

PRINCESS ALEXANDRA HOSPITAL

Making Advances Matter

research, education and
treatment in partnership



2013 PAH Health Symposium
19-23 August • Brisbane Australia



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Making Advances Matter



“Research, education and treatment in partnership”

On behalf of the Organising Committee, I welcome you to the 2013 PAH Health Symposium, which carries the theme: Making Advances Matter: research, education and treatment in partnership.

The PAH Symposium will be augmented by sessions on health systems innovation and new technologies, oral and poster communications, and awards presentations. The Symposium will culminate in a special DHP session on the influence of academic health science enterprises in delivering future healthcare.

Central to the program is Professor Stephen Durham of Imperial College Hospital London, 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 immunologic mechanisms that are translating to novel therapies for allergies and asthma. Professor Durham is also this year’s Kurt Aaron Orator.

The core program this year is aligned to the flagship themes of DHP, the mission of which is to achieve better health through innovation and academic leadership. The themes include:

- Cancer
- Chronic disease
- Trauma and recovery
- Immunity, inflammation and infection
- Neuroscience and mental health
- Clinical practice innovation.

The week will feature engaging educational forums from a ‘CSI’-style hunt for the cause of demise, to the pragmatism of clinical hand over and attracting funding. During the week, over lunchtime, there will be forums on integrated electronic medical records in research, a debate on the use of social media, and a celebratory presentation on the PAH Centres for Health Research.

The PAH Symposium will be augmented by sessions on health systems innovation, new technologies, by oral and poster communication, and awards, culminating in a special DHP session on the influence of Academic Health Science in delivery of future health care.

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 2013



International Plenary Speaker - Professor Stephen Durham

Head of Section
Allergy and Clinical Immunology
NHLI, Imperial College

Professor of Allergy and Respiratory Medicine
Royal Brompton Hospital
London, England.

Professor Durham has studied basic mechanisms of allergic rhinitis and asthma and the influence of treatment. This has involved the development of pharmacodynamic models of allergen challenge in the skin, nose and lung and studies of seasonal hay fever. A particular focus has been translational studies of allergen immunotherapy that have elucidated mechanisms of human antigen-specific tolerance and informed novel treatment approaches. He is principle investigator for a number of international trials that have resulted in Europe-wide registration of an Alum-based grass pollen vaccine for injection and a sublingual grass allergen tablet, the first allergy vaccine to be registered in UK for 35 years.

Professor Durham is current President of the British Society for Allergy and Clinical Immunology and a member of the Immune Tolerance Network Steering Committee of the National Institutes of health. He is former Chair of the Research Committee of the World Allergy Organisation and council member of Collegium Internationale Allergologicum. He has given prestigious lectures including the Dr John Salvaggio and Dr Harold Nelson Lectureships at the American Academy of Allergy, Asthma and Immunology, the John P McGovern Medal from the American College of Allergy, Asthma and Immunology. From the BSACI has been awarded the Jack Pepys Lectureship and William Frankland Medal for outstanding services to clinical allergy. He has written over 350 peer-reviewed articles and chapters and edited 3 books, including the popular BMJ ABC of Allergies.

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

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

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

2006	Dr Michael Wagels "Diabetic control and coronary artery disease. How do they correlate?"
2007	Dr Iain Thomson "Do patients recall the details of consent for colonoscopy?"
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"

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 Pandey 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

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)

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.

Entering into its fifth year, 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

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Dr Leanne Aitken

Dr Leanne Aitken is the Chair in Critical Care Nursing at Griffith University and Princess Alexandra Hospital in Brisbane, Australia. These roles incorporate the conduct and implementation of a range of clinical research and practice improvement projects, as well as postgraduate teaching and supervision. Mentoring clinical staff through the research process is an important component of the role. Leanne's research focuses on recovery after critical illness and injury, decision making practices of critical care nurses and a range of clinical practice issues including sedation management within critical care.

Leanne Aitken has been awarded Life Membership of the Australian College of Critical Care Nurses (ACCCN), is a Fellow of the Australian College of Nursing and a co-editor of the ACCCN Critical Care Nursing text that is published by Elsevier. She is also a Fulbright Alumnus after receiving a Fulbright Senior Scholarship to undertake research examining recovery after trauma with Dr Therese Richmond at the University of Pennsylvania, Philadelphia. Dr Aitken is the representative of the World Federation of Critical Care Nurses on the Global Sepsis Alliance, has led the development of guidelines for nursing care of sepsis patients and has been involved in the revision of the Surviving Sepsis Campaign Guidelines.



Ms Kellie Allen

Kellie Allen is the Communication and Patient Safety (CaPS) Program Manager for Queensland Health, Clinical Governance, Metro South Hospital Health Service and co writer of the CAPS program. As the coordinator, trainer and behavioral coach she leads the CaPS program.

As an extension of the CAPS program, Kellie is leading the development and delivery of the Clinical Handover strategy at Logan Hospital.

Kellie has presented the CAPS program across the state of Queensland from CEO, senior executives and management, mid-level management and multidisciplinary teams from medical through to operational. She has further represented Queensland Health internationally at the IHI 22nd Annual

National Forum on Quality Improvement in Health Care with a poster presentation, forming links with the USA, UK and Canada and delivered the CAPS presentation at the 14th Annual National Patient Safety Congress in Washington, USA. Nationally – Chair and presenter at 10th Anniversary Measuring & Reducing Avoidable Adverse Events Conference, key note Diversional Therapy Association.



Dr Richard Ashby

Dr Ashby is one of the state's most experienced clinicians and clinical administrators. His experience is an invaluable asset in providing direction to the Hospital and Health Service. 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 was most recently the Executive Director and Director of Medical Services at the Princess Alexandra Hospital (PAH). 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 (RBWH) in 2000. In the period 2000-2006, he also acted as District Manager at both the RBWH and PAH for lengthy periods before transferring to his current post in June 2006.

Dr Ashby's experience in health services management combined with his experience in clinical systems will accelerate the delivery of Queensland Health's agenda for the benefit of patients.

Dr Ashby contributes to a significant number of organisations/committees. His roles include:

- Member, Australian Medical Council
- Vice President Royal Australasian College of Medical Administrators (2010-2012)
- Chair, Clinical Council, PAH
- Board Member, Diamantina Health Partners
- Board Member, Australian Health Research Centre
- Member, e-Health Governance Board (Queensland Health)
- Chair, ICT Board, Metro South Hospital and Health Service
- Executive Sponsor, Clinical Redesign Program, PAH

PAH Health Symposium Speakers 2013



Ms Kalpana Atresh

Is the current Occupational Therapist on Acute Neurosciences & Acute Stroke Unit. She completed Bachelor of Occupational Therapy from Auckland University Of Technology in 2002. Kalpana has predominantly worked in Acute care services in New Zealand and Australia and has a special interest in early neuro-rehabilitation.



Associate Professor Andrew Barbour

Associate Professor Andrew Barbour is a Surgical Oncologist at the Princess Alexandra Hospital (PAH), Greenslopes Private Hospital and Mater Private Hospital with a research interest in the treatment of cancer. His academic interests have encompassed the areas of 1) clinical research, including randomised controlled clinical trials, 2) laboratory based research, including molecular biology pertinent to upper gastrointestinal disease, pancreatic cancer and melanoma, 3) translational research integrating the laboratory and clinical domains. As a surgeon, A/Prof Barbour specializes in the treatment of oesophageal, gastric, pancreatic and adrenal diseases, as well as melanoma and soft tissue tumours. He has expertise in minimally invasive treatments of these conditions, including thoracoscopic/laparoscopic oesophagectomy and laparoscopic gastrectomy.

As a clinical researcher, A/Prof Barbour has been active in the conduct of clinical trials at Phase I, II and III levels. He is the Principal Investigator for multicentre phase II trials in oesophageal and pancreatic cancer, funded by the NH&MRC. Both of these national trials include biological substudies with tumour tissue and blood banking and subsequent molecular analyses aimed at answering specific questions, including the identification of biomarkers of response to therapy.

A/Prof Barbour is a translational researcher at the School of Medicine, PAH, The University of Queensland. He is the head of Surgical Oncology Lab at the School of Medicine. His research has focused on using genomic, epigenomic, mRNA expression and next generation sequencing data to classify oesophageal adenocarcinoma (OAC) and identify biomarkers of outcome. In addition, his lab is seeking to identify biomarkers for recurrence following surgery for stage III melanoma.



Dr Johanna Barclay

Since completing her PhD in 2007, Dr Barclay has focussed on the role of the endocrine system in metabolic health. She worked with Professor Mike Waters at the IMB (UQ) on the role of growth hormone signalling in hepatic lipid metabolism, and with Professor Henrik Oster at the Max Planck in Germany on the effects of circadian disruption on the development of obesity and diabetes. She has recently returned to Australia to join Professor Ken Ho and study human brown adipose tissue; its characterisation, regulation and its contribution to energy expenditure in adults.



Dr Helen Benham

Dr Helen Benham is a consultant rheumatologist at Princess Alexandra Hospital and a current PhD student at the University of Queensland Diamantina Institute with her thesis due for completion in August 2013. 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 she has been completing her PhD in Professor Ranjeny Thomas's lab focusing on IL-23 signalling in the SKG mouse model of Spondyloarthritis. An educational grant is currently enabling Helen to lead a project investigating,

“Future pathways and innovation to embed the delivery of healthcare with research through the engagement and support of clinician researchers in Australia.”

PAH Health Symposium Speakers 2013



Ms Emily Brown

Emily has worked as a physiotherapist for the last 4 years at the PA hospital. She has spend most of her career working in the Brain Injury Rehabilitation Unit and on the acute neurological ward where she has developed a keen interest. Emily has been exposed to many patients diagnosed with conversion disorder and understands the challenges faced by physiotherapists when managing this patient group.



Dr Helen Brown

Helen Brown works as a Neurologist with both the Department of Neurology and The Stroke Unit at The Princess Alexandra Hospital



Dr Ellen Burkett

Dr Burketts current postitions are Full-time staff specialist in Emergency Medicine at Princess Alexandra Hospital ,Clinical lead for Aged Care Early Intervention and Management (ACEIM) and CARE-PACT, in collaboration with CNC Dawn Bandiera. She is also a Senior Lecturer University of Queensland.

Dr Burketts current research interests focus on improving ED quality of care and include, developing a quality framework for the management of older persons in the Emergency Department where she is the Lead Clinical Investigator (and PhD candidate) in collaboration with CRGM's Professor Len Gray and Dr Melinda Martin-Khan and improving quality of care of patients with sepsis in the Emergency Department in collaboration with Dr David Looke and the Department of Infectious Diseases



Dr Katrina Campbell

Dr Katrina Campbell PhD APD, is a Senior Research Fellow in the Department of Nutrition and Dietetics, Princess Alexandra Hospital. Katrina has developed a track record in clinical nutrition research and has been successful as a co-applicant in several multi-disciplinary clinical projects, receiving over \$2 million in research funding. Katrina's research interests are primarily focused on the nutritional management of renal disease, and include dietary intervention trials; validation of nutrition assessment tools; body composition assessment in the clinical setting and investigating the adoption and impact of implementing evidence into practice settings. Katrina is the Primary Investigator of the CKD.QLD Nutrition Study, and is funded by fellowships from Office of Health and Medical Research and Lions Medical Research Foundation.

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Ms Veronica Casey

Veronica is currently the Executive Director, Nursing and Midwifery Services, Metro South Health and Executive Director of Nursing Services, Princess Alexandra Hospital.

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.



Ms Renea Collins

Renea Collins is the Integrated Electronic Medical Record (ieMR) Clinical Lead at Princess Alexandra Hospital (PAH), Brisbane, Australia. This position provides clinical leadership and leads change management activities with clinical and business staff during the implementation of the ieMR solution. Her clinical background is as the Venous Thromboembolism (VTE) Clinical Nurse Consultant in which she has coordinated a VTE prevention program at a tertiary hospital & health service district that has led to significant and sustained improvement in appropriate VTE prophylaxis rates.

Among some of her past achievements include the national nursing co-ordinator of multi-centre clinical audit and finalist and runner-up for the American Nurses Credentialing Center (ANCC) Magnet prize 2008 and 2009 respectively. She has participated in oral and poster presentations at international and national conferences and has published several articles related to VTE and nursing.



Professor Jeff Coombes

Jeff is a Professor of Exercise Science in the School of Human Movement Studies at the University of Queensland. In addition he is Leader of the Exercise and Oxidative Stress Research Group and was a Director of the NH&MRC Centre for Clinical Research in Cardiovascular, Metabolic and Kidney Diseases based at the Princess Alexandra Hospital between 2004-2012. Jeff's research interests centre around the roles of exercise, oxidative stress and antioxidants in health and disease. He uses animal models for more mechanistic studies and human trials for clinical questions. He has published over 150 articles and written five book chapters and one book.



Dr Janet Davies

Dr Davies is a mid-career scientist internationally recognized as a leader in subtropical grass pollen allergy. Dr Davies has published 35 papers and her research has been awarded prizes from ASCIA scientific meetings four times. Her post-doctoral training was with Prof Ian Mackay's Autoimmunity Group at Monash University. In 1999, Prof. Robyn O'Hehir at the Alfred Hospital invited Dr Davies to work on IgE antibody responses to grass pollen. Dr Davies initiated her research on characterizing allergens of Bahia grass pollen with a funding from the Asthma Foundation of Victoria in 2005 and later with the CRC for Asthma and Airways disease.

Dr Davies joined The School of Medicine in July 2008 and has built a small research group in the Lung and Allergy Research Center focused on improving diagnosis, treatment and understanding of the immunological mechanism underlying allergic respiratory diseases in Australia. Dr Davies is an inventor on two patents which she is developing to produce a more specific immunodiagnostics and treatments for subtropical grass pollen allergy.

Dr Davies is collaborating with a network of national allergy physicians, research scientists and major national and international industry partners with the goal of delivering translatable results for improved health outcomes for people with allergic rhinitis and asthma.

PAH Health Symposium Speakers 2013



Dr Mark Deuble

Mark Deuble is currently Full-time Senior Staff Specialist in Palliative Medicine at Princess Alexandra Hospital. His background was originally as a community General Practitioner in Brisbane with a major interest in Palliative Care and Geriatrics. During the mid to late 1990's he completed further formal post-graduate training in Palliative Medicine through Melbourne University before beginning full-time work in Palliative Care.

In 1999 he co-founded the first private community palliative care service in Queensland - Brisbane Palliative Care. This then led to becoming the first Medical Director of the Wesley Hospital Palliative Care Service until taking on his current position in Princess Alexandra Hospital in 2006.

Mark's major interests in Palliative Care include End-of-Life care and Ethical Decision-Making. He also is passionate about the need for our society to develop equitable delivery of health care resources and sees Palliative Care as a critical player in the health care debates of the future.



Mr Patrick Eastgate

Patrick is the Clinical Educator for the Department of Medical Imaging at the RBWH. He is the Queensland Board Member and Vice President for the Australian Institute of Radiography. Patrick's areas of interest are training and education and advanced practice.



Dr Liliana Endo-Munoz

Dr. Liliana Endo-Munoz leads the Sarcoma Research Group at the University of Queensland Diamantina Institute. Her work has focused on understanding the mechanisms that drive osteosarcoma metastasis and on finding new treatments that may improve patient survival.



Adjunct Associate Professor Julie Finucane

Julie is the Nursing Director Medical at QE11 Jubilee Hospital, responsible for Emergency, Intensive Care, General Medicine, Cardiology Services, Palliative Care, Acute Stroke, Rehabilitation, Specialist Outpatients Department, and Infection Control Management.

Julie is the Sub Clinical Stream Leader – Nursing Services for Medicine and Chronic Disease Services Stream - Metro South Health.

Julie is a Colonel Consultant, posted to the Directorate of Defence Force Nursing Office, Canberra, Part Time Royal Australian Army Officer.

She is on the Editorial Board of the Australasian Emergency Nursing Journal and the Journal of Emergency Nursing USA. Julie has been employed within Metro South Health area for close to 38 years.

Julie Finucane OAM RFD FACN FCENA Mast Clin Nurs Emerg Nurs.

Inaugural recipient for the Julie Finucane OAM Medal for Leadership in Emergency Nursing in 2009.

Adjunct Associate Professor, Griffith University, School of Nursing and Midwifery.

PAH Health Symposium Speakers 2013



Professor Nicholas Fisk

Professor Nicholas Fisk is Executive Dean of the University of Queensland's Faculty of Health Sciences, overseeing seven schools and several large research centres. Previously he was inaugural Director of The University of Queensland Centre for Clinical Research, a \$70M translational research facility on the Herston Campus.

Professor Fisk spent 15 years as a Clinical Professor at Imperial College where he experienced the transition to UK's first Academic Health Science Centre. Clinically, he practices as an obstetrics and maternal-fetal medicine specialist, while his research group focuses on fetal stem cells and monochorionic placentation.

He has authored several hundred publications, has a Hirsch index of over 50, and is a past President of the International Fetal Medicine & Surgery Society.



Associate Professor Jenny Flemming

Dr Fleming is an occupational therapist and researcher in the field of brain injury rehabilitation. Her PhD completed in 1996 was on the topic of the development of self-awareness following traumatic brain injury. She has continued to pursue collaborative research on role of metacognitive factors in brain injury rehabilitation. Other research interests include prospective memory assessment and rehabilitation, community integration and the transition from hospital to the community, and psychosocial adjustment and outcomes following acquired brain injury. She is employed in a conjoint research appointment between The University of Queensland and the Occupational Therapy Department, Princess Alexandra Hospital, Brisbane.



Professor Ian Frazer

Professor Ian Frazer is the Chief Executive Officer (CEO) of the Translational Research Institute (TRI) in Brisbane, Australia. In his role as CEO, Professor Frazer is charged with leading the \$354 million TRI to achieve its mission of being Australia's first institute, and one of only a few in the world, to research, trial and manufacture breakthrough drugs in the one location, once construction is complete in 2012. The TRI will accommodate up to 650 researchers from the four TRI partners: The University of Queensland, Queensland University of Technology, Mater Medical Research Institute and the Princess Alexandra Hospital.

Internationally-renown for the co-creation of the technology for the cervical cancer vaccines, Professor Frazer began his career as a renal physician and clinical immunologist in Edinburgh, Scotland before emigrating in 1981 to Melbourne, Australia. He continued his clinical training and pursued studies in viral immunology and autoimmunity at the Walter and Eliza Hall Institute of Medical Research with Professor Ian Mackay. In 1985, Professor Frazer accepted a teaching post with The University of Queensland and was appointed Director of The University of Queensland Diamantina Institute in 1991. In early 2011, Professor Frazer relinquished directorship of the Institute to commence in-post as CEO of the TRI. He retains an active research program at the Institute in immune responses to cancer.

Professor Frazer was awarded the 2005 CSIRO Eureka Prize for Leadership in Science and was selected as Queenslander of the Year, and Australian of the Year in 2006. He was also awarded the 2008 Prime Minister's Prize for Science, the 2008 Balzan Prize for Preventative Medicine, the 2009 Honda Prize and was recently elected as a Fellow of the esteemed Royal Society of London.

PAH Health Symposium Speakers 2013



Professor Maher Gandhi

Professor Gandhi is a Senior Staff Haematologist at the PAH and Head of the Experimental Haematology Laboratory, at the Translational Research Institute, University of Queensland. He holds the inaugural John McCaffrey CCQ/HMR Clinical Research Fellowship, and is also Chair of the Metro South Human Research Ethics Committee. The major interest of the group is the immunobiology of lymphoma, with an emphasis on correlative laboratory research using patient samples.



Ms Areti Gavrilidis

Areti Gavrilidis has a business, health and science background with 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 the 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 to assist a working group of the Smart State Council to prepare a report to advance Queensland's health and medical research and development (R&D) outcomes, which led to the establishment of the QH Office of Health and Medical Research. In 2008 she was a recipient of an Australasian Research Management Society – International Network of Research Management Societies (ARMS -INORMS) Scholarship. In the same year she 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.

She has qualifications in science, applied science, with postgraduate in Business and a Masters in Business Administration. Over the years she has served on a number of local, national and international committees and boards including the ARMS International Committee and the 2012 ARMS National Conference Organising and Program Committees. She was past-Secretary of the Churchill Fellows Association of Queensland.



Professor Len Gray

Professor Len Gray is the Director of the Centre for Research in Geriatric Medicine and the Centre for Online Health at the University of Queensland.

His research interests relate to systems of care and quality improvement for older people, service planning, telemedicine, and software development. He leads the international research collaboration "the interRAI network of excellence in acute care of older persons". He is an active tele-geriatrician, currently providing clinical services to Dalby, Miles and Rockhampton



Ms Penny Geraghty

Ms Geraghty has eight years' experience in media, marketing and public relations within the hospital sector gained mainly at Princess Alexandra Hospital. As a credentialed PR practitioner, Ms Geraghty has found a niche in health with respected knowledge in its application to the hospital, political, education and research environment. Ms Geraghty plays a consultative role in fundraising for medical research and has previous experience in the education sector, and revenue development.

Ms Geraghty commenced managing the media and marketing unit at PAH in 2005, taking on a professional role in Metro South in addition to PAH responsibilities from 2009.

Ms Geraghty has previously held a health PR position with Princess Alexandra Hospital, following hospital revenue development, consultancy work and administration in facility management. She has keen interests in clinical efficiency and reputation development. In addition to dedicated loyalty to the network, targeted communications across the spectrum, relationship development and structured reporting are keen areas of interest.

PAH Health Symposium Speakers 2013



Associate Professor Nikolas Haass

Nikolas Haass is an Associate Professor at The University of Queensland Diamantina Institute/ Translational Research Institute, Honorary Associate Professor at The University of Sydney and Adjunct Associate Faculty member at the Centenary Institute. After obtaining his PhD at the German Cancer Research Center/University of Heidelberg, he trained as a dermatologist (focus: cutaneous oncology) at the University Hospital Hamburg-Eppendorf, Germany. He then spent five years at the Wistar Institute/University of Pennsylvania, Philadelphia, as a post-doctoral fellow funded by the German Research Foundation. As a Cameron Melanoma Research Fellow from October 2007 to February 2013, he headed the group, 'Experimental Melanoma Therapy' at the Centenary Institute.

In March 2013 he commenced his current position at UQDI. Using real-time imaging of melanoma cells in 3D culture and in vivo, he and his team investigate the role of differential subpopulations of melanoma cells in melanomagenesis with the goal to develop novel therapeutic approaches by simultaneously targeting these differential subpopulations.



Dr Ron Hazelton

Dr Hazelton has been Medical Director of the Brain Injury Rehabilitation Unit at Princess Alexandra for 14 years. He also attends Casuarina Rehabilitation at Wynnum West where there is a slow to recover program for Acquired Brain Injury.



Professor Amanda Henderson

Professor Henderson has an extensive career in nursing education, research and leadership in both academic and clinical settings. She is a clinical academic title holder at Griffith University, and Nursing Director, Education at the Princess Alexandra Hospital where she supervises education initiatives and directives across Metro South District comprising more than 5,000 nursing staff. During 2010 she was appointed Discipline Scholar (Health) by the Australian Learning and Teaching Council where she lead the identification of common learning outcomes of health professional qualifications across a broad range of health disciplines. She is presently a Queensland Health Research Fellow. Her scholarship is focused on the establishment of clinical settings that promote learning in practice, including the development and utilisation of health care knowledge. She has

over 100 publications in international refereed journals, written ten book chapters and co-edited two books.



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.

PAH Health Symposium Speakers 2013



Dr Katherine Isoardi

Katherine is an emergency physician working at the Princess Alexandra Hospital. She has an interest in trauma, toxicology, ultrasound and pre-hospital medicine. She also works with the Queensland Ambulance on their Trauma Response Team road retrieval unit.



Dr 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 Queensland Statewide Renal Clinical Network, 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 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 540 original manuscripts in peer-reviewed journals and presented over 350 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.



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 Award, and the Canadian Psychiatric Association’s R.O. Jones Award in 08

PAH Health Symposium Speakers 2013



Associate Professor Pim Kuipers

Associate Professor Pim Kuipers originally joined CONROD in 2003, and rejoined since appointment to Griffith University in 2010. Pim Kuipers holds a joint appointment as Principal Research Fellow with Metro South Hospitals and Health Service. He was previously the Head of Research at the Centre for Remote Health in Alice Springs (Flinders University). Pim is a psychologist by training and completed his doctoral research in community based rehabilitation. He has had leadership roles in research on health service delivery, rural, remote and Indigenous primary health care, multi-methods reviews, community based rehabilitation, complexity in health care and disability services, specifically for people with brain injuries and people with spinal cord injuries. Pim maintains an active research interest in community rehabilitation (in Australia and in developing countries) and is engaged in

a number of international projects. He has been a project advisor in the Lao People's Democratic Republic, and received a 4-month Erasmus Mundus (European Commission) Fellowship to University College, London, as well as commissioned project work with the World Health Organisation in Geneva, Switzerland.



Dr Andrew McCann

Andrew is an interventional cardiologist and vascular physician and Director of Vascular Medicine at Princes Alexandra Hospital. He is actively involved in clinical medicine, research and medical education. His interests include thrombosis, venous thromboembolism and renal denervation for resistant hypertension.



Associate Professor Alexandra McCarthy

Alexandra McCarthy holds a joint appointment as Associate Professor, Postgraduate Co-ordinator and Cancer Nursing Subject Area Coordinator at the Queensland University of Technology and Associate Professor, Division of Cancer Services, Metro South Health Services, Queensland Health. Her research program focuses upon the acute and longer-term physical and psychosocial outcomes of cancer therapies, as well as health promotion after treatment. Publications from these projects have advanced current understanding of the complexities involved in the prevention of further morbidity during and after cancer treatment and led to practical interventions such as tailored education programs, and culturally-specific health resources delivered in various languages. She has over 130

journal and conference publications.



Associate Professor Graeme Macdonald

Dr Macdonald is a graduate of the University of Queensland. He completed training in Gastroenterology at the Princess Alexandra Hospital before undertaking a Hepatology Fellowship at the University of Michigan. On his return to Australia he undertook a PhD on Hepatocellular carcinoma with Prof Barbara Leggett as his Supervisor. He was Director of the Department of Gastroenterology and Hepatology at the Princess Alexandra Hospital from 2004 to 2009 and is now a Senior Staff Specialist in the Department. He is a member of the Queensland Liver Transplant Service and heads an active clinical trials group. His research interests include Hepatic steatosis and associated metabolic factors; and outcomes following liver transplantation.

PAH Health Symposium Speakers 2013



Professor Michael McGuckin

Mike McGuckin is a NHMRC Senior Research Fellow and is Deputy Director (Research) at the Mater Medical Research Institute within the new Translational Research Institute in Brisbane, where he leads the Mucosal Diseases Research Group. Mike is the author of over 125 scientific publications with his research currently focused on mucosal infection and chronic inflammation in the gastrointestinal and respiratory tracts. He has particular interests in the role of secreted and cell surface mucin glycoproteins in host defense from infection and inflammation. Mike also has a strong interest in the role of protein misfolding and ER stress in secretory cells in chronic inflammatory disease. He is heavily involved in national and international peer review and is the lead member of the Academy of

the Australian National Health and Medical Research Council for Gastroenterology



Ms Linda Mundy

Linda Mundy is the manager of the Health Policy Advisory Committee on Technology (HealthPACT) Secretariat, which is now seated in Queensland within the HTA team in the Clinical Access and Redesign Unit. HealthPACT is the national committee for the horizon scanning of new and emerging health technologies, excluding pharmaceuticals, and as such, provides jurisdictions with evidence-based advice on the managed introduction of these technologies. Linda oversees all Horizon Scanning activities: scanning the literature and writing briefs, which can be found on the dedicated HealthPACT web site <http://www.health.qld.gov.au/healthpact/>. Linda holds a BSc from the

University of Adelaide majoring in immunology, microbiology and biochemistry and recently completed her Masters of Public Health. Linda has a strong clinical research background in the fields of obstetrics and gynaecology, physiology and HIV infection.



Mr Andrew Murphy

Andrew Murphy is originally from northern NSW, He completed his radiography degree at QUT in 2012. Andrew is currently involved in a research project investigating the uptake of Radiographer Image Alert systems within Qld.

Andrew is also an avid long distance runner, whose ultimate goal is to compete in the 150km event in FNQ later in 2013.



Professor Colleen Nelson

Professor Nelson is the founding Executive Director of the Australian Prostate Cancer Research Centre – Queensland, the Chair of Prostate Cancer Research at Queensland University of Technology, and a member of the Translational Research Institute caucus.

Professor Nelson is also the founder and Director of the Australian-Canadian Prostate Cancer Research Alliance, an initiative developed to coordinate national and international network interactions of more than 200 prostate cancer scientists and clinicians in Australia and Canada, facilitating access to state-of-the-art infrastructure and clinical trials to assist in the translation of a wide range of discoveries in both countries. In 2010, Professor Nelson was instrumental with PAH urology and oncology colleagues in the establishment of the PAH Multi-disciplinary team clinic for advanced prostate cancer.

PAH Health Symposium Speakers 2013



Professor Ken O'Byrne

Dr Kenneth O'Byrne has recently been appointed Professor in Medical Oncology at PA Hospital and is Professor of Health Sciences at QUT. He was clinical director of the HOPE directorate at St James's Hospital and a clinical lecturer at Trinity College, Dublin. Dr O'Byrne has a particular interest in the management of thoracic malignancies. His research focuses on the identification of novel biomarkers and novel targeted therapy in lung cancer and mesothelioma. Ken has published over 200 manuscripts in peer reviewed books and journals and has led over 100 clinical trials.



Dr John O'Donnell

Dr John O'Donnell has been Chief Executive Officer of Mater Health Services since November 2001. A medical graduate of the University of Adelaide, Dr O'Donnell has been managing public and private hospitals since 1984. He completed a Masters in Health Planning at The University of New South Wales. John is a Fellow of the Royal Australasian College of Medical Administrators; a Fellow of the Australian College of Health Service Management; Fellow of the Australian Institute of Management, and a Fellow of the Australian Institute of Company Directors.

Dr O'Donnell is an Honorary Professor in Department of Management of the Griffith University Business School, and an Adjunct Professor of the School of Medicine, University of Queensland. Other roles include Directorships of Mater Medical Research Institute Ltd, Queensland Children's Medical Research Institute Ltd, The Health Round Table Ltd, Mater Appeals Ltd (Mater Foundation), Greater Brisbane South Medicare Local Ltd, Assistant Commissioner of the Queensland Health Quality and Complaints Commission, and Chair of Mercy Super.



Dr Michelle Owens

Born and trained as a doctor in South Africa, Michelle began practicing medicine at 23 in 1996. In 1997 she worked at the notorious Hillbrow Hospital with its heavy daily presentation of gun shot victims, as well as general practices in Johannesburg and Cape Town. Michelle migrated with her young family to Australia at the end of 2002 and completed her AMC examinations by early 2004. Her clinical roles in Australia have been at both Logan Hospital and Beaudesert General Practice.

Michelle's experience as a patient began in 2009 after a car accident left her with a fractured skull and severe brain injury. Transferred straight to the PAH, she spent 3 months in a coma and a total 9 months in hospital including rehab in the Brain Injury Rehabilitation Unit. Waking from her coma, Michelle did not recognise her children, couldn't walk, couldn't talk or coordinate her limbs. Miraculously, she could still recall medical information which follows evidence about memory loss in trauma situations, in that the long-term memory is the last to be affected. Michelle went home in 2010 to continue her work cover rehabilitation. Despite formally completing rehabilitation, the reality Michelle lives is that she will be "rehabilitating" for the rest of her life.



Dr Edward Pink

Dr Edward Pink went to Medical School in the UK before moving to Australia for the first time in 2000. He has since split the last 14 years between the 2 countries and is now settled in Australia. Dr Pink is the Deputy Director at QEII Jubilee Hospital and has a strong interest in Patient Flow. Having seen the benefits and downsides of a 4 hour target in the UK, he is determined to ensure that its attainment is done with the patient's interests very much as a focus. QEII currently has one of the best NEAT figures in Queensland due to extensive work on patient flow and senior clinician-led models of care.

PAH Health Symposium Speakers 2013



Ms Sally Porter

Miss Sally Porter is the Clinical Assistant Director of Pharmacy at Logan & Beaudesert Hospitals in Queensland. Sally has previously worked as a Clinical Pharmacist at Princess Alexandra Hospital between 2003-2011. Sally graduated from the University of Queensland with a Bachelor of Pharmacy in 2002 and Post Graduate Diploma in Clinical Pharmacy in 2009. Sally has worked in rural and metropolitan hospital pharmacy settings within Australia and in the United Kingdom. She has a particular interest in renal and critical care pharmacy. Sally also has a keen interest in the advancement and professional development of pharmacists and technicians and has been involved with the development of the Queensland Health Advanced Level Framework. Sally has recently been working towards finding improvements and efficiencies in pharmacy service delivery and has been involved in the implementation of new technologies and processes working towards this aim.



Professor Joe Proietto

Professor Proietto is the inaugural Sir Edward Dunlop Medical Research Foundation, Professor of Medicine, in the Department of Medicine Austin Health, University of Melbourne. Professor Proietto is a scientist and clinician investigating the genetic and biochemical causes of obesity and type 2 diabetes. He established one of the first obesity clinics in a Victorian public hospital at the Royal Melbourne Hospital. Since moving to the Repatriation hospital he has established the Weight Control Clinic at Austin Health. He is a past president of the Australasian Society for the Study of Obesity and was the Chair of the Program Organising Committee for the 10th International Congress of Obesity Sydney. He has been on the Council of the Australian Diabetes Society and has served on the Board of Diabetes Australia acting as Chairman of its Medical Educational and Scientific Council. He was Chairman of the National Association of Diabetes Centre. Professor Proietto has published over 170 articles, book chapters and books on obesity and diabetes. He is an editor and reviewer of a number of international scientific journals



Mr Ray Quinn

Ray Quinn is the manager of the Acquired Brain Injury Outreach Service, a rehabilitation service for people with brain injury. He is a social worker and health manager with 30 years experience in the rehabilitation and disability fields. Ray has a special interest in community based rehabilitation models.



Dr Ashok Raj

Dr Ashok Raj is a gastroenterologist at the PA Hospital and PhD candidate with the School of Medicine, University of Queensland, based at the Translational Research Institute. He undertook his gastroenterology training in New Zealand, and has a particular interest in Hepatology, working at the NZ Liver Transplant Unit, before coming to Brisbane to gain further experience as the clinical Hepatology Fellow at the PA Hospital. After completing his FRACP in Gastroenterology, he is now investigating the role of small intestinal mucosal permeability and microbiota in the pathogenesis of chronic liver disease, as part of his PhD.

PAH Health Symposium Speakers 2013

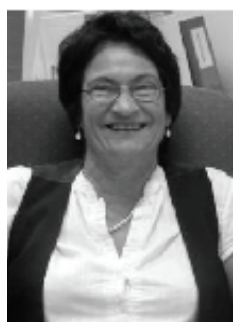


Assistant Professor Jamie Ranse

Jamie is currently employed as an Assistant Professor in Nursing at the University of Canberra. Jamie has research interests in the area of disaster and mass gathering health. Jamie is currently completing a Doctor of Philosophy at the Flinders University Disaster Research Centre, where he is researching the experience of Australian nurses who assist in the out-of-hospital disaster environment.

Jamie has volunteered with St John Ambulance Australia for over 20 years; previously holding the high-level national strategic position of Chief Nurse. Jamie is actively engaged with a number of professional associations. He is a Fellow of the Australian College of Nursing and the College of Emergency Nursing Australasia. Jamie is an Associate Editor for the Australasian Emergency Nursing Journal, holding the disaster portfolio. Additionally, Jamie is an active member of the International Nursing Section for the World Association of Disaster.

Jamie is a user and advocate of social networks / social media within health. Jamie uses four main social network / media platforms: Twitter at <https://twitter.com/jamieranse>, YouTube at <http://www.youtube.com/user/jamieranse>, LinkedIn at <http://www.linkedin.com/in/jamieranse>, Facebook at <https://www.facebook.com/jamieranse>



Professor Liz Reymond

Dr Reymond holds the position of Clinical Director, Metro South Palliative Care Services (MSPCS). MSPCS provides inpatient, outpatient and community-based care across Metro South Health (MSH), Brisbane with a catchment population of over one million. She is also Director of the Brisbane South Palliative Care Collaborative, a research and education partnership between MSH and Griffith University School of Medicine. Her research interests include symptom management in palliative care patients and palliative care service delivery and development



Professor Steffen Ruchholtz

Prof. Dr. med. Steffen Ruchholtz studied medicine from 1985 to 1991 in Ulm and Munich, Germany. He was trained in general surgery from 1992 to 1998 in the Department of Surgery, of the Ludwig-Maximilians-University of Munich. From 1998 to 2007 Ruchholtz practised orthopaedic-trauma and hand surgery at the Department of Trauma Surgery of the University of Essen in leading positions working as deputy head from the year 2000 on. In 2007 he became full professor and chairman of the Department of Trauma-, Hand- and Reconstructive Surgery at the Philipps-University of Marburg, Germany. He is a board certified surgeon in general, orthopaedic-trauma and hand surgery.

An early, important scientific objective has been the care of severely injured patients. In 1993 Ruchholtz was one of the founders of the TraumaRegister DGUB, of the German Society for Trauma Surgery. Ruchholtz was directly involved in planning and establishing the project TraumaNetwork DGUB, and in 2006 became speaker of AKUT (Whitebook Implementation Group / TraumaNetwork DGUB). In this position he is heading the organisation of the TraumaNetwork DGUB, including more than 600 certified Trauma Centres in Germany, Austria, Switzerland, the Netherlands and Luxembourg.

Another strong research interest is the treatment of the geriatric patient with complicated trauma. Ruchholtz published his work on less invasive approaches in the treatment of geriatric fractures of the humerus, the acetabulum and periprosthetic fractures in national and international journals.

Ruchholtz is the editor of two textbooks on the treatment of orthopaedic trauma. He has published more than 150 peer reviewed journal articles and held more than 550 lectures at national and international meetings. He has received awards from orthopaedic and other medical societies. Ruchholtz is a member of the executive committee of the German Society for Trauma Surgery, member of 8 scientific societies and reviewer for 10 national and international medical journals.

PAH Health Symposium Speakers 2013



Dr Washington Y. Sanchez

Dr Washington Y. Sanchez is a post-doctoral research scientist for the Therapeutics Research Centre, in the University of Queensland and University of South Australia, led by Professor Michael Roberts. Dr Sanchez was awarded his PhD in 2009 for prostate cancer research at the Institute of Health and Biomedical Innovation, QUT. He undertook post-doctoral research at the Mater Medical Research Institute investigating metabolic-targeting therapeutics for multiple myeloma. Currently, Dr Sanchez specialises in biomedical and metabolic imaging. His research includes measuring drug penetration and distribution into human skin, liver and other tissues, along with cellular metabolic changes associated with drug therapy.



Professor Michael Schuetz

Professor Michael Schuetz (Fracs, FaOrth, Dr.med.habil) is an Orthopaedic Surgeon and the Director & Chair of Trauma at Princess Alexandra Hospital in Brisbane. He is specialised in the management of acute injuries and severe trauma. Michael Schuetz research team is located at Queensland University of Technology and is focusing on aspects of fracture and soft tissue healing including mathematical modelling, CT/MRI Imaging, and reviewing process management in trauma care. The Australian Research Council, NHRMC and other national and international research grants support the research. Michael Schuetz is author / co-author in >100 pre-reviewed papers and is reviewer for 9 international journals. Beside holding various memberships in professional societies he is active member of PASC (Department Health and Ageing / Canberra). In 2011 he was nominated to become the Chair of the AO

Exploratory Research Board / Switzerland.



Professor Paul Scuffham

Paul scuffham is the Director of the Centre for Applied Health Economics in the School of Medicine and Director of the Population & Social Health Research Program in the Griffith Health Institute and Griffith University.

He specialises in modelling the costs and benefits of health care interventions (especially cardiology, mental health, injury prevention, vaccines and telemedicine) and the valuation of health outcomes. He is a member of Queensland Health's Innovation Board and the Queensland Policy Advisory Committee on new Technology (QPACT).

He has published over 150 articles in peer reviewed journals and economics discussion papers, and has prepared 8 major reports to governments including reports to the PBAC on the pricing of statins and the bDMARDS. He is on the editorial board of five journals (including Medical Decision Making), and is co-editor Value in Health.



Associate Professor Mark Smithers

Director, Upper GI, Soft Tissue Unit Princess Alexandra Hospital. Associate Professor, Department of Surgery, The University of Queensland. Chairman, Melanoma Clinic, Princess Alexandra Hospital, Brisbane; Chairman, Queensland Melanoma Project and Medical Director, Melanoma Patients Australia. The Queensland Melanoma Project co-ordinates trials ranging from Phase I studies of new therapies to multicentre Phase III trials for patients with locally advanced primary disease through to patients with stage IV metastatic melanoma

PAH Health Symposium Speakers 2013



Professor H. Peter Soyer

Professor H. Peter Soyer is an academic dermatologist from Austria with nearly 30 years in the field. He came to Brisbane, Australia, in 2007 to fulfil an appointment with The University of Queensland as the inaugural Chair of Dermatology. He is head of the Dermatology Research Centre at the University of Queensland and was recently awarded a Practitioner Fellowship from the National Health Medical Research Council (NHMRC) in Australia. He was appointed as the Director of the Princess Alexandra Hospital Dermatology Department in Brisbane in 2008.

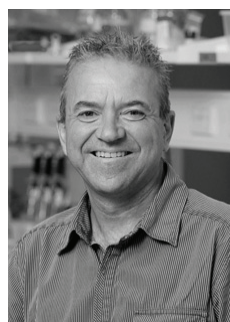
Within the dermatology field he is considered among the pioneers of dermoscopy of pigmented skin lesions, a non-invasive diagnostic method for the early diagnosis of melanoma, and led the development of the morphologic classification system currently used worldwide. His specific research expertise lies in preventive dermatooncology, dermatopathology and clinico-molecular correlation of melanocytic and keratinocytic skin lesions. Recently he developed an interest in open access mobile teledermatology with the vision of “Melanoma Diagnosis by One Click”.

He is well published in these fields with over 450 peer reviewed publications, 5 books and numerous book chapters. He is invited regularly to chair discussions and speak on dermoscopy and teledermatology at the American and European Academy of Dermatology meetings and over the past 10 years have been a speaker at over 100 international conferences. In May 2012 Professor Soyer convened the 3rd World Congress of Dermoscopy in Brisbane and has taken up the role as the program chair in the Global Controversies and Advances in Skin Cancer conference in November 2013. From 2014 to 2016 he will be the ASDR president-elect.



Associate Professor Tony Stanton

Tony Stanton is a cardiologist who originally trained in Glasgow, Scotland. He first moved to Brisbane in 2007. He is now the current Director of the Cardiac Imaging Research Group at the Princess Alexandra Hospital, Brisbane.



Associate Professor Ray Steptoe

Dr Steptoe undertook undergraduate studies in Anatomy and Human Biology and postgraduate studies in Immunology at the University of Western Australia. After further research training as a postdoctoral fellow at the Thomas E. Starzl Transplantation Institute in Pittsburgh, he returned to Australia to pursue research in autoimmune diabetes at the Walter and Eliza Hall Institute of Medical Research. In 2004 he moved to Brisbane to take up a Research Fellowship in the Immunology Program at the UQ Diamantina Institute. Dr Steptoe was awarded an NHMRC Career Development Award (Level 2) in 2008 and an Australian Research Council Future Fellowship in 2012. Dr Steptoe is now an Associate Professor and Group Leader heading a team of researchers investigating how pathogenic immune responses can be turned off. Dr Steptoe's research interests are aimed at

determining the cellular and molecular pathways that are important in determining the fate of T-cell activation with specific reference to tolerance induction. In particular, studies are directed at understanding how to terminate pathogenic T-cell responses with the goal of developing new therapeutic approaches to prevent or treat T-cell mediated diseases. Dr Steptoe pioneered a novel approach to gene therapy of autoimmune diabetes using genetically-engineered hematopoietic stem cells and continues to actively investigate application of this therapeutic approach.

PAH Health Symposium Speakers 2013



Dr Claire Sullivan

Dr Sullivan is an Endocrinologist and the Director of Physician Training at Princess Alexandra Hospital Brisbane. She completed her research doctorate and clinical training in the UK. She has developed an interest in improving quality of healthcare and clinical design. Dr Sullivan is an invited speaker at local and international conferences.



Professor 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 Ranjeny Thomas

Ranjeny Thomas is clinical Rheumatologist at Princess Alexandra Hospital and head of the Autoimmunity programme at the University of Queensland Diamantina Institute. She did a research fellowship with Peter Lipsky in Dallas, Texas and has been a full Professor at UQ since '03. Her research is focussed on the study of autoimmune disease and restoration of tolerance. Through this work, she developed and tested the first rheumatoid arthritis vaccine. Ranjeny is founder and a director of the spin-off company, Dendright, which develops vaccines to suppress autoimmune diseases. Ranjeny is mother of 3 children aged 17, 13 and 13. Besides Science, she loves music, dancing and cooking. She is a passionate mentor and change agent in the Australian academic

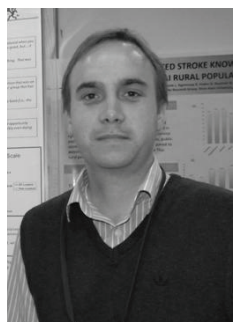
environment.



Ms Lee Trenning

Lee has a post graduate qualifications in Emergency and Critical Care nursing as well as Clinical Education. She has worked extensively across both the private and public sectors in a variety of roles within emergency and critical care environments. Lee has an interest in simulation as a learning modality, trauma nursing and clinical ethics. She is currently the Nurse Educator in the Emergency Department at Princess Alexandra Hospital.

PAH Health Symposium Speakers 2013



Dr Ben Turner

Dr Ben Turner is an Occupational Therapist with the Acquired Brain Injury Outreach Service (ABIOS). He completed his PhD at the University of Queensland in 2011 in which he examined the hospital to home transition phase following Acquired Brain Injury. Ben's current clinical role is Program Co-ordinator of the Skills To Enable People and Communities (STEPS) Program. Ben's clinical and research interests extend to innovative models of community rehabilitation after brain injury.



Associate Professor Jane Turner

My research interests are in the emotional impact of cancer, particularly advanced cancer and the impact of this on families. In addition, I have an interest in strategies to promote wellness in patients who have been treated for cancer.

The field of Psycho-Oncology involves attention to the psychological, emotional and social needs of people with cancer and their family or carers. It encompasses the person's spiritual and cultural concerns, across all phases of the cancer journey from diagnosis, through treatment, survivorship or advanced disease and death.



Associate Professor Paul Varghese

Associate Professor Paul Varghese is the current Director of Geriatric Medicine at the Princess Alexandra Hospital. He practices in clinical geriatric medicine with clinical interests in the areas of amputees, dementia, falls and the acute care of the elderly. He is current Chair of the State Falls Injury Prevention Collaborative, is Chair of the Older Persons Health Network and attends the Clinical Senate. He sits on a number of clinical reference groups at both a State and Federal level. His research interests include falls, clinical database design, tele-geriatrics and the management of patients with dementia.



Dr Phillip Vecchio

Phillip Vecchio is privileged to be Princess Alexandra Hospital's Director of Rheumatology and Chair of Medication Safety Team. He likes everything about Princess Alexandra Hospital, loves efficient safe and effective use of health resources, and gets a buzz from highly functioning teams.



Ms Sarah Winch

Sarah's academic training is in sociology with a clinical background in nursing. She has been consulting in clinical ethics and research ethics for two decades and was responsible for designing the Clinical Ethics Service at PAHHSD, which remains the only secular identifiable ethics service in Queensland. She is an associate editor for Clinical Ethics for the Journal of Bioethical Inquiry.

Sarah has published over 50 academic journal articles and book chapters in a variety of areas including ethics, the history of ideas, evidence based practice and research capacity building.

Sarah's current funded research involves gaining an understanding of the factors associated with the provision of futile treatment in acute care hospitals.

PAH Health Symposium Speakers 2013



Mr Michael Wright

Michael Wright is an experienced senior manager and consultant.

Michael has over 30 years experience in leading and advising Departments, Agencies, Companies and managers on organisational change, strategic planning and leadership development. Michael has broad public and private sector experience, a record of wide ranging consulting and management in the health sector and extensive Board expertise.

Michael has held CEO, Deputy Secretary and Division Head roles in the Victorian public sector. He has had leadership roles in Agencies as diverse as the Department of Premier and Cabinet, the Ministry of Transport, the Victorian Channels Authority, Department of Labour and the Victorian Cancer Agency. In addition, he has extensive Board expertise – having been a member of the Board of the National Rail Authority, the Transport Accident Commission and numerous not for profit Boards.

Michael has spent 20 years running an organisational change consulting firm. Michael's clients have been in the public and private sector in the Commonwealth and all the States, as well as in New Zealand and South Africa. Approximately 30% of Michael's work has been in the health sector. Michael's private sector clients have been in the mining, ports, banking and manufacturing sectors. This diverse mix of clients and issues has provided Michael with a rich source of insights and experiences into the workings of major organisations and an understanding of the challenges facing their leaders.

In addition to his management, consulting and Board activities, Michael has broad expertise in senior leadership coaching. This breadth of experience has proven invaluable in his coaching and professional development roles. In addition to coaching of senior public sector leaders, Michael has also coached senior managers from within police, port, mining and university sectors and also the health industry. He is currently leading a number of public sector learning groups.

Michael is currently the Managing Director of Monash Partners Academic Health Science Centre as well as Project Director for the Monash Health Translational Precinct development at Monash Health. Prior to these roles, Michael had spent 4 years as CEO of the Victorian Cancer Agency (VCA) and had been the Inaugural Chair of the joint TAC/WorkCover Health Committee and Chair of the TAC funded Victorian Neurotrauma Initiative (VNI) – both VCA and the VNI are research funding organisations.

Michael holds an honours degree in Economics from ANU and a Masters degree in Economics and Industrial Relations from London School of Economics. Michael has also completed the AICD Company Director's course.



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 YIA awards and poster viewing and 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 TRI Atrium. 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.

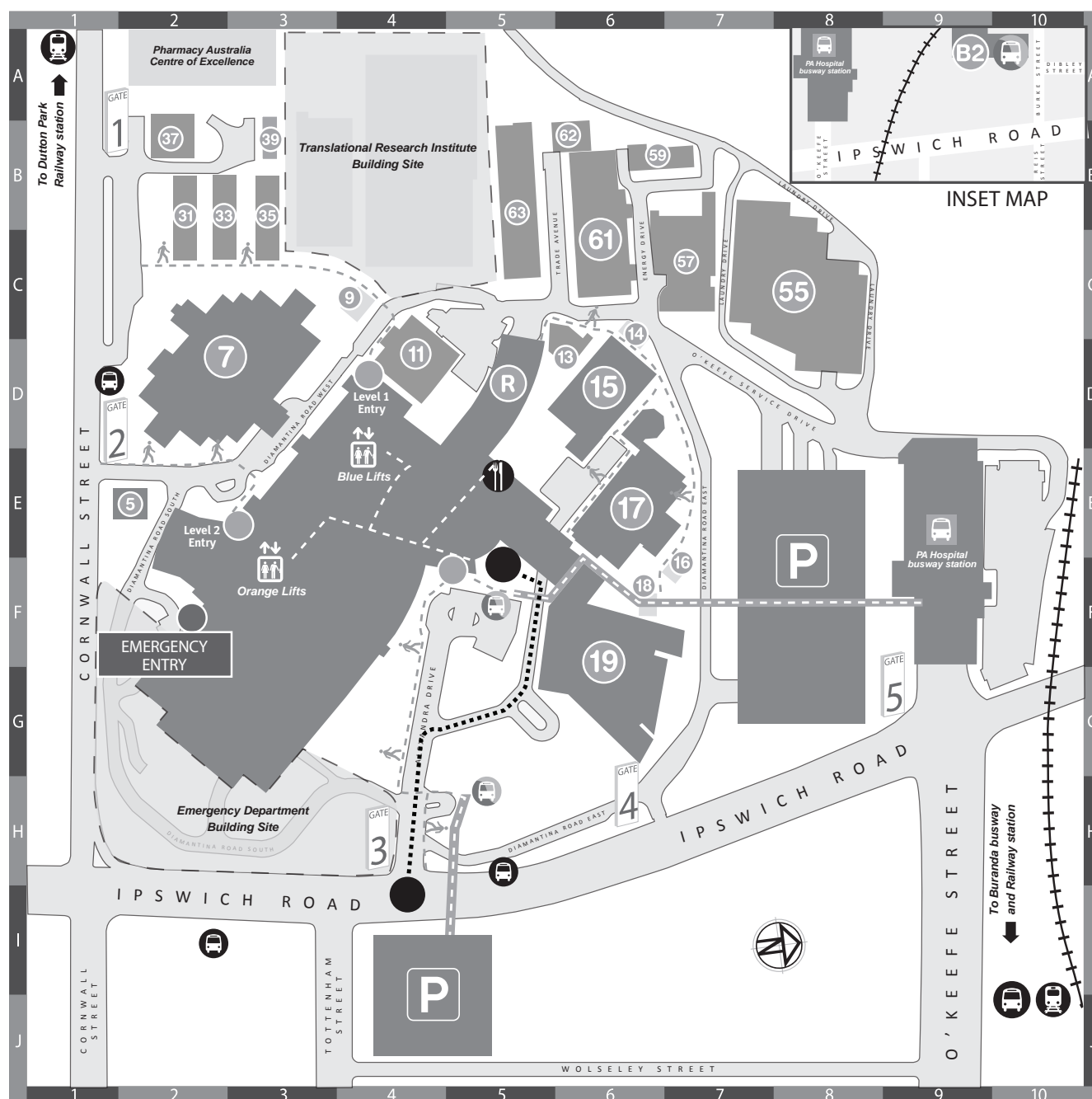
Mobile Phones

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 |
| ● information desk E4 | 19 mental health services F6 | 61 general support services C6 |
| ● public toilets E5, E5, F3 | R research wing D5 | 63 maintenance services B5 |
| ● public café 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, 19th August 2013

Lunchtime Session

12:00 PM - 1:00 PM

Ms Areti Gavrilidis

15th Anniversary of the PAH Centres for Health Research

Russell Strong
Auditorium

Department Research Showcase

1:00 PM - 2:25 PM

Co-chairs: Professor Ken Ho and Professor Ken O'Byrne

Professor Ken O'Byrne - *Cancer*

Medical Oncology

Dr Liliana Endo-Munoz - *UQ Diamantina Institute*

Osteosarcoma

Professor Leanne Aitken - *Nursing*

Critical Care Nursing

Professor Peter Soyer - *UQ School of Medicine*

Dermatology

Dr Andrew McCann - *Medicine*

Vascular Medicine

Associate Prof Pim Kuipers - *Allied Health*

Social Work

Professor Michael Schuetz - *Surgery*

Trauma Services

Dr Ron Hazelton - *Rehabilitation*

Brain Injury Rehabilitation Unit (BIRU)

Russell Strong
Auditorium

Afternoon Tea

2:25 PM - 2:40 PM

Russell Strong
Auditorium Foyer

Department Research Showcase

2:40 PM - 4:00 PM

Co-chairs: Professor Adrian Herington and Professor Gerald Holtmann

Dr Phillip Vecchio - *Medicine*

Rheumatology

Dr Nitish Agrawal - *UQ Diamantina Institute*

Ankylosing Spondylitis

Dr Katrina Campbell - *Allied Health*

Nutrition and Dietetics

Associate Professor Mark Smithers - *Surgery*

Cancer

Associate Prof Nik Haass - *UQ Diamantina Institute*

Melanoma

Professor Len Gray - *Medicine*

Geriatrics

Professor Amanda Henderson - *Nursing*

Nursing Education

Professor Gerald Holtmann - *Medicine*

Gastroenterology and Hepatology

Russell Strong
Auditorium

Networking Drinks Function

4:00 PM - 5:00 PM

Russell Strong
Auditorium Foyer

Trauma Grand Rounds

Trauma Networks – What is in it for the patient, the hospital and the society?

The story of Trauma Networks in Germany

7:15 AM - 8:45 AM - Video Conference

Chair: Professor Michael Schuetz

Professor Steffen Ruchholtz - *Speaker of the German Trauma Network, Director of the Department for Trauma-Hand and Reconstructive Surgery, University Clinic Marburg*

Russell Strong

Auditorium

Morning Tea

10:30 AM - 10:45 AM

Russell Strong

Auditorium Foyer

Official Opening

10:45 AM - 11:00 AM

Mr Terry White AO - *Chairman, Metro South Hospital and Health Board*

Plenary

Advances in allergen immunotherapy for allergic respiratory disease

11:00 AM - 12:00 PM

Chair: Professor Ken Ho

Professor Stephen Durham - *Head of Section Allergy and Clinical Immunology NHLI, Imperial College, Professor of Allergy and Respiratory Medicine, Royal Brompton Hospital, London.*

Russell Strong

Auditorium

Lunch with Chronic Disease Management

Battling the Bulge

12:00 PM - 1:45 PM

Chair: Professor Anthony Russell

Dr Johanna Barclay - *University of Queensland / PAH*

Fighting fat with fat

Professor Jeff Coombes - *University of Queensland*

What is the best form of exercise to improve metabolic parameters in chronic disease?

Professor Joe Proietto - *University of Melbourne*

Why is it so hard to lose weight?

Russell Strong

Auditorium

Minister's Address

1:45 PM - 2:15 PM

Hon Lawrence Springborg - Minister for Health

Russell Strong

Auditorium

Integrated Electronic Medical Records

2:15 PM - 2:45 PM

Russell Strong
Auditorium

Ms Renea Collins - *Princess Alexandra Hospital*

What does the integrated electronic medical record mean for research at PAH?

Afternoon Tea

2:45 PM - 3:00 PM

Russell Strong
Auditorium Foyer

Immunology & Inflammation

Clinical Manifestation of disordered immune responses and targeted interventions

3:00 PM - 4:30 PM

Chair: Professor Gerald Holtmann & Dr Graham Leggatt

Russell Strong
Auditorium

Dr Helen Benham - *University of Queensland / Diamantina Institute*

Towards prevention of Rheumatoid Arthritis - Clinical Introduction

Professor Ranjeny Thomas - *University of Queensland / Diamantina Institute*

Towards prevention of Rheumatoid Arthritis

Dr Janet Davies

Regional variations in grass pollen allergy in Australian patients with
allergic respiratory diseases

Associate Professor Ray Steptoe - *University of Queensland / Diamantina Institute*

Reversing allergic airways inflammatory disease: Exploring the hematopoietic stem
cell / gene therapy axis.

Professor Gerald Holtmann - *University of Queensland / Princess Alexandra Hospital*

Gut - Clinical Introduction

Professor Michael McGuckin - *Mater Medical Research Institute*

Restoring Glucose Control by Suppressing Pancreatic Inflammation in Type 2
Diabetes

Dr Graeme Macdonald - *Princess Alexandra Hospital*

The rapidly increasing burden of obesity-related liver disease

Dr Ashok Raj - *University of Queensland / Princess Alexandra Hospital*

Translational medicine to bridge the gap between the gastrointestinal lumen and the
liver

Wednesday, 21st August 2013

New Technology

9:00 AM - 10:15 AM

Chair: Ms Lynette Loy

Ms Sally Porter - Logan - Beaudesert Hospital

A New Innovation to Address Old Issues

Ms Linda Mundy - Health Policy Advisory Committee on Technology

New Horizons ICT

Dr Washington Y. Sanchez - University of Queensland

Nano technology-Safety?

Russell Strong

Auditorium

Morning Tea

10:15 AM - 10:30 AM

Russell Strong

Auditorium Foyer

Cancer

Improving Cancer Care: Bridging Science and Clinical Practice

10:30 AM - 12:00 PM

Chair: Professor Devinder Gill & Professor Maher Gandhi

Dr Andrew Barbour - University of Queensland

Personalised treatment for oesophageal cancer: from genomics to clinical trials

Professor Maher Gandhi - University of Queensland

A new model of aggressive lymphoma

Associate Professor Alexandra McCarthy - Qld University of Technology / PAH

Comparison of ratings of fitness for chemotherapy using Vulnerable

Elders Survey-13 versus physician's judgments.

Professor Ken O'Byrne - Princess Alexandra Hospital

Overcoming pluripotency and immune tolerance in cancer therapy

Russell Strong

Auditorium

Lunch

12:00 PM - 1:00 PM

Russell Strong

Auditorium Foyer

CPC

1:00 PM - 2:00 PM

Chair: Associate Professor Paul Varghese

Clinico Pathological Conference: The workings of a team based approach.

Russell Strong

Auditorium

Wednesday, 21st August 2013

Afternoon Tea

2:00 PM - 2:30 PM

Russell Strong

Auditorium Foyer

Young Investigator Awards

2:30 PM - 4:45 PM

TRI Auditorium

Chair: Dr Michelle Hill, Dr Janet Davies, Professor Maher Gandhi, Dr David Gillis & Dr Tarl Prow

Guest Adjudicators: Professor John Prins, Professor Ian Frazer, Professor Adrian Herington and
Professor Matt Brown

2:30 PM - 3:30 PM Student Finalists

3:30 PM - 3:45 PM Break

3:45 PM - 4:45 PM Postdoctorate Finalists

Poster and Drinks Function

5:00 PM - 7:00 PM

TRI Atrium

Covidien Surgical Prize

1.4L.2

7:30 AM

Trauma and Recovery -

Russell Strong

Current Thinking in Brain Injury

Auditorium

9:00 AM - 10:15 AM

Chair: Dr Tim Geraghty & Professor Liz Ward

Dr Ron Hazelton - *Princess Alexandra Hospital*

Addressing the challenges in Traumatic Brain Injury

Associate Professor Jenny Fleming - *University of Queensland/PAH*

Optimising early rehabilitation

Dr Ben Turner - *Aquired Brain Injury Outreach Service (ABIOS)*

Innovative models of care for rehabilitation

Mr Ray Quinn - *Aquired Brain Injury Outreach Service (ABIOS)*

Enhancing community Integration

Dr Michelle Owens

The Lived Experience of Rehabilitation

Morning Tea

Russell Strong

10:15 AM - 10:30 AM

Auditorium Foyer

Neuroscience and Mental Health

Russell Strong

Medically unexplained symptoms - not necessarily all in the mind

Auditorium

10:30 AM - 12:00 PM

Co-Chair: Dr Steve Kisely & Dr Helen Brown

Professor Steve Kisely - *University of Queensland*

Medically unexplained symptoms - not necessarily all in the mind

Dr Helen Brown - *Princess Alexandra Hospital*

Conversion Disorders - The Neurology Perspective

Ms Emily Brown - *Princess Alexandra Hospital*

Conversion Disorders - The Physiotherapy Perspective

Ms Kalpana Atresh - *Princess Alexandra Hospital*

Conversion Disorders - The Occupational Therapy Perspective

Lunch

Russell Strong

12:00 PM - 1:00 PM

Auditorium Foyer

Lunchtime Debate -

Social Media.... Friend or Foe?

12:00 PM - 1.00 PM

Moderator: Sarah Bailey

Russell Strong

Auditorium

Education

What can I do to make a difference?

1:00 PM - 1:45 PM

Chair: Ms Bernadette Thomson & Ms Kim Nicolls

Russell Strong

Auditorium

Associate Professor Tony Stanton - *Princess Alexandra Hospital*

5 quick ways to attract the \$\$\$

Ms Kellie Allen - *Communication and Patient Safety (CaPS)*

Life or Death: Does Clinical handover really make a difference?

Panel Discussion

1:45 PM - 2:30PM

Are we saving Too Many Lives?

Moderator: Lee Trenning

Dr Sarah Winch - *Clinical ethicist*

Dr Mark Deuble - *Palliative Care*

Dr Katherine Isoradi - *Emergency Physician*

Associate Professor Julie Finucane - *ND DOM QEII Hospital*

Professor Paul Scuffham - *Health Economist*

Afternoon Tea

2:30 PM - 2:45 PM

Russell Strong

Auditorium Foyer

Health System Innovation

2:45 PM - 5:00 PM

Chair: Dr Michael Daly

Russell Strong

Auditorium Foyer

Professor Liz Reymond - *Metro South Palliative Care Services (MSPCS)*

End of life care in Residential Aged Care Facilities in Metro South Health

Dr Ellen Burkett - *Princess Alexandra Hospital*

Hidden treasures: the ACEIM program

Dr Clair Sullivan - *Princess Alexandra Hospital*

Tidying up to be NEAT

Dr Edward Pink - *QEII Jubilee Hospital*

Radical process change within the QEII Emergency Department to meet the NEAT

Friday, 23rd August 2013

Diamantina Health Partners

The influence of Academic Health Science Enterprises in delivering Future Healthcare

Russell Strong

Auditorium

9:00 AM - 10:45 AM

Chair: Professor David Theile (Snr)

Professor David Johnson - *Metro South Nephrology and Transplant Services.*

Clinician perspective

Professor Nick Fisk - *Faculty of Health Sciences, University of Queensland.*

Educationist perspective

Professor Ian Frazer - *Translational Research Institute.*

Researcher perspective

Dr John O'Donnell - *Mater Health Services.*

Private enterprise perspective

Dr Richard Ashby - *Metro South Health*

Health Service perspective

Panel Discussion -

Moderator: Professor Ross Young - *Faculty of Health, Queensland University of Technology*

Morning Tea

10:45 AM - 11:00 AM

Russell Strong

Auditorium Foyer

Awards Ceremony

11:00 AM - 11:30 AM

Russell Strong

Auditorium Foyer

Dr Jennifer King - *Executive Director, PAH-QEII Health Network*

Kurt Aaron Oration

Allergy and immunotherapy: a historical perspective

11:30 AM - 12:25 PM

Professor Stephen Durham

Closing Address

12:25 PM - 12:30 PM

Professor Ken Ho

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HIGH PREVALENCE OF FUNCTIONAL VITAMIN DEFICIENCIES IN A PSYCHOGERIATRIC WARD.

W Abbott-Johnson¹, N Squelch², K Schilling², P Varghese³, M Rozario⁴, D Lie²

1. School of Medicine, University of Queensland

2. Metro South Mental Health Service

3. Geriatrics, Princess Alexandra Hospital

4. University of Queensland

Background: Although vitamin B12 and folate affect cognition, little is known about functional deficiencies of vitamin B12 and folate in psychogeriatric patients.

Aims: 1) determine vitamin B12, folate and homocysteine.
2) examine the relationship between methylmalonate and vitamin B12.
3) determine the relationship between vitamin B12 levels and use of proton pump inhibitors (PPI).
4) compare vitamin status between various diagnoses.

Methods: 100 consecutive patients (38 M, 62 F, mean age 74.6) admitted to Grevillea were assessed for vitamin B12 (RR 133-680 pmol/L), methylmalonate (RR < 0.4 µmol/L) [for vitamin B12 levels ≤ 220 pmol/L], red cell (RC) folate (RR > 356 nmol/L), homocysteine (RR < 15 µmol/L) and creatinine. Diagnoses were determined according to DSM IV criteria, Major Depressive Episode 44, Psychotic 26, Mania 11, Dementia 8, other 10. Vitamins and PPIs taken at admission were recorded.

Results: Three of 99 (3%) and 32 (32%) patients had vitamin B12 < 133 and 134-220 respectively. Mean (SD) RC folate was 1309 ± 547. 41 of 97 (42%) had elevated homocysteine including 73% of patients with renal failure. Six of 32 (19%) of patients with lower normal vitamin B12 had impaired methylmalonate. Vitamin B12 levels were similar for patients on PPI and not on PPI. Vitamin B12, RC folate and homocysteine did not vary between diagnoses.

Conclusions: Functional vitamin B12 deficiency existed within the lower normal reference range. Vitamin B12 levels were not related to use of PPIs. Folate deficiency was rare and elevated homocysteine was common especially in renal failure.

HSSB1: AN ESSENTIAL REGULATOR OF GENOMIC INTEGRITY IN LUNG CANCER

M N Adams^{1,2*}, V Leong^{1,2}, N Paquet^{1,2}, E Bolderson^{1,2}, D Fennell³, K O'Byrne^{1,2}, D J. Richard^{1,2}

1. Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia

2. Translational Research Institute, Brisbane, Queensland, Australia

3. University of Leicester, Leicester, United Kingdom

Lung cancer remains a leading cause for cancer mortality worldwide. A key feature of lung cancer development is genomic instability resulting from an accumulation of DNA lesions. In normal settings, these DNA lesions, such as double strand breaks and oxidised DNA, are rapidly repaired to prevent cytotoxicity and loss of genetic information. However, the molecular basis for the loss of genome integrity during cancer development remains to be determined.

Herein, we have examined the involvement of hSSB1 in maintenance of genome stability and its potential role in lung cancer progression. hSSB1 is a critical component of the repair of DNA double strand breaks. We identified that hSSB1 is universally overexpressed in TMA staining of lung cancer tissues from 550 patients. Survival curves generated from patient data indicated a poorer prognosis for patients with increased hSSB1 expression versus lower expressing tumours. As oxidative stress is prevalent in lung cancers, we also tested whether hSSB1 orchestrates the repair of oxidised DNA lesions. These lesions are directly repaired by the enzyme OGG1. Interestingly, we identified that following oxidative DNA damage induced by H₂O₂, hSSB1 localises rapidly to

chromatin. hSSB1 also directly interacts with OGG1 to facilitate OGG1 recruitment to chromatin and repair of DNA damage. Importantly, cells lacking hSSB1 display ineffective repair of oxidised DNA.

Our data highlight a potential role for hSSB1 in lung cancer progression and a novel role in maintenance of genome integrity. Taken together, these data present hSSB1 both as a prognostic marker and a novel therapeutic target.

FIRST CASE OF BILATERAL PALLIDAL STIMULATION FOR DYT4 DYSTONIA

C A Airey¹, A C Lehn¹, S Olson¹, R Wilcox², R Boyle¹.

1. *Princess Alexandra Hospital*

2. *Flinders Medical Centre*

We describe the case of a 31 year old woman with DYT4 dystonia (whispering dysphonia) from a known family in North Queensland. She is the first known case of DYT4 dystonia to undergo DBS.

Although DYT4 dystonia is rare, there is a large kindred of affected patients in Australia and the UK. Pallidal GPi stimulation has not previously been attempted in DYT4 dystonia. Pallidal DBS has been shown to be a safe and effective treatment in other primary forms of dystonia, and in particular in DYT1 dystonia, however not in DYT6 dystonia.

There has been significant improvement in our patient at 6 months, with a 50% improvement in the UDRS and Fahn-Marsden scores, but more importantly, a substantial improvement in quality of life - as although relatively severely affected still, she can now eat, talk and walk. Our patient has had a marked response to bilateral GPi stimulation in all symptoms previously experienced, including adductor spasmodic dysphonia and laryngeal dystonia.

This suggests pallidal stimulation may be a safe and effective treatment for patients with DYT4 dystonia, however further cases are needed. Long term follow up of the patient is required to determine whether the response to pallidal stimulation is sustained.

WNT SIGNALLING DRIVES PRO-INFLAMMATORY CYTOKINE RESPONSES AND LIMITS BACTERIAL CLERANCE IN A MODEL OF GRAM-NEGATIVE SEPSIS

M G Andrades¹, T T K Nguyen¹, I H Frazer^{1,2}, A Blumenthal^{1,2}

1. *The University of Queensland Diamantina Institute, Translational Research Institute, Brisbane*

2. *Australian Infectious Diseases Research Centre, University of Queensland, Brisbane*

Sepsis describes an acute severe infection that results from a poorly controlled primary infection and is mostly caused by the Gram-negative bacterium *E. coli*. Management of septic patients remains challenging and mortality rates for severe sepsis remain high. The initial insult can cause strong systemic inflammation, which if uncontrolled leads to organ failure, which is often followed by impaired defence against pathogens. Strategies that control severe inflammation and aid the antimicrobial defence in this context bear great potential for novel therapeutic avenues.

Wnt's are secreted molecules that play a central role in embryonic development and tissue homeostasis. Recent observations in patients and model systems have associated them with infections, including severe sepsis and *E. coli* infection. Emerging concepts suggest that Wnt's promote inflammation by amplifying inflammatory cytokine production. However, most findings to date are from in vitro systems and functional insights into complex in vivo settings are needed. To address this, we studied the impact of interference with the Wnt pathway in mouse models of *E. coli* infection as well as systemic inflammation induced by the Gram-negative bacterial cell wall component, LPS. We observed differential expression of Wnt ligands in organs of LPS-challenged mice. Interference with key elements of the Wnt pathway reduced systemic and local LPS-induced cytokine responses. Wnt pathway inhibition also resulted in decreased bacterial burden during *E. coli* infection in vivo as well as in macrophages in vitro. Our results warrant evaluation of the Wnt pathway as a potential therapeutic target for the management of severe sepsis.

CHROMATIN-BOUND HUMAN SINGLE-STRANDED DNA BINDING PROTEIN 1 IS MONO-UBIQUITINATED

NW Ashton¹, N Paquet¹, KJ O'Byrne^{1,2}, DJ Richard¹

1. Genome Stability Laboratory, Cancer and Ageing Research Program, Institute of Health and Biomedical Innovation, Translational Research Institute

2. Medical Oncology Department, Princess Alexandra Hospital

The loss of genomic stability is responsible for all stages of cancer development, including initiation of tumorigenesis, metastatic transformation, and drug resistance. Accommodating this, the deregulation of DNA damage repair mechanisms is common amongst all cancer types, and indeed most known cancer pre-disposing genetic abnormalities involve disruption of at least one of these key proteins. Recently we identified human single-stranded DNA binding protein 1 (hSSB1) as a central DNA repair protein (Richard et al. Nature 2008), and consistent with the aforementioned trend, have found deregulation of hSSB1 in all tumour specimens analysed thus far.

hSSB1 is required for the efficient resolution of double-stranded DNA breaks, where it binds sites of single-stranded DNA (chromatin) at broken DNA ends, and functions directly in the recruitment of other downstream DNA repair proteins. The significance of these events is demonstrated by severe chromosomal instability in cells depleted of hSSB1, as well as reduced DNA damage repair capacity. Because of this, there is an absolute requirement for hSSB1 in the maintenance of normal cellular function.

In the current work we show that hSSB1 is chemically modified by covalent attachment of an ubiquitin peptide. As we have found chromatin-bound hSSB1 to be predominantly mono-ubiquitinated, this modification may represent a central regulatory mechanism of hSSB1 function. These findings will generate insight into the tumour suppressive activity of hSSB1.

Aims: To determine the regulatory environment surrounding hSSB1 mono-ubiquitination, and the functional significance of this modification in DNA repair.

USE OF BENZODIAZEPINES AND HISTORY OF FALLS IN OLDER PEOPLE ADMITTED TO ACUTE CARE SETTINGS IN AUSTRALIA

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Changes in pharmacokinetics and pharmacodynamics of benzodiazepines (BZDs) during ageing may increase the pharmacological potential of these medications to cause adverse outcomes. This study investigates BZDs in acute care settings and explores the association between use of these medications and falls.

This is a prospective cohort study of 1412 patients aged 70+ admitted to general medical, orthopaedic and surgical wards in 11 acute care hospitals in Queensland and Victoria. Patients were recruited between July 2005 and May 2010. Data were collected using The interRAI Acute Care assessment tool.

Out of 1412 patients (61.6% women, mean age 81.0 ± 6.8), 146 (10.3%) were on BZDs at admission assessment. The three most frequently used BZDs were oxazepam (33.6% of BZD users), temazepam (32.3%), and diazepam (16.8%). Patients on diazepam were significantly more likely to have fallen than all other BZD users (70.0% and 36.1%, respectively, $p=0.002$) and in particular when compared to oxazepam users (70.8% and 25.0%, respectively, $p=0.001$). Multivariate logistic regression model adjusting for cognition, functional status, age and gender confirmed that use of diazepam was positively associated with falls comparing to all other BZDs users (OR 3.7; CI 1.4-9.9, $p=0.008$).

The findings of our study suggest that use of BZDs is still common (10%) in older patients admitted to acute care settings in Australia. There were differences in negative outcomes of particular BZDs in relation to falls. Use of diazepam was independently associated with falls. The indications for, and selection of, a particular BZD to older patients should be carefully evaluated.

IDENTIFICATION OF GENES INVOLVED IN ACQUIRED CISPLATIN RESISTANCE IN NON-SMALL CELL LUNG CANCER CELLS

SS Beard, MP Barr, KJ O'Byrne, DJ Richards.

Lung cancer is responsible for 20% of all cancer deaths in Australia and accounts for 9% of all cancer diagnoses. Cisplatin is a primary chemotherapeutic agent for treatment of lung cancer, however patient responses to the drug are generally transient, with the majority of patients undergoing relapse as the cancer cells acquire resistance. An understanding of the cellular mechanisms of resistance to cisplatin is important for the design of new therapeutic agents and strategies, as well as the identification of biomarkers of cisplatin resistance. We initially generated cisplatin resistant non-small cell lung cancer cell (NSCLC) lines by repeated exposure of NSCLC parental lines (PT) to IC50 concentrations of cisplatin over a 6-month period. Cisplatin IC50 doses were then reassessed and cells were maintained continuously at the new IC50 for a further 6 months, resulting in CisR lines with an increased tolerance for cisplatin (between 4 - 15 fold increase in IC50).

SIRNA SCREENING OF THE KINOME IDENTIFIED AURORA A KINASE AS A POTENTIAL THERAPEUTIC TARGET IN CERVICAL CANCER

FF Bokhari, MV Ranall, TJ Gonda, BG Gabrielli, NAJ McMillan.

HPV oncogenes disable the p53 and Rb tumour suppressor pathways contributing to transformation. Loss of these critical host cell functions may provide an opportunity to selectively target the destruction of HPV-transformed cells. We have performed an siRNA screen using the kinome (788 gene) library to identify genes that when depleted are synthetically lethal with HPV transformation. Primary and validation screens have confirmed Aurora A kinase (AURKA) as a potential synthetic lethal target selective for HPV-transformed cells. AURKA has been further investigated using the selective small molecule inhibitor MLN8237. MLN8237 was significantly more potent towards the HPV-transformed cells. The effect was not a consequence of targeting mitosis as two other mitotic inhibitors, PLK1 and taxol, demonstrated no selectivity. Analysis of the nuclear structure and DNA content showed that Aurora A inhibition promoted a high level of polyploidy in non-HPV-treated cells whilst the same degree of polyploidy was associated with apoptosis in HPV-transformed cells. The pro-apoptotic BH-3 only protein BIM was expressed at higher levels in HPV than non-HPV-transformed cells. No other consistent differences were observed in other apoptotic regulators examined, suggesting that BIM plays a role in triggering apoptosis in the HPV-transformed cells. MLN8237 inhibited growth of HPV and non-HPV cervical cancer xenografts during treatment with 30mg/kg MLN8237 once daily for 10 consecutive days. However, tumour outgrowth was noticed from the second post-treatment day in the non-HPV-transformed tumour group. These findings suggest that MLN8237 may represent a promising novel therapeutic targeted agent towards HPV-transformed cervical cancer.

THERAPIES WHICH LOWER ADVANCED GLYCATION INFLUENCE EXPERIMENTAL AUTOIMMUNE DIABETES IN A TIME DEPENDENT MANNER

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The surge in type 1 diabetes within lower risk genotypes is most likely a result of environmental risk factors. Altered dietary patterns and food processing has led to increasing exposure to advanced glycation end products (AGEs) which have been shown to influence islet secretory function. We examined the effect of reducing AGE exposure with therapies administered either short term prediabetes or long-term for the remainder of life. Female NODShiLt mice (n=10/group) received either (i) No therapy (ii) a diet 4-fold lower in AGE content or (iii) the AGE lowering therapy, alagebrium chloride (ALT; 1mg/kg/day) from day 50 - 100 or day 50 - 200 of life. Mice treated

with ALT short term (day 50- 100), had a considerable reduction in diabetes by day 200 as compared to control mice (80% vs 20%, $p=0.005$). Conversely, mice fed a low AGE diet from day 50 to 100 of life were not protected compared to control mice (80% vs 60%, $p=0.35$). ALT therapy improved glucose and insulin tolerance while a low AGE diet only enhanced glucose tolerance prediabetes compared to control mice. Long-term administration of either low AGE diet or ALT (day 50 - 200) prevented the development of diabetes compared to control mice (90% and 95% respectively vs 50%, $p<0.05$). These results demonstrate protection afforded by targeting AGEs depends upon therapy type and length in experimental autoimmune diabetes. Further insight into mechanisms responsible for this variation is required to better evaluate these approaches in the prevention of type 1 diabetes.

USTEKINUMAB IN ANKYLOSING SPONDYLITIS AND ULCERATIVE COLITIS

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Mr T, 38yrs, presented to the AS Specialist Clinic (April 2012), with severe, active AS and ulcerative colitis (UC) of 8 years duration: BASDAI 8.5, ESR 88, CRP 125, BASFI 10. Radiographs showed bilateral grade III sacroiliitis, severe hip disease, extensive axial and peripheral joint damage. Previously, adalimumab and golimumab had failed; current medications were infliximab, methotrexate (20mg weekly), sulphasalazine (3g daily), and folate (5mg daily).

Following right THR (May 2012) with postoperative heparin prophylaxis, slight thrombocytopaenia occurred resolving spontaneously. Infliximab and methotrexate were withheld peri-operatively but recommenced in July 2012. In September 2012, severe left foot bruising occurred (no known injury). Radiographs excluded fracture but thrombocytopaenia and neutropaenia were noted (platelets $53 \times 10^9/L$, neutrophils $0.39 \times 10^9/L$); all medications were ceased. Bone marrow biopsy suggested a peripheral destructive process, unlikely infliximab-related, but more likely related to severe inflammation. Thrombocytopaenia and neutropaenia progressively deteriorated (23 and $0.10 \times 10^9/L$ respectively). Despite recommencing infliximab, the addition of IV methylprednisolone (1g daily x3, October 2012) prednisone 40mg daily, and Salkofalk enemas, his AS and UC remained active (15-20 movements/day). Thrombocytopaenia and neutropenia continued, with minor temporary improvement post-methylprednisolone. In December 2012, due to extreme AS and UC activity, ustekinumab (anti-IL-12p40 antibodies) 90mg subcutaneously was commenced (infliximab ceased). Thrombocytopaenia, neutropaenia and AS rapidly improved after 2 doses (1 month apart): 204 and $9.15 \times 10^9/L$ respectively, BASDAI 5.1, BASFI 6.1, ESR 18, CRP 17; UC improved to 7-10 movements/day. This case provides further evidence that blocking the IL-23 pathway is a likely effective treatment in AS, including TNF-inhibition resistant patients.

A NOVEL ROLE FOR SASH1 IN THE RESPONSE TO DNA DOUBLE-STRAND BREAKS

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SASH1 (SAM and SH3 domain-containing protein 1) is a recently discovered tumour suppressor gene. Decreased SASH1 protein expression has been observed in 70% of breast cancer specimens tested and SASH1 is also down-regulated in lung, thyroid and colon tumours (Zellar et al. *Oncogene* 2003, Rimkus et al. *Biochem Cell Biol* 2006). Despite the correlation between SASH1 expression and cell malignancy, little is known about the cellular function of SASH1. In this study we report a negative correlation between SASH1 protein expression, and that of the DNA repair protein, hSSB1, in cancers. Further, we demonstrate that SASH1 is required for the normal cellular response to DNA damage. Following ionising radiation treatment, SASH1 is stabilised and eventually becomes exported from the nucleus to the cytoplasm. Cells depleted of SASH1 show an altered response to DNA damage, including increased sensitivity to ionising radiation-induced DNA damage, hyper-phosphorylation of DNA repair proteins and defective homologous recombination. In contrast, over-expression of SASH1 led to morphological abnormalities, such as micronuclei. We also show that SASH1, like many other DNA repair proteins, is localised at telomeres, supporting a role for SASH1 in the normal maintenance of genome stability. In light of the hyper-

phosphorylation of DNA repair proteins and defects in homologous recombination observed in SASH1 depleted cells, we suggest SASH1 has a crucial role in regulating DNA repair signalling pathways and maintaining genomic stability.

CD62L EXPRESSION IS ASSOCIATED WITH CHRONIC LYMPHOCYTIC LEUKAEMIA CELL SURVIVAL IN VITRO AND REPRESENTS A NOVEL THERAPEUTIC TARGET IN CLL

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Background: Recent advances in the treatment of chronic lymphocytic leukaemia (CLL) has improved overall patient survival, however the disease remains incurable. There is accumulating evidence that CLL cell resistance to apoptosis is attributable to microenvironmental factors mediated by cell:cell interactions and dysregulation of cytokines signals.

Methods and Results: To dissect the complex microenvironmental interactions present in vitro, we profiled the immunophenotypic changes that occur in long-term CLL PBMC cultures using flow cytometry. The most highly upregulated marker was CD62L (L-selectin). Furthermore, CD62L expression was present in proliferation and survival niches involved in CLL, the bone marrow and lymph nodes, using confocal microscopy. The pro-survival role of CD62L was examined using a functional blocking antibody which resulted in the significant loss of CLL cell survival. This cytotoxic mediated response was not abrogated by the presence of stromal cell line HS-5, suggesting that anti-CD62L therapy may be effective in vivo where pro-survival signals are intact. Moreover, combining fludarabine or mafosfamide with the anti-CD62L in vitro produced an additive effect both with and without stromal cells.

Conclusion: Immunophenotypic analysis of CLL cultures demonstrated that the expression of several cell surface markers change throughout in vitro culture. These markers are suggestive of cell-cell interactions that provide survival signals. Blocking the activation and homing marker, CD62L, regulates CLL cell survival in vitro and activates a novel prosurvival signal which induces cell death equivalent to current CLL chemotherapeutics. Overall, CD62L is a novel prosurvival effector that may represent an attractive therapeutic target in CLL.

ANTIBIOTIC POINT-PREVALENCE SURVEYS AT AN AUSTRALIAN TERTIARY HOSPITAL: MEASURING THE IMPACT OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM

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Background: Inappropriate antibiotic use is associated with adverse outcomes, increased costs and antibiotic resistance. To combat this, a revised antimicrobial stewardship program (ASP) including a hospital antibiotic formulary, guidelines and restriction policy, was relaunched in June 2012.

Methods: We conducted an antibiotic point-prevalence survey (PPS) at the Princess Alexandra Hospital in Brisbane. Results were compared to a PPS conducted in 2011.

Results: 440 patients were reviewed, with 226 (51%) on antimicrobials, compared with 200 (46%) in 2011. Appropriate antibiotic use was 63%, down from 73% in 2011. Surgical prophylaxis and community acquired pneumonia had high rates of inappropriate use. Guidelines were available for 49% of prescriptions and were followed in 72%. Inappropriate use when guidelines were not followed was 80%. Approval was sought for only 44% of restricted antibiotics. When approval was not sought, the rate of inappropriate use was 76%. The number of inappropriate, unrestricted antibiotics was more than double that of restricted antibiotics (85 vs. 39). Admitting teams that engaged in weekly infectious diseases or microbiology rounds had a high rate of

appropriate antimicrobial use (>80%) in both 2011 and 2012.

Conclusion: Appropriate antibiotic use has not improved despite the revision of our ASP. Increased support from pharmacy, including reporting unapproved restricted antibiotics is required. Electronic prescribing with decision support may better enable appropriate prescribing. However, systems directed at restricted antibiotics (such as Guidance) are unlikely to impact the majority of inappropriate use. Greater infectious diseases and microbiology input is imperative to guide correct antimicrobial usage.

DEFINING AN INFECTIOUS DISEASES CONSULTATION SERVICE: A REVIEW OF 13.5 YEARS OF ID CONSULTS AT THE PRINCESS ALEXANDRA HOSPITAL AND DATABASE REVISION

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Introduction: Infectious diseases (ID) consultations at the Princess Alexandra Hospital are tracked on a database, recording information including the requesting team, indication for and outcome of the consult. A review of the data was undertaken to define the scope and evolution of the service, allowing for an informed restructure of the database.

Methods: Formal inpatient consultations between July 1999 and December 2012 were reviewed retrospectively. Phone consultations and ID admissions were excluded. The reasons for final diagnoses classified as "other", from 2008 to 2012, were evaluated. The database was rewritten with improvements targeting areas identified during the review.

Results: 11511 consultations were identified, with annual consultations increasing threefold during this period. Consults were most commonly requested by orthopaedics (14.3%) and general medicine (11.4%). Syndromes triggering a consult were headed by bacteraemia (13.9%) and complicated soft tissue infection (7.8%). The final diagnosis was most frequently "other diagnosis" (10%) and these were frequently malignancy or other non-infective diagnoses (46%), or misclassified (15%). *Staphylococcus aureus* (19.4%), *Pseudomonas aeruginosa* (8.3%) led the list of microbiological diagnoses.

Conclusion: The demand for ID consultations has increased, likely reflecting the ongoing subspecialisation of medicine and a trend to formal (rather than phone) consultations. Information derived from this review can be used to guide service delivery, trainee education and inform funding or accreditation applications. "Other", as the most common final diagnosis, reflects both the inadequacies of the previous diagnosis list, but also the impressive diversity of infectious diseases practice. Revising the database in this light has enabled improved data validity.

INVESTIGATING THE THERAPEUTIC EFFECT OF RESVERATROL IN NON-ALCOHOLIC FATTY LIVER DISEASE: A RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Non-alcoholic fatty liver disease (NAFLD) is a common liver disease in the obese population, featuring hepatic triglyceride accumulation (steatosis), insulin resistance (IR), inflammation and dyslipidemia. NAFLD is a precursor of type 2 diabetes, significantly increasing cardiovascular risk. Weight-loss is effective, but clinically challenging. No pharmacological therapy is currently available. The polyphenol resveratrol, found in red wine, has shown promising results in pre-clinical models. In over-fed animals, resveratrol prevented the development of steatosis, IR, inflammation, oxidative stress, and dyslipidemia.

Aim: To investigate the clinical efficacy of resveratrol on hepatic and cardiometabolic dysregulation in NAFLD.
Methods: Twenty obese non-diabetic men with NAFLD were randomized to 3000mg resveratrol or placebo daily for 8 weeks. **Outcomes:** peripheral IR (euglycemic-hyperinsulinemic clamp); hepatic steatosis and abdominal fat distribution (magnetic resonance spectroscopy and imaging); plasma biochemistry (liver function, inflammation, lipids, oxidative-stress and antioxidant capacity); target-gene transcription in peripheral blood mononuclear cells; resveratrol pharmacokinetics.

Results: At baseline, subjects presented with profound IR: glucose disposal rate (GDR)= 2.7 ± 0.4 mg/kg/min, and steatosis ranged from 6 to 54%. Resveratrol treatment did not result in change in GDR, steatosis, abdominal fat distribution, antioxidant capacity, lipids, or gene transcription. Resveratrol was associated with significant increase in aminotransferases (ALT: 57 ± 24 to 73 ± 34 U/L, $p=0.03$, AST: 36 ± 9 to 45 ± 15 U/L, $p=0.03$), suggesting hepatocyte burden.

Conclusion: Resveratrol supplementation over 8 weeks did not demonstrate apparent therapeutic benefit in patients with established disease. Evidence of clinical efficacy and safety is paramount before high-dose nutraceuticals, with purported claims of therapy for obesity-related complications, are available to the public.

CLINICAL BENEFITS OF LONG-TERM, LOW-DOSE ERYTHROMYCIN IN BRONCHIECTASIS ARE NOT DUE TO ANTI-INFLAMMATORY EFFECTS

ACH Chen, ML Martin, R Lourie, L Burr, SZ Hasnain, SD Bowler, MA McGuckin, and DJ Serisier

Background: Macrolide antibiotics have demonstrated clinical efficacy in inflammatory airway diseases. Airway immunomodulatory effects are widely believed to be responsible for these benefits, however comprehensive evaluations of these mechanisms in vivo have not been reported to date.

Hypothesis: We hypothesized that low-dose erythromycin would significantly reduce markers of inflammation in bronchiectasis subjects.

Methodology: The Bronchiectasis and Low-dose Erythromycin Study (BLESS) randomized 117 subjects to either low-dose erythromycin ($n=59$) or placebo ($n=58$) for 48 weeks. All subjects underwent sputum induction at weeks 0, 4, and 48. A subgroup of 41 subjects (erythromycin $n=20$) also underwent bronchoscopy for collection of bronchoalveolar lavage fluid. Markers of airway inflammation were thoroughly evaluated.

Results: Erythromycin significantly reduced protocol defined pulmonary exacerbations and 24h sputum volume. Pro-inflammatory cytokines associated with innate and adaptive immunity were highly elevated in bronchiectasis vs healthy controls. However, there was no significant change in concentrations in bronchoalveolar lavage fluid or induced sputum of erythromycin-treated subjects after 4 or 48 weeks, indicating that long-term low-dose erythromycin treatment does not have a direct anti-inflammatory effect in patients with bronchiectasis. There was no significant effect of erythromycin upon airway inflammation in the subgroups demonstrating particular clinical benefits (*Pseudomonas aeruginosa* positive subjects and subjects reporting ≥ 4 pulmonary exacerbations in the 12 months preceding enrolment).

Conclusion: In spite of significant clinical improvements with erythromycin in bronchiectasis, the current analysis

failed to show suppression of inflammation. The mechanism by which macrolides achieve clinical benefit in bronchiectasis relates to an alternate pathway such as a 'non-antibiotic' antimicrobial effect.

NON-CF BRONCHIECTASIS SUBJECTS DEMONSTRATE A COMPLEX AND CONSISTENT AIRWAY INFLAMMATORY PROFILE

ACH Chen, R Lourie, M Martin, L Burr, G Price, SZ Hasnain, SD Bowler, MA McGuckin and DJ Serisier

Background: Except in cystic fibrosis (CF), the pathophysiology of bronchiectasis remains poorly defined. A comprehensive understanding of the pathophysiology of airway mucosal inflammation in non-CF bronchiectasis is a critical first step to developing preventive and therapeutic strategies.

Methods: Induced sputum was collected from participants in the Bronchiectasis and Low-dose Erythromycin Study (BLESS; n=117) and 20 normal healthy controls. Control subjects and 41 BLESS subjects underwent bronchoscopy for collection of bronchoalveolar lavage fluid (BALF) and endobronchial biopsies. Markers of inflammation were comprehensively evaluated in sputum and BALF. Gene expression was measured in biopsies following identification of candidates from screening microarray analysis.

Findings: Every inflammatory marker in respiratory secretions was significantly higher in bronchiectasis compared to controls including BALF levels of innate, Th1, Th2, Th17 and regulatory immune mediators ($p < 0.001$ for all except CXCL10 < 0.05). Median levels of inflammatory markers in bronchiectasis subjects were at least 3 times higher than control, with BALF IL-1- (120-fold) and IL-8 (35-fold) demonstrating the greatest increases. Median BALF MPO concentration was 12-fold, and MPO activity >2000-fold higher in bronchiectasis than control subjects (both $p < 0.001$). Levels of inflammatory markers were significantly lower in bronchiectasis subjects with milder disease according to airway microbiology, lung function and serum CRP levels.

GROWTH HORMONE REGULATION OF MUSCLE FUNCTION: ROLE OF THE ANAEROBIC ENERGY SYSTEM

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Background: Growth hormone (GH) regulates muscle function such as strength and aerobic fitness. It has recently been reported that GH improves sprinting (1), a performance activity dependent on anaerobic glycolysis, suggesting stimulation of anaerobic energy production by GH in muscle. The effects of GH on the anaerobic energy system are unknown.

Aim: To investigate the regulation of the anaerobic energy system in muscle by GH and its functional significance.

Method: Nine adults with GH deficiency (GHD) and 10 age- and body mass index (BMI)- matched normal subjects were compared. Anaerobic capacity was assessed by the Wingate test and aerobic capacity by VO₂max. The functional significance of anaerobic capacity was assessed by the stair-climb test, chair-stand test and 7-day pedometry.

Results: In the GHD group, mean anaerobic capacity (3.7 ± 0.3 vs. 4.9 ± 0.4 watts/kg, $p = 0.02$) and VO₂max (23.5 ± 1.3 vs. 33 ± 2.2 ml/kg/min, $p = 0.002$) were significantly lower than the normal group. These measures were lower in women than in men. The mean duration for completion of the stair-climb test was longer (19 ± 0.8 vs 15.2 ± 0.6 seconds, $p < 0.001$) in the GHD group and correlated with mean anaerobic capacity. In a multivariate analysis after correcting for age, gender and BMI, GH status significantly ($p < 0.05$) predicted anaerobic capacity and VO₂max. Anaerobic capacity but not VO₂max significantly ($p < 0.004$) predicted stair-climb performance.

Summary: Anaerobic capacity, VO₂max and stair-climb performance are reduced in GHD. Anaerobic capacity independently predicts stair-climb performance.

Conclusion: GH regulates the anaerobic energy system, which plays an important role in activities of daily living such as climbing stairs.

UTILITY OF URINARY BIOMARKERS IN PREDICTING LOSS OF RESIDUAL RENAL FUNCTION: THE BALANZ TRIAL

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Background: The ability of urinary biomarkers to predict residual renal function (RRF) decline in peritoneal dialysis (PD) patients has not been defined. The present study aimed to explore the utility of established biomarkers from kidney injury models in predicting loss of RRF in incident PD patients, and to evaluate the impact of neutral pH, low glucose degradation product (GDP) PD solution use.

Methods: The study included fifty randomly selected participants from the balANZ trial who had completed 24 months follow-up. A change in GFR was used as the primary clinical outcome measure. The baseline measurements of eighteen novel urinary biomarkers and albumin were used to predict GFR change using a mixed-effects general linear model. This model was further used to evaluate the impact of the biocompatible PD solutions on RRF adjusted for each biomarker.

Results: Baseline albuminuria was not a useful predictor of change in RRF in PD patients ($P=0.84$). When the effect of the administered PD solutions was examined, higher baseline urinary concentrations of trefoil factor 3 (TFF3; $P=0.02$), kidney injury molecule-1 (KIM-1; $P=0.04$) and interferon gamma-induced protein 10 (IP-10; $P=0.03$) were associated with more rapid decline in RRF in patients receiving conventional solutions compared with those who received biocompatible solutions.

Conclusions: Higher baseline urinary levels of kidney injury biomarkers (TFF3, KIM-1, IP-10), predicted significantly slower RRF decline in patients receiving biocompatible solutions. This is the first study to examine the utility of both traditional and 'novel' urinary kidney injury biomarkers in their ability to predict RRF loss in incident PD patients, and evaluate the impact of biocompatible solutions use.

DIAGNOSTIC SERUM BIOMARKERS FOR CANINE HAEMANGIOSARCOMA: A POTENTIAL MODEL OF HUMAN ANGIOSARCOMA

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Introduction: People suffering from uncommon diseases often do not benefit from the advances in medical research due to lack of research. One such disease is angiosarcoma, a highly aggressive cancer originating from blood vessels with risk factors including toxic exposure, radiotherapy and lymphedema. Angiosarcoma in dogs (commonly called haemangiosarcoma) is a very similar disease with much higher prevalence, comprising up to 7% of all canine malignancies. For both species, an accurate diagnostic method is needed for more favourable outcome.

Method: We have developed a method called Lectin Magnetic Bead Array (LeMBA), utilising 20 individual lectins, or sugar-binding proteins, to enrich for the sub-glycoproteome. By direct coupling to tandem mass spectrometry (MS/MS), the proteins bearing aberrant sugar structures can be identified. Using LeMBA-MS/MS and a customised database, we performed a biomarker candidate screen comparing sera from 10 dogs with haemangiosarcoma with 10 age and sex-matched control sera.

Results: LeMBA and an in-house database developed for the analysis of LeMBA, identified candidates clearly showing differential lectin binding, and demonstrating the utility of LeMBA to identify glyco-biomarkers. We are currently validating the candidates in another 100 samples using customized LeMBA isolation coupled with multiple reaction monitoring (MRM)-mass spectrometry.

Conclusion: The identification of differential lectin binding in normal compared to cancer samples demonstrates the utility of LeMBA and its potential to identify glyco-biomarkers. Validation of identified candidates will allow the development of clinical tests to improve diagnosis and clinical outcomes of angiosarcoma for both dogs and humans.

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EVIDENCE OF A MICROBIAL SIGNATURE IN THE INTESTINAL MICROBIOME OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Ankylosing spondylitis (AS) is a common highly heritable immune mediated arthropathy. AS occurs in genetically predisposed individuals exposed to an unknown but likely ubiquitous environmental trigger. Crohn's disease (CD) is a common form of inflammatory bowel disease, where interplay between host genetic factors and largely undefined environmental factors are thought to drive disease. Microbial involvement from the gut has been implicated in both diseases. To date, no comprehensive characterisation of intestinal microbiota in AS patients has been performed. Our objective was to characterise the intestinal microbiome of newly diagnosed TNF-antagonist naïve AS patients using next generation sequencing and determine if AS gut carries a distinct microbial signature. To explore the effect of host genotype on microbiome composition, we characterised the intestinal microbiome of ERAP^{-/-} and IL23R^{-/-} mice and compared their profiles to wild-type controls. Our results show TI microbial communities of AS patients differ significantly from CD and HC, driven by higher abundance of five families of bacteria. Microbial composition was found to correlate with disease status ($P < 0.001$) and greater differences were observed between than within disease groups. In mice, the loss of ERAP or IL23R alone was sufficient to significantly alter microbiome composition. In conclusion, AS case microbiomes are different from CD and HC, and knockout mouse studies show that AS-associated genes shape the intestinal microbiome. This is consistent with models for AS in which genetic effects lead to changes in the gut microbiome which cause immunological effects that leads to AS.

FUNCTIONAL INTERACTION BETWEEN BLOOM'S HELICASE AND HUMAN SINGLE STRANDED DNA BINDING PROTEIN 1

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Cancer is the single biggest clinical problem facing the world. The WHO has estimated that by 2030, half of all deaths worldwide will be from cancer. The vast majority of these cancers will have developed due to loss of genome stability. Once a cancer forms further genetic variability is induced by the deregulation of the DNA damage response pathways. This genetic heterogeneity within the tumour drives growth, invasion, metastasis and drug resistance. In order to maintain genomic stability, cells possess a complex network of signalling pathways involved in the detection, signaling, and repair of DNA damage. Since the most effective cancer therapies target the DNA damage response, understanding these pathways clearly leads to the identification of new therapies and disease biomarkers. Bloom's helicase (BLM) and the human single stranded DNA binding protein 1 (hSSB1) are both central components of genome stability pathways. Mutations in BLM are associated with a severe predisposition to cancer while hSSB1 overexpression is strongly linked to tumour grade and patient survival. We have recently identified a novel DNA repair protein complex containing both hSSB1 and BLM and shown that hSSB1 affects the stability and chromatin loading of BLM in response to DNA damage. We are currently investigating whether hSSB1 and BLM directly interact in vitro and whether hSSB1 modulates the function of BLM in homologous recombination. Since BLM mutations are strongly linked to cancer predisposition, knowledge of its role in DNA repair will help us understand how BLM may contribute to tumourigenesis.

IMPROVING ED PATIENT FLOWS THROUGH PROCESS-ORIENTED DATA MINING

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Improving patient flows in terms of processing time, costs, and patient outcomes is one of the priority research themes in the healthcare domain. To achieve this, an in-depth understanding of patient flows, especially the knowledge of what has actually happened, is crucial. Combining insights from real practices with the information already available in clinical guidelines will inform the development and evaluation of evidence-based improvement strategies. This project aims towards a detailed analysis of ED patient flows based on an innovative process-oriented data mining methodology (known as process mining) through which evidence-based patient flow improvements can be realised. Process mining exploits the wealth of patient-flow-related data stored in health service systems, to discover actual process flows, conduct performance analysis, understand the relationships between care process characteristics and outcomes, and check conformance to clinical guidelines. The results of these analyses will then form the basis for improvement recommendations.

IN VITRO RESISTANCE SCREEN TO IDENTIFY POINT MUTATIONS IN FGFR2 THAT CAN PROVIDE RESISTANCE TO THE FGFR INHIBITOR, BGJ398.

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Purpose: Targeting cancers expressing activated FGFRs with anti-FGFR kinase inhibitors is currently being tested in the clinic, however, emergence of acquired or intrinsic resistance is expected. We will use an in vitro approach to identify potential resistance mutations and determine the most effective FGFR inhibitor.

Experimental Design: Ba/F3 cells expressing FGFR2b will be mutagenized with ENU and then treated with the FGFR-specific inhibitor BGJ398. The resistant clones will be expanded and intracellular region of the FGFR2 will be

sequenced to identify any resistance mutations. To validate this finding, we will create independent Ba/F3 cells expressing these FGFR2 mutants and measure their sensitivity/resistance to BGJ398 and other FGFR inhibitors. Furthermore, we will lentivirally transduce several FGFR2 mutations into the FGFR2 mutant endometrial cancer cell line JHUEM2, and assess BGJ398 sensitivity to confirm these results.

Results: An initial BaF3 screen yielded ~80 resistance clones however sequencing DNA from 46 clones revealed no resistance mutations. We will repeat the assay with a different BaF3 stable cell line expressing higher levels of FGFR2 and a higher drug concentration. We transduced JHUEM2 with FGFR2WT and FGFR2N550K and the stable cell lines showed some resistance to PD173074 although the relative expression of the transduced FGFR2 was low. Lentiviral stocks of HA tagged FGFR2WT, FGFR2N550K and FGFR2V565I have been prepared to remake these lines using a higher viral titre.

Conclusion: We will be able to identify the point mutations that will confer resistance to BGJ398, and identify other FGFR inhibitors that may have better activity against these mutations.

ENHANCING MONOCLONAL ANTIBODY THERAPY AGAINST B CELL MALIGNANCIES

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Tumor resistance to anti-CD20 monoclonal antibody therapy, Rituximab, can occur due to internalisation of the Rituximab/CD20 receptor complex, thereby limiting antibody-mediated cellular cytotoxicity by immune cell populations. We demonstrated internalisation of Rituximab in a human lymphoma cell line, then investigated whether this internalisation can be prevented by the Dynamin inhibitor, Dyngo-4a. Immunofluorescent microscopy indicated that the internalisation of Rituximab is not Dynamin mediated. In addition, we investigated the combination of Rituximab and an NKT cell adjuvant vaccine. We have previously demonstrated this vaccine promotes activation and expansion of effector cells important for the efficacy of Rituximab. We hypothesised that the anti-tumour actions of Rituximab will be augmented by combination with this therapeutic vaccine. Firstly, to determine whether B cell depletion affected vaccine function, we used a CD20- mouse lymphoma model treated with anti-CD20 antibody and vaccine. Although prolonged activation of NK cells and T cells was reduced in B cell depleted mice, overall tumour progression was not affected by B cell depletion. We then investigated the combination of anti-CD20 antibody and vaccine in a CD20+ subcutaneous lymphoma model. The combination therapy did not provide additional benefit to vaccine or anti-CD20 antibody when given individually. This work has implications for endocytosis inhibitors, and combination immunotherapy in the treatment of B cell malignancies.

EYA4 IS A NOVEL BREAST CANCER GENE.

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One in eight women worldwide (12%) develop invasive breast cancer during their lifetime. Recent reduction of hormone therapy after menopause helped decrease breast cancer incidence, and years of awareness campaigns dramatically improved early detection of the disease by the patient themselves. However, aside from non-melanoma skin cancer, breast cancer is still the most common cancer among women in the United States and in Australia. For the US only, the 2013 American Cancer Society's estimates for breast cancer predict that about 232,340 new cases of invasive breast cancer will be diagnosed and about 39,620 women will die from breast cancer. Understanding the molecular basis of breast cancer is therefore of uttermost importance for improving the outcome/ treatment of patients diagnosed with this disease. Together with our collaborator at the Garvan Institute (NSW), we have identified new genes that are deregulated in triple negative cancer and could be used to develop new diagnostic tools and new treatments. In the past year, we started investigating the function of EYA4 and have knocked-down the gene in breast cancer cell lines. We observed a very strong phenotype of cell death and aberrant divisions, indicating that EYA4 is essential for cell proliferation.

Aim: We hope to decipher the function of EYA4 in a normal cell, and the role it plays in cancer development and progression.

WHOLE NUMBERS, PLEASE!

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BACKGROUND: Intrinsic problems in comprehending pathology results expressed in decimals are a potential source of systemic medical error. The Task Force for the Universal Definition of Myocardial Infarction stated that Troponin values should be presented as whole numbers. However this recommendation and similar ones for other diagnostic tests do not state any empirical evidence upon which this recommendation is based. Our study tested the hypotheses that clinical staff have difficulty in the comprehension of numbers presented as decimals with leading zeros, and would prefer results to be presented as whole numbers.

METHODS: Medical and nursing personnel from the Emergency and Cardiology Departments were recruited. Comprehension of how individuals interpret decimal notation used the SMART test. Additional questions identified whether participants had experienced issues in interpreting decimals, their understanding of concentrations and reference ranges, and their views on the presentation of results.

RESULTS: Poor comprehension of decimals was determined in 40 percent of the 85 participants. Errors included sorting numbers containing decimals, understanding changes in concentration and determining whether numbers were above or below a reference value. Sixty percent of participants thought that it would be safer for results to be presented as whole numbers (e.g. 40 ng/ml) and not as decimals with leading zeros (e.g. 0.04 nmol/L)

CONCLUSIONS: The study confirms the hypotheses and provides supporting evidence for the recommendation that Troponin results should be presented as whole numbers.

The authors acknowledge funding support from the Queensland Emergency Medicine Research Fund

AN INHIBITOR OF UPA REDUCES OSTEOSARCOMA METASTASIS BY BLOCKING SIGNALING IN TUMOUR CELLS AND THE BONE MARROW MICROENVIRONMENT

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Pulmonary metastasis is the major untreatable complication of osteosarcoma (OS) resulting in 10-20% long-term survival. We have previously shown that OS metastasis can be attributed to inherent properties of OS cells and the surrounding microenvironment. The factors and pathways regulating these processes remain unclear, yet their identification is crucial in order to find new therapeutic targets. In this study we used a multi-omics approach to identify molecules that may contribute to OS metastasis. We found elevated levels of urokinase plasminogen activator (uPA) and of uPA receptor (uPAR) in metastatic OS cells compared with non-metastatic OS cells. In addition, uPA was expressed and secreted by bone marrow cells (BMC). Osteosarcoma- and BMC-derived uPA significantly and specifically stimulated migration of metastatic OS cells via uPA-dependent signaling pathways but independent of uPA proteolytic activity. Silencing of uPAR in metastatic OS cells abrogated the migratory response to uPA and decreased metastasis in vivo. Finally, a new small-molecule inhibitor of uPA significantly ($P = 0.0004$) inhibited metastasis in an orthotopic mouse model of OS. Thus, we show, for the first time that malignant conversion of OS cells to a metastatic phenotype is defined by activation of the uPA/uPAR axis in both an autocrine and paracrine fashion. We go on to show that metastasis is driven by changes in both the OS cells as well as the microenvironment in which they reside. Finally, our data show that pharmacological inhibition of the uPA/uPAR axis with a novel small-molecule inhibitor can prevent the emergence of metastatic foci.

ASSESSMENT OF ALCOHOL HISTORIES OBTAINED FROM PATIENTS WITH LIVER DISEASE: OPPORTUNITIES TO IMPROVE EARLY INTERVENTION

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Background: Alcohol is an important primary and co-morbid cause of liver injury in patients referred for investigation and management of liver disease. Early assessment and documentation of alcohol consumption is therefore essential, and recommended in both general practice and hospital settings.

Aims: To determine the extent and accuracy of documentation of alcohol consumption in patients referred for evaluation of liver disease.

Methods: Patients were interviewed using a structured questionnaire. The medical records of all patients interviewed were reviewed to obtain information from the referral letter and the hepatology consultations.

Results: 83 patients were surveyed. Only 14 referrals had an informative alcohol history, despite 27 patients admitting risky alcohol consumption at the initial hepatology consultation. 90% of initial consultations had an informative alcohol history documented, whereas only 56% of patients attending a follow-up appointment had informative documentation. Assessment of alcohol consumption was comparable between the hepatology consultation and the structured questionnaire, but 4 subjects had substantially different alcohol histories. AUDIT identified all patients reporting harmful alcohol consumption on the questionnaire.

Conclusions: Hazardous alcohol use is prevalent in subjects attending hepatology clinics, but informative alcohol histories which are crucial to patient management, are rarely documented in referrals. Screening tools improve documentation and accuracy of alcohol histories and their use by general practitioners and hospital clinicians would improve detection rates of hazardous drinking and allow earlier intervention. Systematic use of screening tools in hepatology clinics will provide opportunities for education and reinforce recommendations to reduce hazardous or harmful alcohol consumption.

DESIGN OF A RANDOMIZED, NON-INFERIORITY TRIAL TO EVALUATE THE SAFETY AND RELIABILITY OF VIDEOCONFERENCING FOR REMOTE CONSULTATION OF DIABETES

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Background: For an estimated 366 million people are living with diabetes worldwide, optimal glycaemic control is necessary to minimize complications, but less than 70% of diabetic patients achieve target levels of blood sugar, partly due to poor access to qualified health care providers. Telemedicine has the potential to improve access to health care, especially for rural and remote residents. If video consultation is to be offered as an alternative to face-to-face consultation in diabetes assessment and management, then it is important to demonstrate that this can be achieved without loss of clinical fidelity.

Methods/Design: A total of 160 people with diabetes will be randomised into either a Telemedicine or a Reference group. Participants in the Reference group will receive two sequential face-to-face consultations whereas in the Telemedicine group one consultation will be conducted face-to-face and the other via videoconference. The primary outcome measure will be the change in the patient's medication. Secondary outcome measures will be findings in physical examination, detecting complications, and patient satisfaction. A

difference of less than 20% in the aggregated level of agreement between the two study groups will be used to identify if videoconference is non-inferior to traditional mode of clinical care (face-to-face).

Discussion: Despite rapid growth in application of telemedicine, little is known about the reliability and safety of videoconferencing for remote consultation of people with diabetes. Results of this proposed study will provide evidence of the reliability and safety of video-consultation for people with diabetes.

Trial registration number: ACTRN12612000315819

TELEHEALTH FOR DIABETES CONSULTATION – A PROCESS ANALYSIS AND CLINIMETRIC STUDY

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Diabetes has been the context of research in telehealth over past few years, but most studies have targeted education, monitoring and self-management of people with diabetes. The aim of this research was to explore the process of care and identify the clinimetric characteristics of specialist consultations for diabetes in a telehealth clinic.

We analysed the video tele-consultations provided by two endocrinologists in the PA Telehealth. A 114-item questionnaire was developed and used to capture the details of the clinical process of care for 54 patients with diabetes consulted remotely using interactive videoconferencing.

The patients (mean age: 50 years; 46% female) were suffering from type 1 and type 2 diabetes in 32% and 66% of the cases respectively; 43% of them had at least one diabetic complication. The consultations were provided to ten cities located 210 to 1800 Km from Brisbane. In 68% of consultations a nurse accompanied the patient. However, the specialist requested the nurse to perform a physical examination in 18% of these cases.

No change in medications was made in 35% of the consultations. Most frequent recommendations were lab test order (76%), insulin dose adjustment (37%), and referral to an allied health professional (13%). Out of 54 consultations, the specialists indicated the need to a physical examination for 12 patients that was not possible remotely. However, they requested an in-person visit only for three patients. Nevertheless they believed that in 35% of the cases they could make a better decision if the consultation was in-person.

CHARACTERISING AND CONTRASTING THE PHENOTYPE OF JAK2 POSITIVE MYELOPROLIFERATIVE NEOPLASMS IN YOUNGER AND OLDER PATIENTS

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Aim/Background: JAK2 positive myeloproliferative neoplasms (MPN) are clonal disorders of myeloid progenitors. Clinical manifestations are highly variable and the phenotype differs according to the gender and age of the patient. Therefore we chose to review our patient population in order to clarify the disease phenotype of younger patients (≤ 40 years of age) and compare it to our older (>40 years of age) patient cohort and published literature.

Methods: This was a retrospective review of the disease characteristics of the 12 patients ≤ 40 years of age and 142 patients >40 years of age when diagnosed with a JAK2 positive MPN at Princess Alexandra Hospital Queensland between December 2005 and April 2013.

Results: We found that portal and hepatic vein thromboses were the most common clinical presentation in the

younger patient cohort (50% of cases). Similarly, splenomegaly was very common in the younger patient cohort (75% of cases). Despite the latter we noted that haematological parameters at diagnosis were similar in both cohorts. Females predominated in both cohorts, and in the younger cohort the median age at diagnosis was lower in females than in males, although vascular complications were similar in both sexes in this cohort

Conclusion: We have confirmed that the clinical phenotype of JAK2 positive MPN varies with age, and to a lesser extent sex. This needs to be considered when managing patients with JAK2 positive MPN and the possibility of a MPN should be actively considered in younger patients with unexplained abdominal vein thromboses.

GLYOXALASE-1 INHIBITION LEADS TO DIABETIC KIDNEY DISEASE ASSOCIATED WITH PODOCYTE INSULIN RESISTANCE

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Background: The plasma concentration of the reactive carbonyl, methylglyoxal (MGO), is elevated in diabetes. Increased accumulation of MGO may contribute to insulin resistance at peripheral sites of glucose uptake. A deficiency in podocyte insulin signalling impairs podocyte function resulting in chronic kidney disease. Glyoxalase-1 (GLO-1) is an enzyme considered to detoxify MGO. Hence, we examined the effects of a GLO-1 inhibitor on podocyte insulin signalling and renal function under diabetic conditions.

Methods: Human podocytes were exposed to a GLO-1 inhibitor and insulin sensitivity assessed using pAKT/AKT and membranous GLUT4 protein expression. Male db/db mice (reminiscent of human type 2 diabetes) and db/H control mice were administered with GLO-1 on alternate days from weeks 6 to 9 of life (50mg/kg body weight) and renal function and glycaemic control were assessed.

Results: Human podocytes exposed to an inhibitor of GLO-1 showed reduced insulin signalling with lower pAKT/AKT ratios and GLUT4 membrane translocation. In the db/db mouse, serum cystatin C was elevated at 9 weeks, and this was exacerbated with GLO-1 inhibition. Peripheral insulin resistance in db/db mice however, was not different in the presence of GLO-1 inhibition. Decreased insulin signalling and expression of GLUT4 in human podocytes exposed to an inhibitor of GLO-1 were consistent with the degree of renal dysfunction in diabetic mice.

Conclusion: Alterations to the glyoxalase system in diabetes may contribute to renal impairment by adversely affecting podocyte insulin sensitivity.

RADIOTHERAPY UTILISATION IN BRAF-MUTATION TESTED METASTATIC MELANOMA IN THE TARGETED THERAPY ERA

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Purpose: To perform a retrospective analysis evaluating radiotherapy (RT) utilisation rates, patterns of care, and survival in a contemporary cohort of patients with metastatic melanoma undergoing BRAF-mutation testing.

Methods: Patients who underwent BRAF-mutation testing between April 2010 and August 2012 were reviewed for demographics, BRAF-mutation status, site(s) and RT fractionation schedules delivered, and systemic agents used.

Results: 158 patients were identified, two of whom had insufficient tissue for testing and 15 had no follow-up data. Of the remaining patients (n=141), 69 (49%) tested BRAF-mutant (BRAF-m) and 72 (51%) tested BRAF-wildtype (BRAF-w). All time points were taken from the date of diagnosis of metastatic disease or unresectable recurrence. Median age for BRAF-m was 47 years (range 21-79) and BRAF-w 62 years (range 25-84). Median follow-up for the cohort was 12 months (range 1 - 147); BRAF-m and BRAF-w were 11 months (range 1-147) and 12 months (range 1-101), respectively. Overall RT utilisation was 68% for BRAF-m and 69% for BRAF-w. Of those that had RT, BRAF-m had an average of 1.70 treatments and BRAF-w 2.36 treatments (Pearson chi-squared 3.92, $p=0.05$). Patients requiring >1 RT course were 56% for BRAF-w and 51% for BRAF-m. 46% of BRAF-m compared to 29% BRAF-w received RT to the brain ($p=0.04$). Median overall survival was 18 months for BRAF-m and 19 months for BRAF-w.

Conclusion: In this modern Australian cohort undergoing BRAF-mutation testing, high RT utilisation rates were observed irrespective of mutation status. Significantly more BRAF-w received RT, however more BRAF-m received brain RT.

PREDICTING CHANGE IN ADIPOKINE LEVELS FOLLOWING OMEGA-3 SUPPLEMENTATION IN OVERWEIGHT AND OBESITY: UNDERSTANDING INCONSISTENCIES IN PREVIOUSLY PUBLISHED DATA

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Background: Adipose tissue contributes to the regulation of energy homeostasis through the production of hormones including adiponectin and leptin. Literature suggests that circulating levels of these hormones are impacted by intake of specific fatty acids.

Aims: Results of studies pertaining to the effects of omega-3 fatty acids on adiponectin and leptin have been inconsistent. This study aims to identify potential compounding factors that may explain these differences.

Methods: Forty non-diabetic adult subjects (body mass index (BMI) ≥ 25.0) were recruited. Anthropometric measures and fasting blood samples were taken at baseline and following 8 weeks of supplementation with 2g/day of omega-3. Blood samples were utilised to quantify adiponectin, leptin, markers of insulin sensitivity, liver function parameters and blood lipids.

Results: Omega-3 derived changes in circulating adiponectin levels demonstrated no significant correlation to anthropometric measures, markers of insulin sensitivity or blood lipids ($P \geq 0.05$), however, significant inverse correlations were observed with alkaline phosphatase and corrected calcium levels ($P < 0.05$). Omega-3 derived changes in leptin levels were positively correlated with BMI and inversely correlated with metabolites associated with potassium, bicarbonate, osmolality, urea:creatinine, and estimated glomerular filtration rate ($P < 0.05$).

Conclusion: With minimal contributing factors identified as impacting omega-3 derived changes in adiponectin levels, inconsistencies in results of previous studies may pertain primarily to the dose of omega-3 supplemented. Correlations between omega-3 derived changes in leptin and both BMI and renal function parameters provides significant insight into inconsistencies in the results of previously studies which have assessed the effects of omega-3 on this hormone.

THE SELF-PERCEPTIONS IN REHABILITATION QUESTIONNAIRE: MONITORING CLIENTS' SELF-PERCEPTIONS, MOTIVATION, AND EMOTIONAL REACTIONS RELATED TO THERAPY

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Background and Aims: Following a traumatic brain injury a person's motivation for therapy and emotional adjustment to their new circumstances can be influenced by their self-perceptions of the everyday consequences of their injury. The Self-Perceptions in Rehabilitation Questionnaire (SPIRQ) is a brief measure that was developed to monitor emotional reactions, motivation, and self-perception throughout rehabilitation. The aim of this study was to describe the development and preliminary psychometric evaluation of the SPIRQ.

Method: 105 adults with traumatic brain injury (79% male) attending occupational therapy sessions at one of two brain injury rehabilitation units completed the SPIRQ. The SPIRQ was completed twice over a 5-7 day interval by a subset (n = 33) to examine test-retest reliability.

Results: Three factors, Changes in Self and Life Plans, Self in Rehabilitation, and Emotional Reactions were yielded by exploratory factor analysis. Internal consistency of the three factor derived SPIRQ scales was sound. Test-retest reliability was generally acceptable ($r = .67-.81$) and scores did not significantly change between testing occasions ($p > .05$).

Conclusions: Preliminary support for the reliability and construct validity of three scales of the SPIRQ has been provided. Further empirical evaluation and potential clinical applications of the SPIRQ in occupational therapy are discussed.

THE EFFECT OF A HIGH FAT DIET ON INTESTINAL INFLAMMATION AND THE MUCUS BARRIER

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The gastrointestinal tract is covered by a mucus barrier that provides protection from external insults and pathogens. Endoplasmic reticulum (ER) stress can occur when the folding mechanism for secreted proteins fails. This halts protein synthesis and activates inflammatory signals. ER stress in intestinal secretory cells has been shown to underlie the pathology in various murine models of intestinal inflammation. Obesity, induced by prolonged feeding on high-fat diet (HFD), has been shown to induce low-grade inflammation in the intestine. We hypothesised that during obesity and HFD feeding, ER stress occurs in secretory cells and this both exacerbates inflammation and reduces the protective mucus barrier. We fed a HFD to both wild type mice and Winnie mice, which have a defective gene encoding for major mucus protein Muc2 and develop intestinal inflammation. Using RT-PCR and immunohistochemistry, we examined changes in gene and protein expression of cytokines, the major constituents of the intestinal epithelial layer, and mucus-producing goblet cells. Winnie mice on a HFD showed reduced neutrophil infiltrate, with greater number of goblet cells compared to those fed on a regular diet. We observed goblet cell hyperplasia in the intestine of wild-type mice following a high fat diet, without any alterations in ER stress markers. Interestingly, this was accompanied by a significant decrease in Muc2 mRNA, which is the major product of intestinal goblet cells. These results suggest that a HFD has important modulatory effects on the protective mucus barrier of the gut in a manner that may be independent of ER stress.

AUTOMATED LOCATION OF ACTINIC KERATOSES IN CLINICAL PHOTOGRAPHS

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Actinic keratoses are important precursor lesions associated with the development of squamous cell carcinoma. We propose and test a method of automatically locating actinic keratosis lesions in high quality clinical photographs. The method focuses on detecting the erythema associated with actinic keratosis by using morphological analysis to extract peaks in a colour space that combines the blue and red chrominance of the input image. Test images were acquired from two groups of six volunteers - one group with severe photodamage and the other group with low photodamage. Images were acquired of each dorsal hand and forearm as well as front, left and right views of the face. Performance was assessed by comparing the automated method with an expert dermatologist's assessment of the same digital image files. The chosen parameters produced a colocalised area sensitivity and specificity of 59% and 94% on images of the face and 59% and 90% on the arms. When considering distinct lesions counted by the dermatologist, 52% of the lesions on the face and 51% of the lesions on the arms were successfully colocalised by the automated method. The positive predictive value of a lesion automatically detected on the face was 9.4% and on the arms 34%. In addition, there was a significant difference between the severe and low photodamage groups ($p < 0.001$) when counting both distinct lesions and total lesion area. This work shows the potential for automated, non-invasive assessment of actinic keratosis.

INVESTIGATIONS INTO THE ROLE OF THE CELL SURFACE PROTEIN CDCP1 IN OVARIAN CANCER PROGRESSION.

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Ovarian cancer is the fifth leading cause of cancer related death in women, with estimates of more than 22,000 new cases expected each year in the USA and a five year survival rate around 40-44% (Siegel, Naishadham et al. 2013). This can be attributed to the fact that most patients present at an advanced stage with disseminated disease which presents a different disease phenotype and challenges in targeting this disease. Ovarian cancers disseminate through the peritoneal cavity and form multiple tumour nodules. A distinctive set of cellular capabilities is required for ovarian cancer cells to disseminate, survive in suspension, migrate and invade other tissues within the peritoneum.

The cell surface protein CUB domain-containing protein 1 (CDCP1) has been shown to promote migration, invasion and tumour cell survival in a number of cancers. These cancer promoting properties and the signalling pathways that are affected downstream of CDCP1 will be assessed in vitro and in vivo to determine if CDCP1 has potential as a therapeutic target for ovarian cancer.

The aims of this project are focussed on understanding the functional role of CDCP1 expression in ovarian cancer, how it promotes disease progression and if it is a pursuable therapeutic target for ovarian cancer.

PROFILING THE TRANSCRIPTOME OF PATIENTS WITH ANKYLOSING SPONDYLITIS USING RNA-SEQ

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RNA-Seq based transcriptomic profiling has the potential to identify new pathways involved in the pathogenesis and progression of complex human diseases. It has previously been utilized with great success on many types of cancer, and some infectious diseases. However, RNA-Seq has not yet been applied to any rheumatic diseases. In a pilot study we have extracted RNA from peripheral blood mononuclear cells obtained from 2 patients with

ankylosing spondylitis, an inflammatory arthritis of the spine, and 2 healthy controls. We have sequenced the long RNA fraction (>200nt) using the Illumina HiSeq platform, including coding and non-coding transcripts. Approximately 55 million reads were sequenced from each sample. Greater than 80% of these paired-end reads mapped to the genome using Bowtie. Assembly with Cufflinks revealed almost 800,000 transcripts across the four samples. Analysis with software packages HTSeq and DESeq showed alternative promoter usages, transcription start sites and coding sequences between patient and control samples. Despite sequencing only 2 patient and 2 control samples, DESeq was still able to clearly differentiate between the two groups on clustering analysis. Using a threshold p value of 0.05 (after correction for multiple testing) 270 genes were identified as differentially expressed between AS patients and healthy controls. Based on the findings from this first small scale pilot RNA-Seq study, we will now expand the study to 65 patient and 65 control samples, to generate a comprehensive picture of the AS transcriptome, to elucidate further the molecular changes involved in this disease.

TUMOUR DERIVED EXTRACELLULAR VESICLE FUNCTION IS MODULATED BY CAVIN-1

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Tumour-derived extracellular vesicles (ECVs) function as intercellular communications through transfer of their biologically active material (protein, DNA and RNA) and are emerging mediators of tumourigenesis. We previously reported that cavin-1 expression reduced in vivo tumour growth and metastasis in an orthotopic prostate cancer xenograft mouse model and that cavin-1 modulates the contents of ECVs derived from prostate cancer PC3 cells. Here we explored ECVs as a potential mechanism for the observed cavin-1 mediated reduction in tumourigenesis. Given that prostate cancer has the propensity to metastasize to the bone, we assessed ECVs function on bone-derived cell models: osteoclast differentiation and osteoblast proliferation. PC3 ECVs differentiated RAW264.7 cells to osteoclast-like multi-nucleate cells, and stimulated human primary osteoblast proliferation compared to control. In the same assays, cavin-1 derived ECVs failed to induce osteoclasts and had reduced ability to stimulate osteoblast proliferation. Using fluorescently-labelled ECVs, we demonstrated that cavin-1 reduced ECV uptake to target cells when compared to control. Treatments to remove ECV surface proteins modulated ECV uptake into target cells. To evaluate ECVs uptake in vivo, fluorescently labelled ECVs were intravenously injected into mice and their tissue distribution was evaluated after 24hr. Confocal microscopy revealed ECVs efficiently migrated to the bone marrow and lung tissue in mice. Furthermore, cavin-1 expression selectively reduced miRNA-148a, previously reported to mediate osteoclastogenesis, in ECVs. In summary, our data show that cavin-1 modulates ECVs contents, uptake and function on bone derived cells. The results suggest a role for ECVs in tumourigenesis that importantly, can be mediated by cavin-1.

NUTRITION SCREENING AND RISK FACTORS PRIOR TO CHEMOTHERAPY IN CANCER PATIENTS 65 YEARS AND OLDER

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Background: The largest proportion of cancer patients are aged 65 years and over. Increasing age is also associated with nutritional risk and multi-morbidities—factors which complicate the cancer treatment decision-making process in older patients.

Objectives: To determine whether malnutrition risk and Body Mass Index (BMI) are associated with key oncogeriatric variables as potential predictors of chemotherapy outcomes in geriatric oncology patients with solid tumours.

Methods: In this longitudinal study, geriatric oncology patients (aged ≥ 65 years) received a Comprehensive Geriatric Assessment (CGA) for baseline data collection prior to the commencement of chemotherapy treatment. Malnutrition risk was assessed using the Malnutrition Screening Tool (MST) and BMI was calculated using anthropometric data. Nutritional risk was compared with other variables collected as part of standard CGA. Associations were determined by chi-square tests and correlations.

Results: Over half of the 175 geriatric oncology patients were at risk of malnutrition (53.1%) according to MST. BMI ranged from 15.5–50.9 kg/m², with 35.4% of the cohort overweight when compared to geriatric cutoffs. Malnutrition risk was more prevalent in those who were underweight (70%) although many overweight participants presented as at risk (34%). Malnutrition risk was associated with a diagnosis of colorectal or lung cancer ($p=0.001$), dependence in activities of daily living ($p=0.015$) and impaired cognition ($p=0.049$). Malnutrition risk was positively associated with vulnerability to intensive cancer therapy ($\rho=0.16$, $p=0.038$). Larger BMI was associated with a greater number of multi-morbidities ($\rho=.27$, $p=0.001$).

Conclusions: Malnutrition risk is prevalent among geriatric patients undergoing chemotherapy, is more common in colorectal and lung cancer diagnoses, is associated with impaired functionality and cognition and negatively influences ability to complete planned intensive chemotherapy.

OPTIMISING THE DETECTION AND REPRODUCIBILITY OF HUMAN BROWN ADIPOSE TISSUE BY PET-CT IN A SUBTROPICAL CLIMATE

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Background: Environmental factors are likely to contribute to the detection and poor reproducibility of Brown Adipose Tissue (BAT) by PET-CT. It is 6 fold higher in winter than in summer and 4 fold lower in tropical than in cooler regions.

Aim: To develop a standardised protocol for improved detection of BAT by PET-CT

Method: We undertook two studies. The first examined BAT detection under ambient conditions in PET-CT scans for oncological indications at a tertiary hospital located in subtropical environment during 2011-2013. The second involved two cold stimulation protocols in healthy volunteers: a) 6 subjects (3M/3F, age 36 ± 6 years, BMI 20.9 ± 0.9 kg/m²) underwent PET-CT scans with hands and feet immersed in ice water for 30-60 minutes in a room at 24°C, and b) 9 subjects (7M/2F, age 39 ± 4 years, BMI 27.6 ± 2.6 kg/m²) stayed in an air-conditioned room at 19°C for 3h prior to scanning. Scanning was repeated in these 9 subjects under identical conditions within 6 weeks.

Results: In first study, BAT was detected in 0.7% of 2284 clinical scans. From ice water immersion, BAT was detected in 16.7% of 6 scans and from cool room exposure in 66.7% of 9 scans. On repeat scanning in the latter, 8 were concordant and one discordant.

Summary: 3h cold stimulation protocol in cool room improved detection from 0.7% to 67% with 89% reproducibility.

INDIVIDUALISING TREATMENT OF ORAL CAVITY CANCER WITH MARKERS OF GENOMIC STABILITY

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Treatment outcomes and prognostic accuracy for oral tongue cancer have had little substantial improvement in the last 20 years. Adjuvant therapy toxicity is high, and there are no clinical tests that accurately stratify which high-risk cancers are likely to benefit from, and which will recur despite treatment. The driving force underpinning carcinogenesis and development of adverse features is genomic instability. Limited studies in chemoprotective DNA repair mechanisms have confirmed an important role of protein expression in treatment prediction (Chiu et al. (2011) *J Transl Med*, 9, 31.; Jun et. Al. (2008) *Br J Cancer*, 99(1)). This study is the first to evaluate novel markers in the double-strand DNA break repair system, which has a fundamental role in the chromosomal rearrangements that underpin carcinogenesis.

Aim: Assessment of the prognostic and predictive implications of a protein expression marker panel for genomic instability in primary oral tongue cancer.

Methods: Patients are selected from a serial cohort of one-hundred and fifty (150) stored oral cavity tumour specimens (both excisional and biopsy) from 2006 to 2011 at the Princess Alexandra Hospital. A high-throughput tissue microarray method is used to stain for twenty-two immunohistochemical markers of genomic stability and DNA repair, and each sample is graded for expression by a pathologist and investigator. Patient data is collected from chart review, and mortality data is obtained from the Queensland Cancer Registry mortality database. Overall survival is calculated using Cox's proportional hazard model, and a survival graph generated for the most prognostically influential markers.

CD163 IDENTIFIES A HIGHLY IMMUNOSUPPRESSIVE SUBSET OF MOMDSC IN POOR-RISK DIFFUSE LARGE B-CELL LYMPHOMA.

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Purpose: In diffuse large B-cell lymphoma (DLBCL), raised monocyte and low lymphocyte blood counts are associated with inferior outcome. This is believed to be mediated by suppression of effector (NK and T) lymphocytes by CD14+HLA-DRlo monocytoïd-myeloid derived suppressor cells (moMDSC), but has not been prospectively validated. Intra-tumoral CD163 expression (a M2 tumor associated macrophage marker) also appears prognostically adverse. The relationship between CD163 and moMDSC, and their influence on antiCD20

monoclonal antibody NK-cell antibody-dependent cellular cytotoxicity (ADCC) in DLBCL is unknown.

Methods: We prospectively analysed circulating moMDSC, lymphocytes, CD163+monocytes, plasma and tissue CD163 in 140 patients with poor-risk DLBCL enrolled in the NHL21 Australasian Leukaemia and Lymphoma Group trial. Patients underwent centrally-reviewed (day 17-20) interim-PET/CT after cycle 4 R-CHOP.

Results: Pre-therapy, circulating moMDSC and CD163+monocytes were elevated in patients (each $P \leq 0.001$), and levels of moMDSC and CD163+monocytes correlated. CD163^{hi}moMDSC were strongly enriched in migratory and immunosuppressive markers. Plasma CD163 was markedly elevated pre-therapy ($P < 0.0001$), correlated with intra-tumoral CD163, and associated with lower lymphocytes, age, stage and prognostic score ($P = 0.004$, $P = 0.014$, $P = 0.007$ and $P = 0.0003$ respectively). Pre-therapy moMDSC and CD163+moMDSC were higher in patients remaining interim- PET/CT+ve (both $P < 0.0001$). Effector lymphocyte/moMDSC and particularly effector lymphocyte/CD163+moMDSC ratios were higher in interim-PET/CT-ve than interim-PET/CT+ve patients ($P \leq 0.03$ and $P \leq 0.0002$), implying that lymphocyte and monocyte subsets are inter-related. In-vitro, monocytes suppressed T-cell proliferation, and rituximab but not obinutuzumab mediated ADCC. Post-cycle 4, monocytes were 'reset' towards a normal profile.

Conclusion: CD163 identifies a highly immunosuppressive subset of moMDSC in DLBCL that is potentially overcome by obinutuzumab.

CHARACTERISATION OF THE ADIPONECTIN RECEPTORS: DIMERISATION AND PALMITOYLATION OF ADIPOR1 AND ADIPOR2 ARE REQUIRED FOR EFFICIENT CELL-SURFACE EXPRESSION.

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The adiponectin axis is a major regulator of metabolic, cardiovascular and inflammatory tone, and area of therapeutic opportunity. The receptors for adiponectin, AdipoR1 (R1) and AdipoR2 (R2), are distant relatives of the largest single class of drug targets, the G-protein coupled receptor (GPCR) family. Current understanding of R1 and R2 is rudimentary, constraining our ability to target these receptors.

Using a series of C-terminal, epitope-tagged R1 and R2 WT, chimeric and truncated constructs we demonstrated that only R1 was readily-detected on the cell surface under steady-state conditions. A non-conserved, intracellular, N-terminal region of R2 (R2(1-81)) restricted cell-surface expression. Co-expression of R1 with R2 lead to the formation of hetero-dimers and cell-surface expression of R2. Complementary investigations revealed that a conserved GxxxG dimerisation motif present in both R1 and R2 was required for homo- and hetero-dimerisation and essential for efficient cell-surface expression. A dimerisation incompetent R1 mutant failed to promote cell-surface expression of R2, but was without effect on WT R1, further highlighting the dependence of R2 on functional R1. Finally, we demonstrated that palmitoylation of a conserved Cysteine, situated in the juxtamembrane region of the N-termini of R1 and R2, was required for efficient cell-surface expression of both R1 and R2.

Aims: To investigate the role of Dimerisation and Palmitoylation in cell surface expression of R1 and R2.

A SYSTEMATIC REVIEW OF CHANGE MANAGEMENT PRACTICES AND ORGANIZATIONAL READINESS FOR TELEHEALTH

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Background and Aim: Healthcare organisations are implementing a number of unprecedented organisational and technological changes to reduce costs, improve quality, increase efficiency and raise patient or client satisfaction. One such change to the health system is the use of telehealth services. This study will offer a

comprehensive review of how change management practices and organizational readiness tools have been applied to the implementation and adoption of telehealth services within health care organizations.

Methods: This review analyzed and identified published peer-reviewed studies that have focused and mentioned telehealth change management practices or assessed telehealth readiness within health care organizations. Change management practices and readiness tools varied across settings such as rural outpatient practices, hospice programs, rural communities and other organizations.

Conclusion: Although, telehealth literature indicates the importance of readiness for change and stated in brief about the consideration of other change management practices for telehealth implementations, health service researchers have only began to theorize about the application of change readiness assessments and the implications of change management practices. Broad dissemination of change readiness tools and the use of change management practices are necessary for the facilitation and sustainability of telehealth practices.

TOWARDS A MOLECULAR DIAGNOSIS FOR THE MYELOPROLIFERATIVE NEOPLASMS USING NEXT-GENERATION SEQUENCING

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BACKGROUND: The myeloproliferative neoplasms (MPN) are a set of clonal malignancies that affect the myeloid cell lineage during haematopoiesis. In 2005, an activating mutation within the pseudokinase domain of JAK2 was found to be present in approximately 60% of patients with MPN. Since that time the remaining 40% of cases have been shown to possess a multitude of different mutations in genes such as: growth factor receptors, negative regulators of the JAK-STAT pathway, cell cycle regulators, transcription factors and epigenetic modifiers. In clinical practice, only one or two of these genes are examined, leaving many patients without a molecular definition of their disease. **AIM:** To develop a diagnostic assay using next generation sequencing to investigate the molecular biology of JAK2-ve MPN patients in South-East Queensland.

METHODS: Ampliseq technology was used to amplify the coding exons of 65 genes, covering a total genomic region of approximately 160 kilobases. Ion Torrent semiconductor sequencing was used to sequence the amplified DNA of 30 JAK2-ve MPN patients from South-East Queensland. The molecular lesions uncovered were correlated with patient clinical data to investigate relationships between specific mutations and clinical course.

RESULTS: A number of well characterised activating mutations were discovered within MPL (the receptor for thrombopoietin) as well as other novel mutations affecting the JAK-STAT pathway. **CONCLUSIONS:** Ampliseq technology with Ion Torrent semiconductor sequencing has been shown to be a useful tool for discovering the molecular basis of MPN and has potential to become the first line of diagnosis for these diseases.

HYPERTONICITY: CLINICAL AND RESEARCH INTERVENTION

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Hypertonicity (spasticity and tissue stiffness) is a common consequence of moderate to severe acquired brain injury. In combination with muscle weakness, hypertonicity leads to immobilisation and contracture, reducing functional capacity and rehabilitation outcomes. Australian evidence indicates that up to 60% of stroke patients have a contracture 6 months post-stroke. The PAH Hypertonicity Service provides specialised intervention to patients with upper or lower limb hypertonicity across the care continuum, from intensive care through acute care, inpatient rehabilitation and outpatient settings. In addition, research is addressing early intervention, post-stroke shoulder pain and evaluation of patient goals. This presentation will describe hypertonicity, the Hypertonicity Service, patient outcomes (including video) and research

ANGIOPOIETIN 2-MEDIATED MODULATION OF THE IMMUNOSUPPRESSIVE PHENOTYPE OF TUMOUR ASSOCIATED TIE2-EXPRESSING MACROPHAGES

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Breast cancer comprises nearly a quarter of new cancer cases reported in 2008 (Ferlay, 2010). Like most solid tumours, the progression of breast cancer is promoted by the ability to form new blood vessels via angiogenesis for tumour survival, and the development of an immunosuppressive microenvironment for tumour evasion from the immune system.

We previously described a population of TIE2-expressing monocytes (TEMs) that are specifically recruited from the bone marrow to the tumors and are required to promote angiogenesis and tumor growth (De Palma 2005, Venneri 2007, Pucci 2009). More recently, others and we reported that the TIE2 ligand Angiopoietin 2 (ANG2), a cytokine highly expressed in tumours and at sites of tissue remodeling by activated endothelial cells, is able to modulate the in vitro (Coffelt 2010) and in vivo (Mazziari 2011) pro-angiogenic activity of TEMs. Furthermore, we have found that the in vivo blockade of ANG2 downregulates TIE2 levels on tumor associated TEMs.

In comparison to TIE2-negative macrophages, tumor associated TEMs are found to express higher levels of IL-10, which is a known immunosuppressive factor that is able to suppress T cell proliferation and promote T regulatory cell expansion. In vitro, IL10 was shown to be upregulated by ANG2 in TEMs (Coffelt 2011). Hence, there is a possibility that TEMs, through the TIE2/ANG2 pathway, modulates both neo-angiogenesis and immunosuppression in tumors.

Aims: To characterize the ANG2/TIE2 pathway by determining if ANG2 induces upregulation of TIE2 receptors and to determine and understand if ANG2-mediated upregulation of TIE2 is modulated by IL-10.

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Coffelt et al., *J. Immunol* 2011

De Palma et al., *Nature Medicine* 2005

Ferlay et al., *Globocan* 2008

Mazziari et al., *Cancer Cell* 2011

Pucci et al., *Blood* 2009

Venneri et al., *Blood* 2007

FOREIGN LANGUAGE SPEAKING PATIENTS' SATISFACTION WITH EMERGENCY DEPARTMENT SERVICE

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Background: It is becoming increasingly difficult to ignore the importance of patients' satisfaction with health and medical care nowadays. Despite the growing number of immigrants in Australia, scarce data exist about patient satisfaction among this group and in particular among non-English speaking immigrants.

Aim: To compare the satisfaction with hospital emergency department (ED) service among patients from Non-English speaking backgrounds (NESB) to those from English speaking backgrounds (ESB).

Methods: A cross-sectional survey was conducted at the ED of Princess Alexandra Hospital in metropolitan Brisbane. Patients who were assigned an Australasian Triage Scale scores of 3, 4 or 5 were surveyed after their ED service over a four-month period. Pearson X2-test and multivariate logistic regression analyses were performed to examine the differences in patient reported satisfaction between the ESB and NESB groups.

Results: A total of 828 patients participated in this study. Overall, although the satisfaction with service was high (ESB 80.7%, 95% CI 77.4, 83.7, NESB 63.2%, 95% CI 56.8 - 69.2, $p < 0.05$), the patients from NESB were less satisfied with their ED service than the ESB patients (Odds Ratio (OR) 0.4, 95% CI 0.3 - 0.6, $p < 0.05$). The promptness of service received the lowest satisfaction rates (ESB 64.7% (60.7-68.4), NESB 51.1% (44.7-57.5), $p < 0.05$), while courtesy and friendliness received the highest satisfaction rates (ESB 90.5 (87.3-92.6), NESB 78.8 (73.1-83.6), $p < 0.05$).

Conclusion: Among the high satisfaction rates with ED service, patients from NESB were significantly less satisfied than the ESB patients.

IS GINGER SUPPLEMENTATION EFFECTIVE IN AMELIORATING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING?

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Chemotherapy-induced nausea and vomiting (CINV) is a common side-effect of cytotoxic treatment. It continues to affect a significant proportion of patients despite the widespread use of anti-emetic medication. To determine the potential use of ginger as an adjuvant prophylactic or treatment for CINV, a systematic literature review was conducted.

Seven studies met the inclusion criteria. Of the seven RCTs published to date five reported favourable results. Of these, three studies found ginger reduced either acute nausea only or both acute and delayed nausea and vomiting when combined with the standard anti-CINV treatment.¹⁻³ The two remaining studies found ginger reduced either acute or delayed nausea and vomiting equal to metoclopramide.^{4,5} However, limitations were identified within the literature which reduce the clinical significance of these findings.

In conclusion, while there exists multiple supportive studies for its use, the considerable limitations in the methodology employed in some studies present genuine uncertainty about its efficacy in the chemotherapy setting and future trials are therefore required to resolve these uncertainties. This review provides recommendations for future research which have been incorporated into a RCT that we are currently conducting. In particular, issues regarding the inconsistent use of rigorous blinding procedures, patient screening, validated tools to assess CINV, and standardised ginger preparations have been addressed in our trial and should be considered for future research in this area. Until these trials have been conducted, professional opinion will be required when choosing ginger as a treatment option.

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DEVELOPMENT AND DELIVERY OF GENE SILENCING THERAPIES FOR ACUTE RESPIRATORY VIRAL INFECTION

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The development of therapeutic agents to treat acute viral infections has historically resulted in a limited number of treatments progressing into the clinic. RNAi can be used to block expression of specific genes, which is highly advantageous for the treatment of viral infections.

To investigate the effectiveness of RNAi in the treatment of respiratory viral infections we designed siRNAs targeting highly conserved regions of Hendra virus (HeV) and Respiratory Syncytial virus (RSV). We have confirmed their silencing efficiency in vitro via qRT-PCR, plaque assay, Western blotting and immunofluorescence microscopy. From these experiments we have identified siRNA sequences that displayed potent gene silencing of <95% as indicated by significant reductions in virus titre, RNA and protein.

A major barrier to the adoption of siRNA therapy is efficient delivery. Our laboratory has developed and tested a number of nanoparticle systems for in vivo siRNA delivery. Here, we have characterised our stealth liposomal vector for its ability to deliver siRNA to virus target cells in the lung upon intravenous injection. We show that greater than 60% of endothelial and 45% of epithelial cells were positive for siRNA liposome delivery in the lung. We are currently testing our liposomal RNAi vector system to determine the ability of our HeV and RSV targeting siRNAs to reduce viral burden in the pulmonary system. The novel combination of intravenous delivery to the lung and RNAi technology potentially offers a superior means to treat acute respiratory viral infection.

PERCEPTION OF METALLIC TASTE IN END STAGE LIVER DISEASE AND ITS RELATIONSHIP WITH FOOD CHOICES

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Taste changes are frequently reported by patients with end stage liver disease. The aim of this study was to determine the prevalence of a perceived metallic taste in patients with end stage liver disease, and to evaluate its relationship with food choices and energy and protein intake. Nineteen consecutive patients (15 male, 4 female, age 44 ± 14 yrs) awaiting liver transplant were recruited. Participants completed taste identification testing of the five basic tastes (bitter, sour, sweet, salty and umami) in accordance with International Standards Organisation (ISO 3972:2011). Participants were able to select from seven possible responses (including 'metallic' and 'no taste') for each of the five stimuli. Usual dietary intake was assessed by diet history. Nine patients (47%) perceived metallic taste for at least one of the five known taste stimuli. Metallic taste was not associated with severity or aetiology of disease. When participants who reported metallic taste were compared with those who did not, there was no difference in total energy (8565 ± 2820 kJ vs 9840 ± 3122 kJ; $p = 0.39$) or protein intake ($97 \text{ g} \pm 32 \text{ g}$ vs $121 \text{ g} \pm 27 \text{ g}$; $p = 0.12$) and no difference in total protein serves per day from dairy ($p = 0.38$), meats ($p = 0.37$) or alternative ($p = 0.73$) sources. Perception of metallic taste is common in people with end stage liver disease however does not appear to be associated with differences in total energy and protein intake or food choices. Longitudinal assessment of taste detection and perception after transplant is underway.

SELF-ADMINISTRATION OF OUTPATIENT PARENTERAL ANTIBIOTIC THERAPY IN A TERTIARY HOSPITAL IN AUSTRALIA

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Introduction: Outpatient parenteral antibiotic therapy (OPAT) has become established as a standard of care in most Australian hospitals to treat a variety of infections. The Alternate Site Infusion Service (ASIS) has provided OPAT service to 5 hospitals in Southern Brisbane, Queensland, using predominantly a patient or carer administration model (S-OPAT). This study was conducted to evaluate outcomes of S-OPAT programme.

Methods: Consecutive patients treated by ASIS at the PAH from 1 January 2011 till 31 December 2011 were reviewed. Data on patient demographics, diagnoses, microbiology, antimicrobial therapy, duration, outcome and complications were sourced from a prospectively collected database and from patients' medical records.

Results: There were 150 episodes in 144 patients resulting in 3,520 days of OPAT; median duration 22 days (range 4-106 days). Patient or carer administration occurred in majority of episodes. The commonest indication was bone/joint infection (47% of patients) and infective endocarditis (9%). *Staphylococcus aureus* was the most frequently isolated organism. The overall cure rate was 93%. On multivariate analysis, patients with 2 or more co-morbidities had increased risk of failure. Line-related complications occurred in 1.4/1,000 catheter days. The cost of OPAT per patient excluding drug administration and home visits was approximately \$150.00/day; significant lower than the cost of an inpatient bed which is estimated to be \$500-\$800/day.

Conclusion: OPAT using a patient or carer administration model is effective and safe option for the management of selected patients with infection requiring intravenous antibiotics.

SODIUM RESTRICTION CONSIDERABLY REDUCES BLOOD PRESSURE, FLUID VOLUME AND PROTEINURIA IN CKD PATIENTS: RESULTS OF A RANDOMISED CROSSOVER TRIAL AND 6-MONTH FOLLOW-UP

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There is a paucity of high-quality evidence to support the efficacy of sodium-restriction for reducing cardiovascular risk in CKD patients. The LowSALT CKD study was a double-blind randomised-crossover trial (period-1) with 6-month follow-up (observational arm/period-2) examining in CKD patients 1) the degree of blood pressure (BP) and proteinuria reduction achievable on a low- versus high-sodium diet, and 2) whether these benefits are maintained with longer-term sodium-restriction. Stage III-IV CKD patients with BP 130-169/>70 mm Hg consumed a low- and high-sodium intake (median [75 [interquartile range (IQR) 58-112] versus 168 [146-219] mmol sodium/day) each for 2-weeks in random order (period-1). In period-2, participants were counselled to continue a low-sodium diet (target <100 mmol/day) with outcomes measured at 6-months. Outcomes (primary: 24-hour ambulatory BP; secondary: 24-hour proteinuria/albuminuria, extracellular fluid (ECF, bio-impedance)) were analysed using paired t-test or Wilcoxon signed-rank test. Twenty patients (age 68±11 years; eGFR 31.6-10.6 ml/min/1.73m²) completed the study. In period-1, mean ambulatory SBP/DBP was reduced by 9.8 [95% confidence interval (CI)] 4.5-15.1 / 4.0 [1.6-6.4] mm Hg (P<0.01), and ECF by 0.8 [95% CI 0.4-1.2] L (P<0.01) from high- to low-salt period. At 6-months, SBP/DBP reductions were maintained (increase of 1.3 [95% CI -4.8-7.3]/1.2 [-1.5-3.9] mm Hg (P>0.05) when compared with low-sodium period), as was ECF (P>0.05). Median protein/albumin excretion were reduced by 40-50% in period-1 and this was maintained at 6-months. Sodium restriction considerably reduced BP, ECF and proteinuria in CKD patients, and, with the assistance of ongoing dietary-counselling by an accredited dietitian, these benefits were maintained at 6-months.

DEVELOPING AN EVIDENCE-BASED CLINICAL PATHWAY FOR THE ASSESSMENT, DIAGNOSIS AND MANAGEMENT OF ACUTE CHARCOT NEURO-ARTHROPATHY: A SYSTEMATIC REVIEW

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Background: Charcot Neuro-Arthropathy (CN) is one of the more devastating complications of diabetes. To the best of the authors' knowledge, it appears that no clinical tools based on a systematic review of existing literature have been developed to manage acute CN. Thus, the aim of this paper was to systematically review existing literature and develop an evidence-based clinical pathway for the assessment, diagnosis and management of acute CN in patients with diabetes.

Methods: Electronic databases (Medline, PubMed, CINAHL, Embase and Cochrane Library), reference lists, and relevant key websites were systematically searched for literature discussing the assessment, diagnosis and/or management of acute CN published between 2002-2012. At least two independent investigators then quality rated and graded the evidence of each included paper. Consistent recommendations emanating from the included papers were then fashioned in a clinical pathway.

Results: The systematic search identified 267 manuscripts, of which 117 (44%) met the inclusion criteria for this study. Most manuscripts discussing the assessment, diagnosis and/or management of acute CN constituted level IV or EO evidence. The included literature was used to develop an evidence-based clinical pathway for the assessment, investigations, diagnosis and management of acute CN.

Conclusions: This research has assisted in developing a comprehensive, evidence-based clinical pathway to promote consistent and optimal practice in the assessment, diagnosis and management of acute CN. The pathway aims to support health professionals in making early diagnosis and providing appropriate immediate management of acute CN, ultimately reducing its associated complications such as amputations and hospitalisations.

CAVIN-1 ALTERS ONCOGENIC EFFECTS OF CAVEOLIN-1 MICRODOMAINS IN PROSTATE CANCER

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Caveolin-1 is associated with prostate cancer progression and has been suggested to be a biomarker and therapeutic target. Mature caveolin-1 resides in lipid raft domains at the plasma membrane, where it forms caveolae upon co-expression of cavin-1 (also known as PTRF; polymerase I and transcript release factor). In the absence of cavin-1, caveolin-1 does not form caveolae but are found on flat membrane. To determine if oncogenic caveolin-1 in prostate cancer is present in caveolae, we examined the relative expression of caveolin-1 and cavin-1 in normal, non-malignant and malignant prostate tissues. We found that caveolin-1 is induced in prostate cancer without cavin-1, an expression pattern mirror in the PC3 cell line. Previously we showed that expression of cavin-1 in PC3 cells recruits flat membrane caveolin-1 to caveolae and reduced transmigration. Here we report that cavin-1 expression reduces tumour size and metastasis of PC3 cells in vivo, using an orthotopic prostate cancer xenograft mouse model. To determine if cavin-1 acts by neutralizing oncogenic caveolin-1, we expressed cavin-1 in caveolin-1 negative LNCaP and 22Rv1 cells. While caveolin-1 over-expression increased anchorage-independent growth of LNCaP and 22Rv1 cells, cavin-1 over-expression had no effect. Furthermore, co-expression of cavin-1 in LNCaP+caveolin-1 cells reversed caveolin-1 effect. Taken together, these results suggest that caveolin-1 in prostate cancer is present outside of caveolae, and caveola formation by cavin-1 co-expression alters the oncogenic effect of non-caveolar caveolin-1 microdomains.

UNDERSTANDING THE ROLE OF HSSB2 IN GENOME STABILITY AND CANCER.

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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 analyze 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 utilized to unravel how hSSB2 interplays with the damaged genome. This research will answer some important questions relating to hSSB2 function, including its role in DNA repair and its interaction with other repairing proteins such as the MRN complex and ATM kinase. This study will generate further understanding of the DNA damage response, outlining new anti-cancer therapeutic targets.

EVALUATING A STUDENT-LED GROUP OCCUPATIONAL THERAPY PROGRAM IN INPATIENT BRAIN INJURY REHABILITATION.

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Background & aims: Groups are commonly used in brain injury rehabilitation to increase the intensity of intervention, and provide opportunities for social interaction and peer feedback and support amongst clients. Limited research however has demonstrated the effectiveness of using groups in an inpatient rehabilitation setting. This study aims to evaluate a student-led group therapy program in occupational therapy in an inpatient brain injury rehabilitation context.

Method: The student-led group therapy program was implemented over a two year period and involved patients in meal preparation groups (breakfast and lunch), upper limb, community access and cognition focused groups. All groups involved clients working towards individualised therapy goals and followed structured group formats. A mixed methods study design incorporating surveys and focus groups with clinician, student, patient and university stakeholders was used to formally evaluate the groups program. Survey data were collated and focus group data were transcribed and analysed thematically.

Results: Results indicate the benefits of the program include autonomy and variety of learning opportunities for students leading the therapy groups. Benefits to patients included increased occasions of service and intensity of rehabilitation. From an organisational perspective, positive outcomes included increased numbers of clinical placements offered to students with reduced ongoing planning for clinical educators.

Discussion: Findings have indicated this is a successful model of clinical placement within an inpatient brain injury rehabilitation setting. Further research investigating the effectiveness of groups in terms of patient outcomes is recommended.

NILOTINIB AND MEK INHIBITORS INDUCE SYNTHETIC LETHALITY IN DRUG-RESISTANT CHRONIC MYELOID LEUKEMIA

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Background and Purpose: The BCR-ABL inhibitors imatinib and nilotinib are approved first-line treatments for chronic myeloid leukemia (CML). The majority of CML patients respond well to imatinib treatment. However, a significant proportion of patients demonstrate primary or acquired resistance to imatinib and nilotinib. Resistance can occur through point mutations in BCR-ABL that block drug binding, and also via BCR-ABL independent mechanisms. It has been shown that imatinib and nilotinib induce activation of MEK/ERK signalling in resistant leukemia cells. We aimed to understand the mechanism underlying the activation of MEK/ERK signalling by imatinib and nilotinib in resistant CML and whether this survival pathway may be utilized in combination therapy to treat drug-resistant CML.

Results: Similar to RAF inhibitors in RAS mutant melanoma, we show that nilotinib possesses weak off-target activity against RAF and drives paradoxical activation of RAF proteins in a RAS-dependent manner. RAS is usually switched off downstream of BCR-ABL inhibition by nilotinib. However, when BCR-ABL is mutated and nilotinib cannot bind and inhibit BCR-ABL, RAS activity persists. This leads to paradoxical activation of RAF/MEK/ERK signalling. We found that nilotinib causes an unexpected survival dependency on the MEK/ERK pathway in resistant CML cells as inhibition of this pathway using a MEK inhibitor induced cell death in imatinib/nilotinib-resistant CML cell lines, primary cells from patients and blocked tumour growth in mice.

Conclusions: We have uncovered a synthetic lethal interaction between nilotinib and MEK inhibitors that can be used to kill drug-resistant CML cells in vitro and in vivo.

LESSONS LEARNT FROM DIABETIC KETOACIDOSIS (DKA)

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Background: DKA is a significant complication of diabetes with profound metabolic ramifications, particularly hyperglycaemia, hypokalemia and ketoacidosis. This analysis aims to identify demographic characteristics of patients, in this region, presenting with DKA and draws attention to methods of monitoring ketosis resolution.

Methods: This was a retrospective chart review of 14 patients who presented with DKA to a peripheral metro south Brisbane hospital between January 2011 and December 2011. Demographic information was analysed along with other important metabolic parameters including blood glucose levels, serum bicarbonate and ketones.

Results: The mean cohort age was 45.7 years, with 10 females and 4 males. Mean HbA1c at presentation was 11.9%. The leading precipitant of DKA was found to be infection (43%), followed by compliance issues (22%). The mean overlap time between administration of subcutaneous insulin and discontinuation of intravenous insulin was 1.62 hours. 2 patients who had an overlap time less than 1 hour required re-commencement of their infusions secondary to rebound ketosis. Serum ketone monitoring was a useful indicator of DKA resolution and was more reflective of improvement when compared to serum bicarbonate levels.

Conclusions: Early septic screens along with aggressive intravenous fluid rehydration and insulin therapy, remains the cornerstone of management. Overlap times between subcutaneous insulin and intravenous insulin cessation should be at least 1-2 hours to prevent rebound episodes. Serum ketone monitoring can be useful in detecting simple rebound hyperglycaemia versus true ketosis recurrence. It is also more indicative of DKA resolution when compared to serum bicarbonate levels which lag behind.

SINGLE-STRAND DNA BINDING PROTEIN HSSB1 IS ESSENTIAL FOR HOGG1 MEDIATED BASE EXCISION REPAIR FOLLOWING OXIDATIVE STRESS.

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The oxidized base 8-Oxoguanine is amongst the most common lesion damaging DNA. Its accumulation is linked to several cancers, neuro-degenerative diseases as well as aging. In human cells, Base Excision Repair (BER) of oxidized purine bases is initiated by the oxoguanine glycosylase 1 (protein OGG1). A small number of proteins are known to interact with OGG1, while very few appear to have functional consequences.

Here we report a direct physical interaction between OGG1 and SSB1. SSB1 is an OB-fold containing protein known to bind ssDNA and to be essential for DNA double strand break repair. In this study, we demonstrate that SSB1 undergoes a homodimeric to homotetrameric conversion under oxidative conditions. This higher ordered organization contributes to the modification of SSB1 affinity for DNA substrates, allowing an efficient binding to dsDNA containing 8oxoG adducts. We identified C41 as a key residue mediating the formation of SSB1 tetramer. Our data suggest that the physical interaction between the tetrameric SSB1 and OGG1 results in an increase of the 8-oxoG/C incision activity of OGG1, indicating an important role for hSSB1 not only in Homologous recombination but also in the initiation of BER.

This interaction may be a relevant therapeutic target to sensitize cancer cells to DNA damaging therapies.

STABILITY INDICATING DEGRADATION STUDY OF CYCLOSPORINE EYE DROPS IN ARTIFICIAL TEARS.

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Cyclosporine A (CsA) is a lipophilic cyclic polypeptide composed of 11 amino acids, seven of which are N-methylated. It has been utilized clinically as a potent immunosuppressant to prevent allograft rejection in various organ transplantations and to treat systemic and local autoimmune disorders [1, 2]. Study by E.Demiryay et al concluded that Ophthalmic administration of Cyclosporine in artificial tears significantly increases goblet cell density, decreases the signs of DTS (dysfunctional tear syndrome) and improves ocular surface health[3]. Although Cyclosporine ophthalmic emulsion has been on the market for a few years now, exact guidelines on how often and how long dry-eye patients should use it are still debatable. So therefore a high-performance liquid chromatography (HPLC) method was developed and validated to be stability-indicating by stress degradation tests.

Due to the cyclic structure and inherent intra-molecular hydrogen bonds, cyclosporine is very stable under normal conditions. However, degradation occurs under stress conditions. Separation of multiple components by HPLC analysis of stability samples possess high accuracy and sensitivity for even small quantities of degradation products produced. In this work, an Acetonitrile-based HPLC method with short run time, with better peak shape and resolution from the excipients has been developed and validated according to the guidance regulated in FDA, and USP. The separation was on a Waters Spherisorb® S5 ODS2 4.6 x 250mm 1.d. reversed phase column at 80° using 80:20 Acetonitrile: water as Mobile phase. Detection was by UV at 210nm, maintained a flow rate of 1mL /min with 20µl injection volume.

Three stress conditions were applied: Acid, Alkali, and heat for degradation study.

It has been found potential degradation products Isocyclosporine, and Dihydrocyclosporine were produced as a result of forced degradation with well resolved and separated peaks from the active indicating successful degradation and stability indicating.

Key words: Cyclosporine A, stability, known degradants, RP-HPLC, degradation

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LONG-TERM CARDIOVASCULAR OUTCOMES WITH EXENATIDE TWICE DAILY COMPARED TO INSULIN: A RETROSPECTIVE LONGITUDINAL STUDY

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Glucagon-like peptide (GLP-1) Receptor Agonists have been shown to reduce cardiovascular risk factors. Data on long-term cardiovascular effects of treating Type 2 Diabetes Mellitus patients with GLP-1 receptor agonists are limited. Using the GE Healthcare database, we evaluated the risk of heart failure (HF), myocardial infarction (MI) and stroke in patients initiating exenatide twice daily (EBID; n=2,795) or any insulin (INS; n=51,547) in routine clinical practice. A cohort of 54,342 patients who received a first prescription of EBID or INS between June 2005 and May 2009, combined with oral antidiabetes agents (OADs), was selected and followed for a minimum of 3 years (till June 2012) with minimum 6 months under the same drug regimen. EBID/INS patients were 39%/47% men, 56/59 years of age, 54%/48% white, 11%/12% history of cardiovascular disease, 89%/61% MET, 55%/46% SFU, 47%/33% TZDs, 74%/82% ACE-ARB, 43%/56% β -blocker, and 85%/84% statins. During median 4.3 years follow-up for EBID and 4.2 for INS, 2.1%/5.8%, 0.5%/0.9% and 0.9%/2.1% had HF, MI and stroke events respectively.

Cardiovascular event rates per 1000 person-years were significantly lower among patients treated with EBID vs. INS (HF: 4.8 vs. 13.6, MI: 1.1 vs. 2.1, stroke: 2.0 vs. 4.9). EBID patients had significantly lower risk of HF by 53% (HR CI: 0.36, 0.61) and MI/stroke by 48% (HR CI: 0.38, 0.72).

Treatment with exenatide twice daily resulted in significantly lower risk of HF and MI/stroke during 4-year follow-up compared with insulin.

QUANTIFICATION OF METAL SCREW ARTIFACTS IN CT, 1.5T AND 3T MRI IMAGES OF THE PILON

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Plain radiographs fail to accurately delineate fragment specific fixation and reduction of tibial pilon fractures three dimensionally. CT and MRI, however, limit the assessment of joint reduction due to metal-generated artifacts. This study aims to quantify these artifacts with fixation of the pilon using CT, 1.5T and 3T MRI.

Three identical screws were inserted into one intact human cadaver ankle specimen proximal to the distal articular surface, and scanned with the three modalities. Four types of screws were investigated: titanium (Ti), stainless steel (SS) (\emptyset = 3.5 mm), cannulated Ti (CTi) and cannulated SS (CSS) (\emptyset = 4.0 mm, \emptyset empty core = 2.6 mm). 3D artifact models were reconstructed. Artifact sizes were measured from the central screw axis to the artifact boundary in four anatomical directions.

The artifact sizes (Ti, SS, CTi and CSS) from CT were 2.0, 2.6, 1.6 and 2.0 mm; 1.5T MRI were 3.7, 10.9, 2.9, and 9 mm; and 3T MRI were 4.4, 15.3, 3.8, and 11.6 mm. The pilon can be clearly visualised if the screws are at a safe distance of about 2 mm for CT or at least 3 mm for MRI (exception of SS and CSS) from the articular surface. MRI enables superior assessment of articular surface reduction if titanium screws are further than 3 mm from the joint line. This allows assessing the accuracy of reduction for clinical management and the degree of post-traumatic arthrosis in long term follow up without exposing patients to ionizing radiation with CT.

LOSS OF PLACENTAL SULFATE TRANSPORT IS LINKED TO FETAL DEATH.

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Sulfate is an essential nutrient during mammalian development. In humans, the fetus is unable to generate sulfate and therefore relies on sulfate being supplied from the mother. To meet the gestational needs of the fetus, maternal blood sulfate concentrations increase from $\approx 230\mu\text{M}$ in non-pregnant women to $465\pm 10\mu\text{M}$ ($n=109$) at 12-20 weeks gestation, with levels peaking (506 ± 10 , $n=109$) at 30-37 weeks gestation. These findings are remarkable since most circulating analytes usually decrease slightly due to haemodilution. Sulfate transporter proteins, expressed on the plasma membrane of cells, maintain sulfate levels in the body. To date, 10 sulfate transporters have been identified in both the rodent and human genomes belonging to the solute linked carrier 13 (SLC13) and SLC26 gene families. Recently, we identified SLC13A4 to be the most highly abundant sulfate transporter at the interface of maternal and fetal nutrient exchange in both mouse and human placentae. Based on these findings, we generated a Slc13a4 knockout mouse to study the role of this sulfate transporter in placental and fetal physiology. Our findings show that loss of Slc13a4 is embryonic lethal due to a multitude of pronounced developmental phenotypes including skeletal underdevelopment, oedema and a possible defect in lymphangiogenesis.

The current study is providing valuable insight into the critical role of placental sulfate transport during gestation, and how increasing sulfate requirements of the fetus are met by the Slc13a4 sulfate transporter. Future studies will be important for understanding the consequences of maternal and fetal sulfate deficiency on health outcomes for mother and child.

NON-SURGICAL TREATMENTS FOR LENTIGO MALIGNA

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Lentigo maligna (LM) is a pre-malignant disease which if untreated has the potential to develop into invasive LM melanoma. It most frequently arises in areas of chronic sun exposure, and is the most common melanocytic malignancy of the head and neck. Primarily affecting elderly and fair skinned people, LM represents a common problem encountered in the Australian population.

Due to the slow-growing nature of the disease and excellent prognosis when detected in the early stages, surgical excision remains the gold standard of treatment. However the frequently large size of LM lesions, technically difficult anatomical locations in which they predominate, and the generally advanced age of the affected population mean that surgical options are not always appropriate. As such, in recent years there has been a renewed emphasis on alternative treatment modalities in patients where the risks associated with operative treatments are considered too high.

The literature describing alternative therapies for the treatment for LM are heterogenous and management protocols vary significantly between institutions. This review will summarise the literature reporting the use of radiotherapy, topical imiquimod and laser therapy as non-surgical alternatives for the treatment of LM. We conducted a comprehensive search of the United States National Library of Medicine using the MEDLINE and Cochrane Library databases and included the most relevant studies. This review included seven significant studies on radiotherapy, laser therapy, and topical imiquimod respectively. The strengths and weaknesses of each treatment were examined independently and a summary of findings presented in a poster format.

MECHANISMS OF MYC-ONCOGENE DRIVEN TUMOR ESCAPE FROM VACCINE-INDUCED IMMUNITY IN A MURINE MODEL OF NON-HODGKIN B CELL LYMPHOMA

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Advances in the treatment of non-Hodgkin B-cell lymphoma (NHL) have recently contributed to a slight reduction in the rate of NHL-associated mortality. Notable therapies include monoclonal antibodies, such as Rituximab that acts directly on CD20+ lymphomas. The efficacy of such treatments is dependent upon the functionality and longevity of host immune populations, including natural killer (NK) and T cell subsets. Thus, stimulation of these subsets with immunotherapy is a promising candidate for combination therapies. Notwithstanding these advances, over 50% of patients still relapse despite initial responses to treatment. Limited evidence suggests that relapsing human lymphomas present with lower immunogenicity and a greater immunosuppressive phenotype than the parental tumor. Here, we present evidence of a murine c-myc oncogene driven B cell tumor utilizing several modes of immune escape from an NKT-targeting immunotherapy. After initial suppression by immunotherapy, Eμ-myc tumors develop an immunotherapy-resistant phenotype, observed when escaped clones were transferred to and treated in immunocompetent mice. Eμ-myc tumor escape from vaccine-induced immunity is dependent upon the presence of regulatory T cells (T_{reg}) at the time of therapy. Furthermore, repeated immunotherapy fails to inhibit or prolong tumor relapse due to host effector cell unresponsiveness to secondary vaccination. We anticipate these results will provide targets for future functional investigations and eventual development of combination therapies that could prevent relapse from NKT-targeting immunotherapies, potentially translating into clinical application against similar myc-oncogene driven lymphomas.

SPHINGOSINE KINASE1 IS A NOVEL E2F7-DEPENDENT EFFECTOR THAT REGULATES CHEMOTHERAPEUTIC SENSITIVITY IN SQUAMOUS CELL CARCINOMA (SCC)

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SCC is a common and potentially fatal malignancy and there is considerable need for selective agents to treat SCC. There is indisputable data implicating the E2F family of transcription factors as key regulators of keratinocyte (KC) differentiation, apoptosis and neoplasia.

We have characterised another novel, important, and non-redundant role for E2F7 (one of the recently identified E2Fs) in the regulation of sensitivity to cytotoxic stimuli. We showed that E2F7-deficient KCs are selectively sensitive to the cytotoxic actions of doxorubicin and not to other chemotherapeutic agents. Sensitivity to doxorubicin was E2F7-dependent, as reintroduction of E2F7 in E2F7-deficient KCs protected against doxorubicin-induced cell death. These results indicate that doxorubicin toxicity is modulated by an E2F7-dependent mechanism. We examined the cytotoxicity of doxorubicin in SCC cell lines and showed that sensitivity to doxorubicin varies in accordance with the ratio of E2F7/E2F1 protein expression. These data also show that E2F7/E2F1 ratio is disrupted in SCC and this contributes to insensitivity to doxorubicin.

A series of microarray studies were undertaken in order to identify the downstream effector of E2F7 axis in SCC cells. We showed that E2F7-mediated sensitivity to doxorubicin is regulated by Sphingosine kinase 1 (Sphk1). Importantly, a number of Sphk1 inhibitors have been described and tested in preclinical setting. Significantly, doxorubicin-insensitive SCC cells treated with combination of low doses of doxorubicin and Sphk1 specific inhibitor (CAY10621) showed attenuated cytotoxic response to doxorubicin.

Collectively, these data demonstrate a novel oncogenic pathway and a potentially novel combination therapy for treating patients with advanced SCC.

THE EFFECT OF A NEPHRECTOMY ON KIDNEY FUNCTION AND UREMIC TOXIN ACCUMULATION: A LONGITUDINAL STUDY

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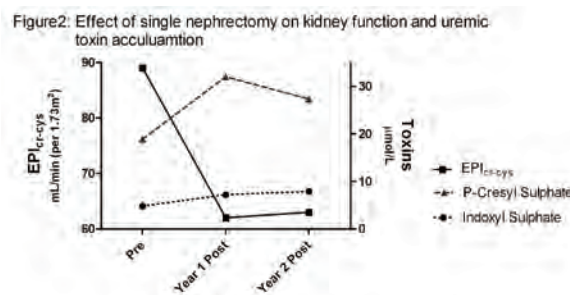
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New research indicates that the bacterial environment in the gut drives the production of kidney failure toxins which play a significant role in cardiovascular and kidney disease progression. These toxins, Indoxyl Sulphate (IS) and P-Cresyl Sulphate (PCS) are known to damage the blood vessels through oxidative stress and inflammatory pathways. This study was the first to investigate the impact of a single nephrectomy in non-CKD patients on uremic toxin accumulation.

A cohort of 42 living kidney donors (Caucasian; 76% female (n=32; 53±10years) were followed up annually for two years (pre-nephrectomy, 1 and 2 years post-nephrectomy). At each time point analysis of both total and free(f) serum IS and PCS was performed using UPLC and fluorescence detection, kidney function by CKD-EPI and Cystatin-C(EPICr-cys) formula, and urate and high sensitivity C-reactive protein (CRP) using standard automated laboratory techniques.

Along with a 30% decrease in kidney function post-nephrectomy, the mean concentration of free and total serum toxins levels significantly increased by 44-100% (mean change IS=2.4±2.6µmol/L; PCS=13.1±10.8µmol/L; ISf=0.1±0.1 µmol/L; PCSf=1.4±1.2µmol/L) which remained elevated at two years post (all p<0.001). Both toxins were associated with other markers of cardiovascular risk including increased urate and CRP levels overtime (all p<0.02).



In conclusion living kidney donors have an increased concentration of key nephrovascular toxins which remain elevated at two years post nephrectomy and correlated well with reduction in kidney function and other clinically relevant markers. Whether chronic elevation of IS and PCS in living donors cause deterioration in kidney function and pose heightened cardiovascular risk warrants investigation.

BEST PRACTICE POTENTIALS FOR THE MANAGEMENT OF OLDER PEOPLE WITH COGNITIVE IMPAIRMENT PRESENTING TO EMERGENCY DEPARTMENTS: A SYSTEMATIC REVIEW

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This paper reviews the research-based literature to identify care practices that meet the specific care needs of the older cognitively impaired ED population.

The study was a systematic literature review of papers describing ED interventions aiming to prevent adverse events and improve health outcomes for older ED patients with cognitive impairment. Interventions carried out in acute care hospitals were also considered. Relevant papers' reference lists were hand searched for additional articles. Two authors independently reviewed the papers by abstract and full text. Discrepancies were decided by consensus discussion.

The literature outlines a number of strategies to improve the care for older ED patients with cognitive impairment, including interventions to improve cognitive impairment recognition and clinical approaches to reduce falls and delirium. Supplemental studies carried out in acute care settings regarding primary and secondary prevention of delirium were also relevant. Intervention studies that reduced the prescription of potentially deliriogenic drugs in older persons, reduced behavioural symptoms, and improved patient comfort and nutritional intake in hospitalised older persons with dementia were also identified.

Useful information was available from several studies testing interventions that improved cognitive impairment

recognition and a single study that investigated the effectiveness of a fall prevention program. Other than this, there is little research carried out to improve the quality of care of older ED patients with cognitive impairment. Although this study found additional evidence obtained from the acute care setting, additional research is needed to identify whether these interventions are beneficial in fast-paced emergency settings.

IL-10 RECEPTOR AND ENDOPLASMIC RETICULUM STRESS IMPAIRS STAT3 ACTIVATION IN TYPE 1 DIABETES PATIENTS AND THEIR HEALTHY FIRST DEGREE RELATIVES

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Autoimmune diseases including type 1 diabetes (T1D) result from disordered immune tolerance. We showed that an endoplasmic reticulum (ER) stress signature predicted poor outcome in recent-onset T1D patients, and is observed in a proportion of at-risk first degree relatives (FDR). To determine the relationship of ER stress to immune cell signalling, we compared monocyte and T cell STAT3 phosphorylation in response to IL-6 and IL-10 in 30 T1D, 35 FDR, 11 healthy controls, and 22 rheumatoid arthritis (RA) disease controls. Cytokine-stimulated signalling was detected in peripheral blood monocytes and T cells by flow cytometry. Expression of ER stress genes GRP78 and DDIT3 was quantified from PBMCs by RT-PCR. Induction of phospho (P)-STAT3 by IL-10 but not IL-6 was significantly reduced in T1D and FDR monocytes and T cells relative to healthy or RA controls. Basal levels of total STAT3 were comparable in all groups. This reduction in P-STAT3 response in T1D patients and FDR was associated with reduced IL-10-, but not IL-6-receptor expression by monocytes and T cells. IL-10 receptor expression and P-STAT3 induction in response to IL-6 and IL-10 were negatively associated with GRP78 and DDIT3 ER stress gene expression. IL-10 was shown to block ER stress in gut epithelium. Thus, our data implicate a disease-specific IL-10 receptor defect and its consequences on excess ER stress and disordered peripheral tolerance in T1D pathogenesis

A POSITIVE FEEDBACK MECHANISM OF IL-6 THROUGH PHOSPHORYLATED AND UNPHOSPHORYLATED STAT3 IN INFLAMMATORY ARTHRITIS

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Background : The molecular mechanisms that link pro-inflammatory cytokines with disease activity in inflammatory arthritis remain incompletely understood. Signal transducer and activator of transcription (STAT) 3 is a signalling protein downstream of IL-6, IL-10, IL-21 and IL-23 receptors. Phosphorylated (P-) STAT3 translocates into the nucleus, where it regulates transcription of its target genes. IL-6 induces P-STAT3, and P-STAT3 promotes un-phosphorylated (U)-STAT3 transcription. We determined peripheral blood (PB) constitutive and induced P-STAT3 and total (T)-STAT3 in early stage inflammatory arthritis.

Methods: We used flow cytometry to determine basal and IL-6 or IL-10-stimulated induction of P-STAT3 in PB CD3+ T-cells of 22 untreated RA patients (median symptom duration 16 weeks), 18 treated RA patients (median symptom duration 88 weeks), and controls (23 healthy, 22 non-RA inflammatory arthritis and 35 non-inflammatory arthritis patients). Serum cytokine levels were measured by chemiluminescence.

Results: Constitutive P-STAT3 and T-STAT3 levels were significantly higher in T cells of RA patients compared to healthy controls, and P-STAT3 and T-STAT3 were correlated. Constitutive T cell P-STAT3 was positively associated with clinical and laboratory measures of inflammatory activity and with serum IL-6. In longitudinal analyses of RA

patients, constitutive P-STAT3 correlated with response to treatment.

Conclusions: Our observations are consistent with a positive feedback mechanism for IL-6 through STAT3 in inflammatory arthritis. This mechanism may underlie the potent therapeutic effect of IL-6 inhibitors.

DOING ANTIMICROBIAL STEWARDSHIP IN OUTER METROPOLITAN HOSPITALS: EXPERIENCE FROM A LARGE HEALTH SERVICE

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Background : The molecular mechanisms that link pro-inflammatory cytokines with disease activity in inflammatory arthritis remain incompletely understood. Signal transducer and activator of transcription (STAT) 3 is a signalling protein downstream of IL-6, IL-10, IL-21 and IL-23 receptors. Phosphorylated (P-) STAT3 translocates into the nucleus, where it regulates transcription of its target genes. IL-6 induces P-STAT3, and P-STAT3 promotes un-phosphorylated (U)-STAT3 transcription. We determined peripheral blood (PB) constitutive and induced P-STAT3 and total (T)-STAT3 in early stage inflammatory arthritis.

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DIFFERENTIAL GLYCOSYLATION OF CIRCULATING PROTEINS AS DIAGNOSTIC BIOMARKERS FOR BARRETT'S OESOPHAGUS AND OESOPHAGEAL ADENOCARCINOMA

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Oesophageal adenocarcinoma (EAC) is the most rapidly increasing cancer with 5-year survival of <15%. Gastro-oesophageal reflux and obesity leads to the development of metaplastic condition, Barrett's oesophagus (BE) which may develop dysplasia and progress towards EAC. To diagnose early EAC, currently BE patients are monitored for dysplastic changes by upper gastro-oesophageal endoscopy-biopsy however, being an asymptomatic condition only a fraction of BE patients are diagnosed who get benefit of this screening. Moreover, endoscopy-biopsy requires patient hospitalisation and specialist appointment hence it is neither convenient for patients nor cost-effective. The aim of this project is to identify altered glycol-forms of serum proteins as biomarkers to diagnose BE-EAC.

We screened serum samples from Healthy(n=9), BE(n=10) and EAC(n=10) patients using lectin magnetic bead array-coupled tandem mass spectrometry (LeMBA-MS/MS) which comprised of a panel of 20 lectins to isolate different glycan structures on serum glycoproteins (Electrophoresis 2011; 32,3564 & J Proteome Res 2010;

9,5496). The data was analysed through “GlycoSelect”, a customised database incorporating outlier detection and sparse Partial Least Squares-Discriminant Analysis (BMC Bioinformatics 2011; 12,253).

We identified a ranked list of candidate protein-lectin pairs that distinguish EAC, BE and healthy phenotypes from one-another. Mass spectrometric results were confirmed for top two candidates at protein levels by LeMBA-Western Immunoblotting in same patients. Future work will validate all candidate protein-lectin pairs using a customised lectin-affinity array-coupled with quantitative mass spectrometry for an independent cohort of patients. The specificity and sensitivity of panels of glycobiomarkers will be determined for formulating a serum screening test for BE/EAC.

HARD OF HEARING: THE IMPACT OF CISPLATIN-BASED CHEMORADIATION ON SENSORINEURAL HEARING LOSS

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Background: An increasing number of patients are presenting with Human Papilloma Virus associated head and neck cancer (HNC). The survival rates in this cohort are improving due to these patients responding well to definitive chemoradiation. As a consequence, these patients are more likely to live longer with the side effects of their treatment and may require prolonged support from medical services. Sensorineural hearing loss (SNHL) is a significant long term side effect of such therapy with potential major quality of life issues for patients with HNC, particularly in those receiving cisplatin-based chemoradiation. The relative contributions of each treatment on SNHL are unknown and further investigation is needed in order to increase the quality of life of these cancer survivors.

Methods/Design: A retrospective review of 150 patients with mucosal squamous cell carcinoma of the head and neck, who received treatment at the PAH Radiation Oncology Centre is currently being undertaken. We will review the rates of SNHL in this cohort to identify whether there are associations with prescribed chemotherapy, organ at risk delineation, radiotherapy parameters and patient demographics. These outcomes will be analysed to see if any significant correlations exist.

Discussion: To our knowledge there have been no detailed reviews of the rates of SNHL in HNC associated with HPV and its therapy. We believe the outcomes of this study may influence the way this disease is treated in the future.

PROTEOMIC SCREENING OF KALLIKREIN-RELATED PEPTIDASE 7 SUBSTRATES IN OVARIAN CANCER

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Kallikrein-related peptidase 7 (KLK7) is a serine protease that is over-expressed in ovarian cancer cells, compared to normal ovarian tissues. KLK7 over production in ovarian cancer cells has been predicted to enhance cell migration, invasion and resistance to chemotherapy, three of the hallmarks of cancer progression. To target KLK7 action in ovarian cancer as a potential therapy, its functional role must be elucidated. As KLK7 exerts its function through cleaving protein targets, we sought to identify substrates of KLK7 in ovarian cancer.

To screen for protein cleavage sites of KLK7, trypsin generated peptides of proteins produced by human cells were treated with KLK7, or a catalytically inactive mutant KLK7, as a control, and analysed by liquid chromatography-tandem mass spectrometry to identify the peptide fragments. Protein databases (MatrixDB) were screened for potential proteins with these peptide sequences and proteins were further interrogated using

three-dimensional (3-D) conformation data in the Protein Data Bank (PDB) database to check the accessibility of these predicted cleavage sites.

Through both bioinformatics screening and biochemically, we demonstrated that KLK7 cleave Integrin Beta 6 (ITGB6) that plays a role in cell adhesion and cell-extracellular matrix interactions. ITGB6 expression has shown to increase in late stage ovarian tumour tissues and is associated with increased invasiveness of cancer cells. Identification of substrates of KLK7 in the ovarian cancer microenvironment will help demonstrate the diverse role played by KLK7 in the progression of ovarian cancer, by re-modelling the extracellular matrix and enhancing cell invasiveness.

INTRAOBSERVED AND INTEROBSERVER VARIABILITY IN ACTINIC KERATOSES COUNTING – CURRENT TRENDS AND FUTURE PROSPECTS

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Introduction: Actinic Keratoses (AKs), also known as solar keratoses are lesions commonly encountered in fair skinned and photodamaged individuals and occur as a consequence of long-term ultraviolet (UV) exposure¹. The clinical significance of an AK is mainly related to its malignant potential because AKs are presumed to be surrogate biomarkers for Non-Melanoma Skin Cancers (NMSCs) such as SCC 2,3. For this reason, AKs are one of the most commonly treated conditions by dermatologists and General Practitioners. Evaluation of AK therapies are vital to allow accurate assessment of their effectiveness, this relies on measures of AK that are consistent and reproducible. We performed a prospective study to explore the reliability of AK counting using high definition photographic equipment and direct lesion counting. The primary end point was to measure the interobserver and intraobserver variability in AK counting.

Methods: 6 participants were selected for the purposes of the study. The body sites included in the counts were the dorsal forearms, hands and face. Counting was performed by 4 dermatologically trained clinicians and this was compared with the practical reference standard (gold standard), a senior consultant dermatologist.

Results: Our results show that excellent to good agreement exists across and within the clinicians and the Gold Standard for Clinical and Photographic counts of AKs. In this technology driven era, this may allow automated techniques to be trialed for treatment evaluation and open doors to teledermatology of AKs in the future.

EXPECT THE UNEXPECTED: PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR GAMMA (PPAR γ) AGONISTS ARE NOT PROTECTIVE IN AN OXIDATIVE STRESS-INDUCED MODEL OF KIDNEY DISEASE

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Background: PPAR γ agonists are renoprotective in diabetic nephropathy, but the mechanisms are not well-understood. PPAR γ upregulates proteins required for mitochondrial biogenesis. PPAR γ agonists may protect against mitochondrial dysfunction and oxidative stress, both known to contribute to kidney disease of various origins.

Aim: To determine the role of PPAR γ in protecting kidney proximal tubular epithelium (PTE) against mitochondrial destabilisation during oxidative stress.

Methods: Human kidney HK-2 PTE cells were treated with 0.2-1.0mM hydrogen peroxide for 2&18h. Treated and untreated cells were compared for: apoptosis, mitosis (morphology/biomarkers); cell viability (MTT); superoxide

(dihydroethidium/DHE); mitochondrial function (MitoTracker-Red; JC-1); ATP (luminescence); and mitochondrial ultrastructure. Western immunoblotting was used to study PPAR γ , phospho-PPAR γ , PPAR γ -coactivator-1 α (PGC-1 α ; mitochondrial biogenesis), and Pak2, p62 and LC3-II (mitochondrial autophagy). PPAR γ was modulated using agonists (rosiglitazone, pioglitazone, troglitazone), and the inhibitor GW9662.

Results: At 2&18h, mitochondrial destabilisation increased dose-dependently: MitoTracker-Red and ATP decreased; JC-1 fluorescence indicated mitochondrial leakiness; and superoxide increased (18h) ($p<0.05$). Ultrastructurally, mitochondria were sparse with disrupted cristae. Alterations in Pak2 (increased), p62 (decreased 2h, increased 18h), and LC3-II (increased) ($p<0.05$) indicated mitochondrial degradation. Phospho-PPAR γ increased but PGC-1 α decreased, indicating reduced mitochondrial biogenesis. Cell viability decreased (18h; $p<0.05$). PPAR γ agonists did not ameliorate mitochondrial dysfunction, and caused increased PTE cell death ($p<0.05$). PPAR γ inhibition had negligible effect.

Conclusions: Oxidative stress promoted mitochondrial destabilisation in kidney PTE, in association with PPAR γ activation. However, PPAR γ agonists did not provide protection. Despite positive effects in other tissues, PPAR γ activation appears to be detrimental to kidney PTE with oxidative stress-induced damage.

NOVEL PERSPECTIVES ON RED BLOOD CELL DISEASE

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Erythropoiesis, the process whereby erythrocytes are produced by the haematopoietic stem cells of the bone marrow, is a complex process involving carefully regulated changes in gene expression. The transcription factor KLF1 is a master regulator of this process and regulates a diverse suite of genes to ensure red cells are viable and that they contain adequate stores of functional haemoglobin.

Recently, human mutations in KLF1 have been discovered that result in changes to red cell antigen expression and the persistence of foetal haemoglobin. These observations are in agreement with mouse studies that have shown KLF1 regulates red cell membrane and cytoskeletal genes as well as haemoglobin switching. An additional human mutation that results in an amino acid substitution within the DNA-binding domain of KLF1 leads to profound anaemia and has provided insights into how KLF1 functions at the biochemical level. We have made use of technological advances in DNA sequencing to further interrogate the *in vivo* functions of KLF1 in erythropoiesis. We have described KLF1 binding genome-wide by performing chromatin immunoprecipitation coupled to high-throughput DNA sequencing (ChIP-seq). We have also defined the KLF1 dependent transcriptome by making use of RNA sequencing in KLF1 knockout mice.

The combination of these two approaches has provided extensive insights into the biochemical functions of KLF1. We have also determined that KLF1 regulates many genes involved in apoptosis, a process that we believe is co-opted in red cell precursors to result in enucleation. Our studies have advanced the understanding of erythropoiesis and its control by KLF1.

INACTIVATION OF ATM/ATR DNA DAMAGE CHECKPOINT PROMOTES ANDROGEN INDUCED CHROMOSOMAL INSTABILITY IN PROSTATE EPITHELIAL CELLS

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The ATM/ATR DNA damage checkpoint functions in the maintenance of genetic stability and some missense variants of the ATM gene has been shown to confer a moderate increased risk of prostate cancer. However, whether inactivation of this checkpoint contributes directly to prostate specific cancer predisposition is still unknown. Here, we show that exposure of non-malignant prostate epithelial cells (HPr-1AR) to androgen led to activation of the ATM/ATR DNA damage response and induction of cellular senescence. Notably, knockdown of the ATM gene expression in HPr-1AR cells can promote androgen induced TMPRSS2: ERG rearrangement, a prostate-specific chromosome translocation frequently found in prostate cancer cells. Intriguingly, unlike the non-malignant prostate epithelial cells, the ATM/ATR DNA damage checkpoint appears to be defective in prostate cancer cells, since androgen treatment only induced a partial activation of the DNA damage response. This mechanism appears to preserve androgen induced auto phosphorylation of ATM and phosphorylation of H2AX, lesion processing and repair pathway yet restrain ATM/CHK1/CHK2 and p53 signaling pathway. Our findings demonstrate that ATM/ATR inactivation is a crucial step in promoting androgen-induced genomic instability and prostate carcinogenesis.

IMMUNOSUPPRESSION (IST) CAN BE SAFELY CEASED DURING CHEMOTHERAPY FOR POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS (PTLD) IN RENAL TRANSPLANT PATIENTS

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Introduction: The optimal reduction of IST in renal transplant patients with PTLD is uncertain. As chemotherapy is inherently immunosuppressive, IST may be able to be stopped without compromising graft function.

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Methods: We performed a retrospective matched cohort study of adult renal transplant patients where IST was ceased during chemotherapy and resumed at lower dose. Outcomes were compared to matched renal transplant patients without PTLD. The primary endpoint of time from PTLD diagnosis to a 25% increase in creatinine was analysed.

Results: 24 cases of PTLD were compared with 83 controls. 23 cases received CHOP-like chemotherapy, 7 received rituximab and 4 had radiation therapy. The 5 yr overall survival for the cases was 71% with a median follow-up of 11.9 years. 3 cases recommenced dialysis, compared to 3 controls (HR 2.5, $p=0.27$). 11 cases (46%) had a rise in creatinine of $\geq 25\%$ compared to 16 controls (19%) (HR 1.8, $p=0.098$). The 5 yr rate of 25% increase in creatinine was 36% in cases and 20% in controls. Of the 11 cases with $\geq 25\%$ increase in creatinine, only 1 of these occurred within 6 months of IST cessation. Only 2 of these 11 cases received rituximab. In contrast 5 of the 7 patients given Rituximab did not develop a $\geq 25\%$ deterioration in renal function.

Conclusions: IST can be safely ceased during chemotherapy for PTLD in renal transplant patients. Whilst long-term reduction in IST is necessary to reduce PTLD relapse, this is associated with a trend to increased risk of transplant rejection.

ANTIVIRAL ROLE OF CYTOKINE-INDUCED ENDOPLASMIC RETICULUM STRESS

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Recently, a number of inflammatory cytokines have been found to induce endoplasmic reticulum (ER) stress, in-vitro, in a number of secretory cell types. ER stress is a cellular state where misfolded proteins aggregate in the ER, resulting in decreased protein synthesis and inflammatory cytokine release. Viruses require host protein synthesis machinery in order to replicate. It has previously not been investigated whether cytokine induced ER stress affects viral replication.

This project aimed to determine which cytokines induce ER stress in respiratory epithelial cells and whether induction of ER stress had a protective role in early stages of respiratory viral infections.

An ER stress fluorescent reporter or ER stress marker gene expression was used to determine which cytokines induce ER stress in primary and immortalised (16HBE) human bronchial epithelial cells. These cytokines were then administered in-vitro and in-vivo prior to infection with respiratory viruses; respiratory syncytial virus (RSV) and mice pneumovirus (PVM). Viral titre and ER stress was measured using qRT-PCR.

We found that cytokines IL-23, IL-24, IL-17A, IL-17F, IL-33, IFN- and IFN- β 1 were potent initiators of ER stress in human bronchial epithelial cells. Pre-treatment of 16HBE cells with cytokines decreased RSV mRNA replication compared to untreated control, as measured by qRT-PCR. In-vivo these ER stressor cytokines were up-regulated during early stages of PVM infection in C57BL/6 mice and this correlated with an increase in ER stress markers sXBP1 and GRP78.

These results highlight a novel antiviral mechanism of cytokines inducing ER stress to decrease protein synthesis in virus-susceptible epithelial cells.

NON-INVASIVE CARDIAC OUTPUT MONITORING IN EMERGENCY RESUSCITATION - THE NICER TRIAL.

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Background: Resuscitation with boluses on intravenous fluids is central to the treatment of the critically ill patient in the Emergency Department.

Aim: To determine if fluid resuscitation guided by non-invasively measured response in stroke volume improves lactate clearance and haemodynamic indices in critically ill patients in the Emergency Department

Method: Randomized controlled pilot study of adult patients requiring urgent fluid resuscitation and having 2 out of three of the following: heart rate > 100 bpm, systolic blood pressure < 100 mmHg and lactate > 1.5 mmol/L. Participants randomized to standard care vs fluid resuscitation guided by stroke volume response.

Results : 110 participants were enrolled. Primary outcome, 4 hr lactate, showed no difference (2.2 vs 2.7 mmol/L, $P=0.57$). There was no significant difference in mean blood pressure at completion (121 vs 116, $P=0.10$) however both the mean heart rate (104 vs 95 bpm, $P=0.02$) and the proportion of patients achieving normalization of vital signs ($HR<100$ bpm, $SBP>100$ mmHg, 30% vs 51%, $P=0.04$) were significantly improved by the intervention. Other indices of inadequate perfusion (base excess, Shock Index) were similar between the two groups. Survival, ICU admission rates and hospital length of stay were not different.

Conclusion: Stroke volume response guided fluid resuscitation in critically ill ED patients lead to a significantly higher proportion of patients normalizing their vitals signs.

BLOOD PRESSURE TRAJECTORIES BEFORE DEATH IN PATIENTS WITH TYPE 2 DIABETES

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The aim of this study is to examine the trajectory of blood pressure (BP) over two years before death or censoring and its association with mortality in patients with Type 2 Diabetes Mellitus.

A cohort of 19966 patients with minimum 3 years of diabetes duration (DD) was selected from the UK General Practice Research Database (1990-2008), who had four consecutive 6-monthly BP measures over 2 years immediately before death or censoring. In the cohort, 46% were female, mean (SD) age of 68 (11) years and 14% had at least one cardiovascular event (CVE) before diagnosis of diabetes. During 6.5 years of median follow-up, 7% patients died, of whom 83% were aged ≥ 68 years, 53% and 20% patients had CVE respectively in dead and alive groups.

During 2 years immediately before death, patient's systolic and diastolic BP trajectories were significantly higher by 5 and 2 mmHg respectively in those who died, compared to alive patients after adjusted for the effects of age, DD, sex, CVE, glucose-lowering and anti-hypertensive medication usages, baseline weight and HbA1c (Fig 1). Compared to patients with systolic BP level 125 – 130 mmHg, patients with BP < 110 and > 140 mmHg had significantly higher mortality risk by 240% (adjusted odds ratio : 2.4, 95% CI: 1.9, 3.1) and 210% (adjusted odds ratio: 2.1, 95% CI: 1.8, 2.5) respectively.

The population level analyses of BP trajectories up to death provides clear message in terms of the requirement for intensive BP control at primary care level.

INCREASED METABOLISM OF FLUORESCEIN IN STEATOTIC LIVERS EXPOSED TO ISCHEMIA REPERFUSION INJURY

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The liver is important for metabolism of various drugs, and liver disease can impair this, causing increased systemic concentrations. Ischemia-reperfusion injury is a common complication during liver surgery, due to generation of oxidative stress during the reintroduction of blood after ischemia. Steatotic livers are more prone to the injury and may become more prevalent in the growing obese population. This study aimed to investigate the ability of the liver to clear drugs in steatosis exposed to ischemia-reperfusion injury. Liver steatosis was induced in rat by feeding them a high fat diet for 7 days. Partial liver ischemia (median and left lobes) was induced for 1 hour, where after fluorescein (10 mg/kg) was injected. The damage caused by ischemia-reperfusion injury with or without steatosis was characterized by increased ALT levels and apoptosis as well as reduced bile flow. In vivo imaging demonstrated delayed excretion of fluorescein, which was due to an increased intrinsic metabolism of fluorescein. As a consequence, the biliary excretion rate was significantly reduced. Our results show the importance of imaging in combination with modelling to understand drug transport and reflect on careful drug monitoring in surgery of steatotic livers.

THE ROLE OF MYRIP IN THE EXOCYTOTIC RESPONSE TO DNA DAMAGE

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An efficient response to DNA damage is crucial for genome stability and cellular survival. Failures in maintaining genomic integrity are associated with cancer, ageing, and a wide range of genetic disorders. The response to genomic instability is regulated through a diverse network of cellular pathways that identify, repair and remove damaged DNA. These pathways represent clinical biomarkers and therapeutic targets in the detection and treatment of cancer. Preliminary mRNA microarray studies by our laboratory identified Myosin- and Rab-interacting protein (MyRIP), a protein with no known role in the DNA damage response, to be over-expressed in non-small cell lung cancer (NSCLC) cells that were resistant to Cisplatin. Cisplatin based drugs are the primary line of treatment for NSCLC and present their toxicity through the introduction of DNA breaks in replicating cells. In this study we are exploring a potential new role for MyRIP in the exosomal response to DNA damage. MyRIP protein expression increases after DNA damage, and is transcriptionally regulated by p53. Depletion of MyRIP resulted in impairment of DNA repair responses. The results of our preliminary studies suggest MyRIP is necessary for the repair of DNA double-strand breaks induced by IR, and is critical for chemotherapeutic-resistance.

IDENTIFYING NOVEL THERAPEUTICS FOR OSTEOSARCOMA METASTASIS

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Osteosarcoma (OS) accounts for 56% of malignant bone cancers in children and adolescents. Pulmonary metastasis occurs in approximately 50% of patients with a 5 year survival rate of only 20%. Therefore it is crucial to identify genes and pathways that drive the metastatic behavior of OS for the identification of therapeutic targets. To identify markers that may define inherent metastatic OS we conducted microarray-based comparative profiling analysis of clonal variants from an inherently metastatic cell line, KHOS. Two highly metastatic (C1 and C6) and two poorly metastatic clones (C4 and C5) were compared in the transcriptomic screen. Vascular endothelial growth factor A (VEGFA) and two other novel genes were identified as potential markers for OS metastasis with 2-4 fold increased expression in highly metastatic clonal variants when compared to poorly metastatic clonal variants. The transcriptomic expression of VEGFA and the two new markers was also investigated in non-malignant bone (NB), OS patients with non-metastatic (NM) and metastatic (M) disease. All three markers were found to be highly expressed in 29-42% of M-OS with little to no expression seen in NB and NM-OS. Targeting one of the markers with a commercially available drug specific inhibitor, we showed significantly reduced migration and invasion in vitro. In a drug treated orthotopic mouse model of OS, there was a significant decrease in pulmonary metastasis using a number of metastatic OS cell lines. These are promising markers of OS metastasis, which can also be strong and novel therapeutic targets.

ARGINASE-1 MEDIATES AN ENHANCED INFLAMMATORY RESPONSE TO 2,4-DINITROCHLOROBENZENE IN THE SKIN EXPRESSING HUMAN PAPILLOMAVIRUS E7 ONCOPROTEIN

LS Tran, AS Bergot, SR Mattarollo, D Mittal, IH Frazer

Human Papillomavirus (HPV) infects the epithelium and accounts for approximately 5.2% of all types of cancer. In approximately 10% of infections, HPV has established a local immunosuppressive environment that facilitates its persistent infection and eventually invasive cancer. However, a robust acute inflammatory response is able to disrupt this environment. 2,4-Dinitrochlorobenzene (DNCB) that can elicit acute inflammation has been clinically shown to induce the regression of HPV associated genital warts. Although the use of DNCB for treatment is discouraged due to its mutagenic potential, understanding how DNCB induces acute inflammation in HPV infection context remains an essential task for the development of therapeutic strategies. To understand this mechanism, we topically applied DNCB to ear skins of nontransgenic (control) and transgenic mice expressing HPV oncoprotein E7 (K14.E7), a model of HPV associated precancerous lesion. We showed that DNCB application induced an hyperinflammatory response in K14.E7 mice, but not in control mice. Arginase, which is a key mediator of L-arginine metabolism, has been identified as a crucial regulator in a multitude of inflammatory episodes. Therefore, we addressed the role of arginase in the inflammatory response of K14.E7 mice to DNCB. In accordance with enhanced inflammatory response, K14.E7 mice produced significantly higher level of Arginase-1 mRNA and arginase activity than control mice following DNCB application. We also identified that arginase-1 was mainly produced by CD11b+Gr1IntermediateF4/80+ myeloid subset. In addition, inhibition of arginase with a specific arginase inhibitor ameliorates this inflammatory response. Our results demonstrated that CD11b+Gr1intF4/80+ derived arginase-1 promotes DNCB induced

WHAT WOULD FLO THINK? HOW CLEAN ARE YOUR CUFFS?

L Trenning , S Galbraith

Background: The hospital environment is a known potential reservoir for bacteria with documented evidence for surface contamination with resistant bacteria posing a risk factor for infection. Blood pressure cuffs have been shown to have been contaminated leading to recommendation for cleaning and use of liners or disposable cuffs.

Problem: In our ED environment there is currently no effective process around the identification, cleaning and rotation of BP cuffs, thus potentially placing patients at risk.

Hypothesis: Replacement of non-disposable blood pressure cuffs with single patient use cuffs for every ED presentation would minimise a potential source of infection.

Methods and Results: Phase 1 involved swabbing and culturing BP cuffs throughout the ED. Phase 2 involved testing BP cuffs tested for faecal occult blood contamination. Over 50% of the cuffs were either bacterially contaminated or had blood on them. The baseline data from these studies demonstrated marked bacterial and blood contamination.

Discussion: As a result of this study a decision has been made to replace all non-disposable cuffs with single use cuffs. The cost effectiveness of this practice is currently being investigated with a view to implementation across the hospital. Plan to work with infection control and Clinical Consumables and Equipment committee within hospital to extend this process to clinical ward areas.

Conclusion: The hypothesis has been proven and is providing evidence to support the change of practice for the benefits of patient safety in a cost effective manner.

CHARACTERIZATION OF SMARCD3 AS A NOVEL BREAST CANCER GENE.

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Worldwide, one in ten women will develop a breast cancer in their lifetime. While the overall outcome for patients has dramatically improved recently, breast cancer remains a killer among the female population. Indeed, breast cancer is the leading cause of death in women after lung cancer. Still today, very little is known about the genetic background of non-BRCA1, BRCA2 breast cancer predisposed families, and we still poorly understand whole categories of patients such as the 'triple negatives', who are lacking 3 essential cell receptors and thus don't benefit much from commonly-used hormone therapy (e.g. Tamoxifen or Herceptin). We have recently identified genes that are specifically deregulated in triple negative breast cancer and could be novel oncogenes. By over-expressing and knocking down SMARCD3, we are investigating its function in normal breast tissue and breast cancer cell lines to decipher its role in cancer development. Growth rate and cells morphology will be measured to determine how SMARCD3 influence cellular behaviour, as both features impact cancer progression. In silico modelization indicates that SMARCD3 might be involved in DNA damage repair, and we will explore this possibility by comparing sensitivity of our cell lines to genotoxic drugs. We hope that our findings will lead the way toward development of new diagnostic tools and novel therapies.

Aims: To determine the role and function of SMARCD3 in normal tissue and during tumor-genesis

ENDOCHONDRAL BONE FORMATION AND ADVANCED ENTHESITIS ARE KEY FEATURES OF PGISP MOUSE MODEL OF ANKYLOSING SPONDYLITIS

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Ankylosing spondylitis (AS) is a chronic inflammatory arthritis targeting the axial skeleton. Initial inflammation occurs in the enthesis, where the tendon attaches to bone. Syndesmophyte formation later bridges the vertebrae and causes joint fusion. The mechanisms controlling the inflammation-bone formation transition are unknown and no current therapy can halt disease progression.

Aims: To understand the transition from inflammation to bone formation in AS using the proteoglycan (PG)-induced spondylitis (PGISP) mouse model.

Bone samples were collected from PGISP mice at different time points from disease onset to joint fusion. The histological scoring criteria include features of inflammation, destruction and excessive tissue formation. Unsupervised cluster analysis was used to delineate the features associating with different disease stages.

Early inflammation was initially found at the periphery of the intervertebral discs (IVD) and subsequently caused disc destruction and bone erosion. The inflammation peaked in the mid-time points; meanwhile, excessive tissue formation around the IVDs and appearance of ectopic chondrocytes in the ligaments started to increase at this stage. Less inflammation but huge excessive tissue formation and frequent ectopic chondrocytes formation were the features of the late time points. Degree of inflammation, excessive tissue formation and ectopic chondrocyte formation could distinguish mice into different disease stages.

The PGISP mouse model displays many features reported in human AS, such as enthesitis and ectopic chondrocytes formation typical of endochondral/chondroidal ossification. Osteoproliferation continues after resolution of inflammation leading to the ankylosis in PGISP mice. Thus the PGISP mouse model illustrates key functional changes in disease progression in AS.

RADIATION INDUCES SPHEROGENESIS IN BREAST CANCER CELLS IN VITRO

D Veleva, L Croft, K O'Byrne, D Richard

Cancer stem cells (CSCs) represent a small number of cells that retain the capacity to self-renew and differentiate into multiple cell types. They have been identified in a variety of human cancers and are known to be responsible for cancer initiation, recurrence and metastasis. CSCs have also been shown to be resistant to conventional chemo and radiation therapies. Cells with CSC-like properties can be isolated and maintained in vitro for extended periods of time. The maintenance of CSCs in vitro requires growth in hormone-supplemented serum-free media that allows their growth as tumour spheres (Cammareri et al, 2008) Here we report that ionizing radiation can induce spherogenesis in breast cancer cells. Particularly, we found that radiation induces CSCs to grow in suspension as spheres when grown in both serum-supplemented as well as the hormone-supplemented serum-free media. These data suggests that radiation can activate stemness pathways in breast cancer cells leading to an enrichment of a cell population with higher resistance to radiation therapy. These findings also provide a new method for expansion of CSCs for investigating cancer stem cell biology as well as aid in the development of potential new treatments for breast cancer.

Cammareri P, Lombardo Y, Francipane MG, Bonventre S, Todaro M, Stassi G. Isolation and culture of colon cancer stem cells. *Methods Cell Biol.* 2008; 86:311-24. doi: 10.1016/S0091-679X(08)00014-9.

THE ROLE OF FKBP4 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 being produced per day per cell. If DNA damage is not repaired correctly it can be detrimental to the cells, with altered structure and genetic material occurring, leading 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 detects different types of genotoxic stress to raise a versatile and coordinated response that includes control of the cell cycle transitions, transcriptional processes and stimulation of DNA repair (Bekker-Jensen, S. and N. Mailand. *DNA Repair*, 2010). Recently our laboratory discovered the human single strand DNA binding protein 1 (hSSB1), and found it to be involved in the DNA damage-signalling pathway (Richard, D.J., et al. *Nature*, 2008). To increase our understanding of the DNA damage pathway, a connectivity screen was performed with hSSB1, this identified FKBP4 as a potential protein involved in the DNA damage repair pathway. FKBP4 (FK506 binding protein 4) is a HSP90 co-chaperone. This protein has been shown to have a role in hormone dependant cancers and has been implicated in the protection of mitochondria from oxidative damage (Storer, C.L, et al. *Trends Endocrinol Metab*, 2011.)

Aim: To identify the role that FKBP4 in the DNA damage response pathway. This will be established by causing DNA damage and determining how FKBP4 reacts, as well as by knocking down FKBP4 and monitoring the cells response to DNA damage.

DIRECT ADVERSE EFFECTS OF IL-23 ON EPITHELIAL CELLS UNDERLIE THE GREATER THERAPEUTIC EFFICACY OF NEUTRALIZING IL-23 VS TH17 EFFECTOR CYTOKINES IN COLITIS

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IL-23/TH17 inflammatory responses are implicated in the pathogenesis of inflammatory bowel disease (IBD). However, clinical trials demonstrate that targeting IL-17A is not efficacious in treating active Crohn's disease patients, and may predispose patients to fungus infection. Therefore, the approach to target proinflammatory cytokines of the IL-23/TH17 axis needs further examination. In a transfer model of colitis, IL-17A deficient T cells induced similar colitis compared to wild type (WT) T cells, while IL-17Ra deficient T cells were more colitogenic than WT T cells. In Winnie mice with spontaneous colitis arising due to an epithelial defect, genetic deficiency of IL-17A suppressed progression of colitis. However, therapeutic inhibition of IL-17a-IL-17Ra signalling by monoclonal antibodies did not reduce colitis severity. In contrast, neutralizing IL-23 using an anti-p19 antibody significantly alleviated established colonic inflammation in Winnie colitis model, diminished neutrophil infiltration and restored mucin production from goblet cells. Whilst IL-17 is known to boost epithelial barrier function, IL-23 has previously been thought to act only on leukocytes. We show that IL-23 acts directly on epithelial cells, increasing intracellular reactive oxygen species in a STAT3-dependent manner, resulting in decreased mucin production and secretion, and increased proinflammatory chemokine release. Adverse effects of IL-23 on epithelial cells could partially underlie the protective effects of hypomorphic IL-23 receptor polymorphisms for IBD, and contribute to the efficacy of IL-23 neutralizing antibodies in IBD. These findings deepen our understanding of the IL-23/TH17 axis and may guide therapeutic approaches for patients with active inflammatory bowel disease.

ENHANCING STATEWIDE REHABILITATION SERVICES THROUGH THE NATIONAL PARTNERSHIP AGREEMENT

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2. Division of Rehabilitation

3. Spinal Outreach Team

4. Division of Rehabilitation

The Division of Rehabilitation (DoR) provides specialised state-wide rehabilitation services to adults with acquired brain injury and spinal cord injury throughout Queensland. Their subacute rehabilitation services have been enhanced via funding from the National Partnership Agreement (NPA) on Improving Public Hospital Services, with 22 positions provided across inpatient and outreach services, including the Spinal Injuries Unit (SIU), Brain Injury Rehabilitation Service (BIRS) and the Spinal Outreach Team (SPOT).

NPA funding objectives included improving outcomes for people with acquired brain injury and spinal cord injury in Queensland, and improving the quality of and access to specialist rehabilitation services.

This poster will present outcomes achieved by the DoR following NPA funding, in the areas of Activity; Health, Function and Quality of Life; Service Delivery and Service Quality.

Outcomes include:

- Increased activity in SIU, BIRS and SPOT
- Increased outreach services (e.g. 34% increase in outreach clients seen by SPOT), and reduced waiting times
- Increased capacity of services for new admissions (e.g. 32% increase in 'new therapy' BIRU Day Hospital admissions)

- Increased intensity of rehabilitation services (e.g. 56% increase in BIRU SP OOS)
- Changes to service delivery, allowing modern, innovative models of care to be implemented
- Increased quality of services, with development of education, training and evidence based resources for consumers statewide

New service models have resulted in increased efficiency and cost-effective services, with target 'occasions of service' being exceeded by >80%. Outcomes for adults with brain injury and spinal cord injury have improved.

PSYCHOSOCIAL OUTCOMES OF PATIENTS WITH ACQUIRED BRAIN INJURY DISCHARGED HOME FROM ACUTE HOSPITAL CARE: A SIX MONTH FOLLOW- UP STUDY

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Background and aims: Inpatient rehabilitation is a limited resource that is not accessible to all patients with acquired brain injury. In the absence of physical disabilities, a large proportion of patients are discharged home directly from acute care once they are medically stable. These individuals may however be at risk of reduced participation and psychosocial adjustment issues due to subtle cognitive and behavioural changes. This study aimed to profile and compare changes in psychosocial functioning in individuals with TBI and ABI from other causes in the first 6 months after discharge home from acute hospital care without a period of inpatient rehabilitation.

Method: Prospective longitudinal study with data collected at four time points; before discharge, and at 1, 3 and 6 months post discharge. A total of 103 participants with ABI (68% male, mean age 42 years, 55.3% with TBI) were recruited from the acute neurosciences unit of a metropolitan hospital. Participants completed self-report questionnaires at each time point including measures of participation, general functioning, emotional distress, quality of life, and sentinel events.

Results: The sample showed improvements on all measures over the 6-month period and the majority demonstrated good psychosocial outcomes. No significant differences between participants with TBI and other ABI were found on any of the measures. Approximately 20% of participants reported elevated symptoms of depression, anxiety and stress which persisted at 6-months post-discharge. Ongoing problems with pain/discomfort and usual activities were reported by 38.8% and 28.1% respectively. Over the 6 month period, 73.8% returned to work/study, 62.1% returned to driving, but 38.8% reported emotional strain and 26.2% a relationship breakdown.

Discussion: The results suggest a subgroup of patients discharged home from acute care without rehabilitation have compromised psychosocial outcomes.

MAKING THE CALL TO END OBESITY: FEASIBILITY AND EFFECTIVENESS OF A TELEPHONE-BASED WEIGHT LOSS PROGRAM DELIVERED VIA A HOSPITAL OUTPATIENT SETTING

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Engaging patients with a face-to-face, group-based healthy eating and lifestyle program (HELP) is a clinical challenge for tertiary hospital outpatient clinics. This study evaluated the feasibility and effectiveness of a telephone-delivered program (iHELP) as an alternative option. Patients who declined the 2-month HELP program (consists of 8 weekly sessions) were offered the iHELP alternative (16 phone calls over 6-months targeting physical activity, healthy eating and weight loss). Weight (kg), physical activity (accelerometry min/day) and self-reported serves of fruit and vegetables were measured at baseline, 2-months, and 6-months. Changes within the iHELP group were analysed by paired t-tests. Relative differences in weight change between HELP and iHELP at 2-months were compared by linear regression models, adjusting for baseline values. Fifty patients (19% of referrals) commenced the HELP group (60% female, 57±14 years, 20% employed), with 66% completion at 2-months. Sixty-one patients (24% of eligible) commenced iHELP (46% female; 49±12 years, 66% employed), with 64% retention at 2-months and 48% completion at 6-months. Preliminary 6-month results from iHELP completers show significant weight loss (-4.8±5.1%, $p<0.05$) and improvements in vegetable serves but not physical activity. Relative to HELP, iHELP was associated with greater weight loss (mean[95% CI]: -2.0[-3.4, -0.6]; $p=0.007$) at 2-months. Telephone-delivered weight management services can be more effective than usual care, and reach a greater number and broader demographic of patients referred within an acute care hospital setting. Exploring alternative and broader-reaching service delivery models is important for the significant proportion of patients who remain unengaged with these services.

RECENT ADVANCES IN THE GENETICS OF FAMILIAL HYPERTENSION WITH HYPERKALAEMIA (GORDON'S SYNDROME)

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Familial hypertension with hyperkalaemia (FHt or Gordon's syndrome) is an inherited form of hypertension characterised by elevated plasma potassium with normal glomerular filtration rate. The genetic causes of this syndrome were unknown until 2001 when mutations in the 'With No Lysine (K)' kinases (WNK1 and WNK4) genes were found to account for a minority of affected families. In 2012 mutations in two new genes were discovered; KeLch-Like3 (KLHL3) and CULLIN3 (CUL3).

In collaboration with Drs Mark Glover (University of Nottingham, UK) and Kevin O'Shaughnessy (University of Cambridge, UK) With our UK collaborators, we performed next generation sequencing in local families already screened for WNK1/4 mutations and confirmed CUL3 or KLHL3 mutations in six of nine pedigrees, including the first patient described by Gordon. Further work is underway to identify genetic causes for which where mutations have yet to be found, and to explore and compare phenotypic manifestations for each genotype.

These mutations result in FHt by causing dysregulation and excessive activity of the thiazide-sensitive sodium transporter (NCC) in the distal tubule. WNK4 is a potent regulator of NCC, inhibiting trafficking to the cell surface by diverting it down a degradative pathway and also phosphorylating and activating NCC through intermediary proteins. KLHL3 and CUL3 are components of a ubiquitination complex and the WNK kinases may be substrates for this complex. Mutations in these genes may result in reduced ubiquitination of the WNK kinases causing excessive NCC activity.

In conclusion, the genetic causes for FHt are slowly being unravelled, revealing previously unknown pathways involved in the regulation of sodium reabsorption in the distal nephron, and providing exciting new targets for drug development.

OSTEOMAC REGULATE OSTEOCLAST FORMATION IN VITRO BY SECRETING CARDIOTROPHIN LIKE FACTOR -1

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Osteomac are resident macrophage within bone lining tissues that are intimately associated with osteoblasts. They provide osteoblast trophic function with the ability to modulate bone formation. Immunohistochemistry staining of 4 weeks old mouse bone identified the presence of osteomac at sites of bone resorption and remodelling. At both sites, osteomac are juxtapositioned to osteoclasts and constitute the bulk of cells within the canopy structure encapsulating the basic multicellular unit. Based on this observation, the possible interaction of osteomac with osteoclast was examined using in vivo and in vitro models. In vivo treatment of C57/Bl6 mice with RANKL-GST induced osteoclast formation with elevated serum TRAP level detected within 3 days, followed by a delayed induction of osteoblast formation (from day 5). Flow cytometry identified a significant biphasic increase in the percentage of F4/80+ bone marrow macrophages which coincided with an elevated bone resorption and osteoblast formation activity respectively, suggesting macrophage involvement in both biological responses. Conditioned media (CM) collected from bone marrow-derived macrophage (BMM) greatly enhanced sub-optimal RANKL-stimulated osteoclastogenesis in vitro. Proteomic analysis of BMM CM identified cardiotrophin-like cytokine factor 1 (CLCF1) as a candidate macrophage secreted pro-osteoclastogenic molecule, with real time PCR confirming the expression of CLCF1 mRNA by macrophages. The addition of recombinant CLCF1 in sub-optimal RANKL-induced osteoclast assay can enhance osteoclastogenesis. The data implicate osteomacs as stimulators of osteoclast formation potentially via CLCF1. Combined with their ability to enhance osteoblast function, the data indicate that osteomacs regulate both catabolic and anabolic responses in bone.

MOLECULAR CHARACTERISATION OF NON-MELANOMA SKIN CANCER IN RENAL TRANSPLANT PATIENTS

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Non melanoma skin cancer (NMSC) is the most common tumour among populations of European origins. Actinickeratosis (AK) is a common skin lesion and also a precancerous skin lesion that has a risk of developing into a squamous cell carcinoma (SCC). Interestingly, among the single-organ transplant patients, particularly kidney, have been shown 4-20 times more likely to develop precancerous lesions compared to non-transplant patient. In addition, these lesions seem to progress from AK to SCC faster. However, the factors that lead to transformation are debatable with the tumour suppressor gene p53 being a recognized candidate. When p53 is up-regulated, it promotes either growth arrest or apoptosis in response to cellular injury as well as is critical for genomic stability maintenance. UV exposure is a known cause of p53 mutations. The aim of this study was to represent some molecular characterizations of NMSCs and the status of p53. This may help to develop a potential marker for the efficacy of NMSC therapy in renal organ transplant and other skin patients. We collected 25 clinically diagnosed AK lesions by shave biopsy. Half of the lesion was subjected to histopathology and the other half processed for whole transcriptome sequencing. All lesions were histopathologically diagnosed within the AK to squamous cell carcinoma progression lineage. We found that Keratin 10 (K10) was highly expressed in AK lesions from immunocompetent patients. There were also eight point mutations detected in P53 profile and G→A seems to be the most common mutation in renal transplant patients.

THE TOLL-LIKE RECEPTOR RP105 PROMOTES TNF TRAFFICKING IN MACROPHAGES DURING MYCOBACTERIAL INFECTION

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Mycobacterial infections, in particular tuberculosis, remain a significant public health concern worldwide. Macrophages are the major host cells for pathogenic mycobacteria and play a central role in containing the pathogen and initiating inflammatory cytokine responses. Radioprotective 105 kDa (RP105) is a member of the Toll-like receptor (TLR) family that has been demonstrated to facilitate B cell proliferation but limit LPS-driven cytokine production by antigen-presenting cells. Our group recently identified a novel role for RP105 in promoting macrophage cytokine production during infection with pathogenic mycobacteria. RP105-deficient macrophages showed reduced cytokine secretion upon infection with *Mycobacterium tuberculosis* (Mtb) and *Mycobacterium bovis*, BCG. While we previously observed physical and functional interactions between RP105 and TLR2, we now show that classical TLR signalling such as activation of MAP kinase and NF- κ B signalling remained intact in RP105-deficient macrophages during mycobacterial infection. Furthermore, mycobacteria-induced mRNA and protein expression of TNF were comparable in WT and RP105-deficient macrophages. In contrast, RP105-deficient macrophages infected with mycobacteria displayed reduced cell surface-associated TNF suggesting diminished TNF trafficking in these cells. We identified PI3K signalling as a likely molecular mechanism regulating mycobacteria-induced macrophage TNF secretion downstream of RP105. Taken together, our observations identify RP105 as an integral part of the innate immune receptor complex for pathogenic mycobacteria that contributes to macrophage responses by regulating trafficking of TNF and possibly other cytokines.

Support: NHMRC

Aims:

To understand how the molecular mechanism shaped by the innate immune receptor, RP105, to facilitate immune control and long-term protection from mycobacterial infection such as tuberculosis.

Notes
