the MRN complex. *Nucleic Acids Res.* 39, 1692–1702 (2011).
3. Storer, C. L., Dickey, C. A., Galigniana, M. D., Rein, T. & Cox, M. B. FKBP51 and FKBP52 in signaling and disease. *Trends Endocrinol. Metab.* 22, 481–490 (2011).
4. Galigniana, M. D., Harrell, J. M., O'Hagen, H. M., Ljungman, M. & Pratt, W. B. Hsp90-binding immunophilins link p53 to dynein during p53 transport to the nucleus. *J. Biol. Chem.* 279, 22483–22489 (2004).

AGER1 OVEREXPRESSION IN GLOMERULAR PODOCYTES RESULTS IN RENAL DISEASE WHICH IS EXACERBATED BY DIABETES

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Background:

Accumulation of advanced glycation end products (AGEs) is implicated in the pathogenesis of diabetic nephropathy. We investigated the effects of overexpressing the AGE receptor 1 (AGER1) in glomerular podocytes on the development of kidney disease in diabetes.

Methods:

Male heterozygous global AGER1 knock-in mice (AGER1WT/ Δ Ubi), podocyte-specific (AGER1WT/ Δ Pod) and littermate controls (N=8/group) were randomised to either control or diabetes induced by low dose streptozotocin (50mg/kg/day for 5 days) and followed for 24 (AGER1WT/ Δ Ubi) or 12 weeks (AGER1WT/ Δ Pod). Kidney function was determined by 24 hour urinary albumin excretion rate (UAER) and creatinine clearance (CrCl) and renal structural abnormalities assessed. Additionally we examined the localisation of AGER1 in subcellular fractions of the podocyte and concentrations of renal AGEs.

Results:

Non-diabetic mice with podocyte-specific overexpression of AGE-R1 developed advanced kidney disease, matching the pathology seen in diabetic WT mice, while global AGE-R1 KI mice were not protected against renal injury in the context of diabetes. This was evidenced by increased glomerulosclerosis, tubulointerstitial expansion, increased UAER and a decline in CrCl. Interestingly there was greater renal clearance of AGEs seen in non-diabetic mice with podocyte-specific overexpression of AGER1 when compared with both global AGE-R1 KI and WT mice.

Conclusions:

Increased expression of AGER1 in podocytes results in kidney disease which was exacerbated with diabetes. Efforts to increase the expression of AGER1 in an attempt to facilitate renal clearance of AGEs in diabetes may have undesirable side-effects leading to kidney dysfunction.

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