

St Vincent's Institute (SVI) is an independent medical research institute conducting research into the cause, prevention and treatment of diseases that have a major effect on the health of the community.

About us

SVI is an independent research body, which is affiliated with St. Vincent's and the University of Melbourne. Through these links, SVI's research programs provide a valuable service to clinical medicine, graduate education and community welfare. SVI hosts the National Serology Reference Laboratory and is a member of Bio 21, the Victorian Breast Cancer Research Consortium and the Association of Australian Medical Research Institutes. It is a member institution of the Australia-wide healthcare facilities of the Sisters of Charity.

Researchers at SVI study diseases that have a major impact on the health of the community. These include Type 1 and 2 diabetes, obesity and heart disease, arthritis, osteoporosis, cancer and metastasis to bone, leukaemia, Alzheimer's

disease, epilepsy and infectious diseases such as hepatitis and AIDS.

More information on the Institute can be found at www.svi.edu.au or by ringing 03 9288 2480.

Projects in progress or completed

Highlights

- 47 per cent of SVI's NHMRC Project Grant applicants had their grants funded in 2008 – well above the national average of 27 per cent.
- Prof Michael Parker was joint recipient of a \$3.7 million NHMRC Program Grant with his collaborator Angel Lopez from The Centre for Cancer Biology (formerly Hanson Institute), Adelaide.
- Prof Michael Parker and his collaborators at The Centre for Cancer Biology in Adelaide published a paper in *Cell*, describing the structure of the GMCSF receptor bound to its ligand, a finding that may have important implications for leukaemia.
- Three patients at St. Vincent's with Type 1 diabetes have received transplants of insulin-producing islets isolated by a team from SVI. Two of these patients are now insulin independent and one has had a >50 per cent fall in daily insulin usage. The recipients no longer suffer severe hypoglycaemic episodes. This trial is part of the Australian Islet Transplant Consortium which is funded by the Juvenile Diabetes Research Foundation and the Department

of Health and Ageing, and involves collaboration between teams at SVI, St. Vincent's, Austin Health, Westmead Hospital and Queen Elizabeth Hospital in Adelaide.

- Assoc Prof Jörg Heierhorst's group at SVI, in collaboration with Ming Daw Tsai and colleagues from the Academia Sinica and National Taiwan University, published a paper in the prestigious journal **Molecular Cell** describing a new mechanism that allows cells to fine-tune their response to the DNA damage signals.
- SVI alumnus Prof Zihe Rao, President of Nankai University of Structural Biology at Tsinghua University in China gave the annual SVI Pehr Edman lecture on the 14th of April entitled 'Structural biology studies of infectious diseases: from AIDS to SARS to bird flu'.

Research applications in the clinical setting

SVI researcher, Assoc Prof Duncan Campbell, who collaborates closely with St. Vincent's Cardiology Department, was awarded a \$300,000 grant over three years from the Bennelong Foundation. The funds were used to purchase a new cardiac imaging machine for patient care at St. Vincent's and for SVI's research into heart failure prevention. The new echocardiography machine enables doctors to view the heart as a 3D image using an external scanning device. The images captured are then used to determine indications of

heart disease. Assoc Prof Campbell will be using the machine to identify people with increased risk of heart failure. The research aims to identify the mechanisms for heart failure in its earliest stages, allowing the development of improved strategies for heart failure prevention.

'The machine's superior imaging capability, particularly in 3D, is providing new insights into cardiac function and the changes visible in various disease states. We are very excited about the rewards this machine will bring to our research and to patient care,' said Assoc Prof Campbell.

The team

Prof Thomas Kay, Director; Dr Elizabeth Allan; Dr Jan Allison; Dr Juliana Antonipillai; Alicia Arnott; David Ascher; Dr Maria Askmyr; Dr Thein Thein Aye; Dr Brett Bennetts; Dr Ora Bernard; Robin Berry; Dr Sue Best; Tony Blick; Steve Boz; Holly Brennan; Penny Buxton; Liza Cabuang; Assoc Prof Duncan Campbell; Elizabeth Castles; Meryn Chalmers; Dr Rod Chappel; Jonathan Chee; Sheng Chen; Dr Zhiping Chen; Chris Chiu; Matthew Chung; Gabriella Crespi; Dr Blessing Crimeen-Irwin; Joanna Crowston; Assoc Prof Elizabeth Dax; Andrew Deans; Dr Bryce Van Denderen; Stirling Dick; Wayne Dimech; Caroline Dobrzalak; Cathryn Dunkley; Sally Emini; Sarah Emmett; Thu-Anh Erickson; Rosanna Fahmy; Dr Susanne Feil; Dr Barbara Francis; Stacey Fynch; Sandra Galic; John Gooi; Ankita Goradia; Mike Gorman; Dr

Kate Graham; Dr Andrew Hammet; Nancy Hancock; Helen Hasler; Assoc Prof Jorg Heierhorst; Kimberly Hewitt; Patricia Ho; Nicholas Hoch; Jane Honeyman; Dexing Huang; Dr Honor Hugo; Dr David Izon; Gaurang Jhala; Dr Anne Johnston; Michael Jovanovic; Sabine Jurado; Marina Karakaltsas; Frosa Katsis; Assoc Prof Darren Kelly; Prof Bruce Kemp; Dr John King-Scott; Shie Foong Kok; Cameron Kos; Dr Bala Krishna-Murthy; Clare Lacey; Xianning Lai; Sally Land; Dr Mark Lanigan; Sara Lawrence; Virginia Leopold; Dr Rong Li; Dr Tom Loudovaris; Nilukshi Malawa-Arachchi; Julie Malyon; Dr Stuart Mannering; Lina Mariana; Emeritus Prof Jack Martin; Dr Tony Mason; Tamara McDonald; Narelle McGregor; Mark McKenzie; Dr Carol McNeese; Dr Dale McPhee; Dr Belinda Michell; Dr Francis Milat; Dr Luke Miles; Dr Zia Mollah; Hayley Moon; Dr Craig Morton; Dr Rachel Mudge; James Mugg; David Murfitt; Michelle Myers; Hooi Ling Ng; Dr Jon Oakhill; Katherine O'Connell; Dr Done Onan-Asik; Hayley O'Neil; Louie Opasinov; Lena Panagiotopoulos; Alison Parker; Lorien Parker; Prof Michael Parker; Rochelle Ayala Perez; Dr Galina Polekhina; Dr Sueli Pompolo; Ingrid Poulton; Dr David Prior; Dr Louise Purton; David Rees; Kim Richards; Helen Ritchie; Megan Russel; Christopher Ryan; Dr Martin Sadowski; Derya Sahin; Dimitra Samaras; Natalie Sanders; Dr Boris Sarcevic; Alice Schofield; Dr John Scott; Dr Manisha Shah; Dr Natalie Sims; Dr Monique Smeets; Kathy Smeh; Annabel Southey; Dr

Robyn Starr; Dr Rohan Steel; Dr Greg Steinberg; Kher Shing Tan; Julian Tang; Nora Tenis; Dr Helen Thomas; Assoc Prof Rick Thompson; Dr Anne Thorburn; Emma Thorburn; Dr John Tomasov; Peter Tonoli; Frank Torzillo; Jenny Trinh; Bonnie La Velle; Dr Anne Verhagen; Sarah Vickery; Robert Vinoya; Emma Walker; Sandy Walker; Dr Carl Walkley; Dr Kim Wilson

Grants

Bernard O

Regulation of microtubule dynamics by LIM kinase1. NHMRC, (2006-2008), \$377,625

Regulation of the actin cytoskeleton by LIM kinase 2. ARC, (2008), \$195,000

Heierhorst J

Regulation and assembly of nuclear DNA repair centres. NHMRC, (2006-2008), \$447,750

DNA lesions involved in chemotherapy responses and their repair. NHMRC, (2006-2008), \$391,250

Identification of telomere-specific recombination pathways. NHMRC, (2008-2010), \$518,250

Izon D

Discovery of T cell oncogenes by using a functional retroviral cDNA library screen. NHMRC, (2006-2008), \$543,750

Kemp B

Regulation of lipid metabolism by AMP activated protein kinase. NHMRC, (2006-2008), \$466,875

Kemp B, Chen Z, Michell B

Regulation of protein kinases and their substrates. NHMRC, (2008-2010), \$531,000

Loudovaris T

Equipment Grant. Rebecca L Cooper Foundation, (2008), \$14,449

Mannering S

Project Grant. St. Vincent's Research Endowment Fund, (2008), \$15,000

Martin T, Pivonka P, Dunstan CR

Bone regulation – cell interactions to disease. ARC, (2008), \$255,000

McPhee D, Wilson K, Dax E

Potent broadly reactive neutralizing HIV-1 monoclonal antibodies. NHMRC, (2008-2010), \$444,375

Miles L

Structural studies of the interactions of gamm-secretase modulators with amyloid beta peptide. The Mason Foundation, (2008), \$50,000

Parker M

Determining the structure of a soluble cytokine receptor complex. NHMRC, (2006-2008), \$498,750

Structural studies of bacterial pore-forming protein toxins. NHMRC, (2006-2008), \$498,750

Parker M, Chai SY

Structure/function studies of insulin regulated membrane aminopeptidase. NHMRC, (2008-2010), \$505,500

Polekhina G, Waltham M

Structural and drug discovery studies of oxidative stress regulator, thioredoxin-interacting protein. NHMRC, (2007-2009), \$276,750

Purton L

Mechanisms underlying the effects of TNFalpha in bone and haemopoiesis. NHMRC, (2008-2010), \$502,612

Equipment Grant. ANZ Trustees, (2008), \$15,000

Shah M, Thompson EW, Waltham M

Targeting host and tumoral MMP-13 in primary breast cancer and bone metastasis. Komen Foundation, (2008-2011), (USD)\$180,000

Steinberg G

Cytokine signalling and insulin resistance in obesity. NHMRC, (2007-2009), \$492,000

Thompson E

Invasion and metastasis of breast cancer. VBCRC, (2004-2009), \$1,450,000

Thompson E, Waltham M

MMP-13 as a therapeutic target in breast cancer. NHMRC, (2008-2010), \$516,000

Thompson EW, Anderson RL, Yap A, Goodall G, Saunders C, Street I

Targeting tumour dormancy in breast cancer – Think Tank. NBCF, (2008), \$15,000

Thompson EW, Dobrovic A, Choong P, Hill P, Henderson M, Pantel K

Exploring epithelial-mesenchymal interconversions in the breast cancer

metastatic cascade. Cancer Council, (2008-2010), \$285,500

Thomas H, Allison J, Kay T

Apoptotic pathways in pancreatic beta cells leading to type 1 diabetes and transplant rejection. NHMRC, (2008-2010), \$513,750

Walkley C

Understanding the contribution of the blood microenvironment to blood cell regulation. Equity Trustees, (2008), \$16,000

Walsh N

Project Grant. St. Vincent's Research Endowment Fund, (2008), \$15,000

Waltham M

New agents to combat breast cancer metastasis. NBCF, (2008-2009), \$293,250

Molecular profiling vestibular schwannomas. Pratt Foundation, (2006-2008) \$180,000

Watt M

Adipose triglyceride lipase: regulation and implications for the aetiology of insulin resistance. NHMRC, (2008-2010), \$310,500

Wilson K

Detailed investigation of the humoral immune response to HCV to identify diagnostic and prognostic serological markers. NHMRC, (2007-2009), \$372,375

Select international presentations

- Indian Society of Molecular Biology Annual Conference, Mumbai, India
- International Society for Blood Transfusion, Hanoi, Vietnam
- Leukemia and Lymphoma Society Stohlman Scholar Symposium, Kansas City, USA
- National Osteoporosis Foundation of South Africa, Capetown, South Africa
- 13th EASD/JDRF Oxford Workshop, 'Inflammation, islets and immunity', Oxford, UK
- 3e (Evidence, Experts, Exchange) meeting: Methotrexate use in the rheumatic diseases, Paris, France
- 4th International Conference on Bone Involvement in Arthritis, San Margherita Ligure, Italy
- 4th Scientific Meeting of Asia-Pacific Diabetes and Obesity Study Group, Kobe, Japan
- 7th Annual AACR Conference on Frontiers in Cancer Prevention Research, Maryland, USA
- American Diabetes Association 68th Scientific Sessions meeting, San Francisco, USA
- American Society for Bone and Mineral Research Annual Scientific Meeting, Montreal, Canada
- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Melbourne
- BIT's 1st Annual Protein and Peptide Conference (PepCon-2008), 'From Concept to Market', Shenzhen, China
- Cancer Pharmacogenomics Conference, Manipal, India
- Clare Bone Meeting, Clare Valley, SA
- Cold Spring Harbor Symposium on Epithelial Mesenchymal Transitions, Cold Spring Harbor, USA
- Endocrine Society of South Africa, Capetown, South Africa
- FASEB Summer Research Conference 'AMPK in Sickness and Health: From Molecule to Man', Snekkersten, Denmark
- FASEB Summer Research Conference: Yeast Chromosome Structure, Replication and Segregation, Carefree, Arizona, USA
- Gordon Conference on Phosphorylation and G-Proteins mediate signalling networks, New England, USA
- Hypertension 2008, joint congress of 18th Scientific Meeting of the European Society of Hypertension and the 22nd Scientific Meeting of the International Society of Hypertension, Berlin, Germany
- International Bone and Mineral Society Davos Workshops: Bone Biology & Therapeutics, Davis, Switzerland
- International Congress of Endocrinology, Rio de Janeiro, Brazil
- International Society for Blood Transfusion, Macao, China
- International Society of Experimental Hematology (ISEH) 2008, Boston, USA
- Joint MRS-AACR Conference on Metastasis, Vancouver, Canada
- Keystone Meeting on Islet Biology, Utah, USA
- Northern Lights on Prostate Cancer, University of Umea, Umea, Sweden
- Renin Summit, Berlin, Germany
- Second Osteoimmunology Conference, Rhodes, Greece
- The 5th international conference on ubiquitin, ubiquitin-like proteins and cancer, Houston, USA
- The Joint Pacific Rim International Conference on Protein Science and the 4th Asian Oceania Human Proteome Organisation, Cairns
- Tokyo Medical and Dental University Research Symposium, Tokyo, Japan
- US-DOD Era of Hope Conference, Baltimore, USA

Publications

Albiston AL, Morton CJ, Ng HL, Pham V, Yeatman HR, Ye S, Fernando RN, De Bundel D, Ascher DB, Mendelsohn FA, Parker MW, Chai SY 2008, 'Identification and characterisation of a new cognitive enhancer based on inhibition of insulin-regulated aminopeptidase', *FASEB J*, 22, 12, 4209-17

Allan EH, Hausler KD, Wei T, Gooi JH, Quinn JM, Crimeen-Irwin B, Pompolo S, Sims NA, Gillespie MT, Onyia JE, Martin TJ 2008, 'EphrinB2 regulation by PTH and PTHrP revealed by molecular profiling in differentiating osteoblasts', *J Bone Miner Res*, 23, 8, 1170-81

Anderson KA, Ribar TJ, Lin F, Noeldner PK, Green MF, Muehlbauer MJ, Witters LA, Kemp BE, Means AR 2008, 'Hypothalamic CaMKK2 contributes to the regulation of energy balance', *Cell Metab*, 7, 5, 377-88

Androulakis S, Schmidberger J, Bate MA, DeGori R, Beitz A, Keong C, Cameron B, McGowan S, Porter CJ, Harrison A, Hunter J, Martin JL, Kobe B, Dobson RC, Parker MW, Whisstock JC, Gray J, Treloar A, Groenewegen D, Dickson N, Buckle AM 2008, 'Federated repositories of X-ray diffraction images', *Acta Crystallogr D Biol Crystallogr*, D64, Pt 7, 810-4

- Angstetra E, Graham KL, Emmett S, Dudek NL, Darwiche R, Ayala-Perez R, Allison J, Santamaria P, Kay TW, Thomas HE 2008, 'In vivo effects of cytokines on pancreatic beta-cells in models of Type I diabetes dependent on CD4(+) T lymphocytes', *Immunol Cell Biol*
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- Blick T, Widodo E, Hugo H, Waltham M, Lenburg ME, Neve RM, Thompson EW 2008, 'Epithelial mesenchymal transition traits in human breast cancer cell lines', *Clin Exp Metastasis*, 25, 6, 629-42
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- Burgess BR, Dobson RC, Bailey MF, Atkinson SC, Griffin MD, Jameson GB, Parker MW, Gerrard JA, Perugini MA 2008, 'Structure and evolution of a novel dimeric enzyme from a clinically important bacterial pathogen', *J Biol Chem*, 283, 41, 27598-603
- Campbell DJ 2008, 'Can measurement of B-type natriuretic peptide levels improve cardiovascular disease prevention?', *Clin Exp Pharmacol Physiol*, 35, 4, 442-6
- Campbell DJ 2008, 'Can the study of female rats help our understanding of women?', *Hypertension*, 52, 6, e142; author reply e43-4
- Campbell DJ 2008, 'Critical review of prorenin and (pro)renin receptor research', *Hypertension*, 51, 5, 1259-64
- Campbell DJ 2008, 'Interpretation of plasma renin concentration in patients receiving aliskiren therapy', *Hypertension*, 51, 1, 15-8
- Campbell DJ 2008, 'Why do men and women differ in their risk of myocardial infarction?' *Eur Heart J*, 29, 7, 835-6
- Campbell PD, Estella E, Dudek NL, Jhala G, Thomas HE, Kay TW, Mannering SI 2008, 'Cytotoxic T-lymphocyte-mediated killing of human pancreatic islet cells in vitro', *Hum Immunol*, 69, 9, 543-51
- Chai SY, Yeatman HR, Parker MW, Ascher DB, Thompson PE, Mulvey HT, Albiston AL 2008, 'Development of cognitive enhancers based on inhibition of insulin-regulated aminopeptidase', *BMC Neurosci*, 9 Suppl 2, S14
- Chan AC, Smeets MF, Izon DJ 2008, 'An in vivo functional genetic screen for suppressors of the Rag1^{-/-} T-cell defect', *Mol Immunol*, 45, 3, 682-9
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