PROMIS

PROSTATE CANCER METASTASIS
ProMis is a new collaborative International Prostate Cancer research consortium dedicated to addressing the mechanisms behind, and ultimately developing new treatments for, lethal prostate bone metastasis.
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ProMis draws on highly experienced Prostate Cancer investigators as well as experts from other fields including bone biology, breast cancer research, transcriptomics and genomics.

Together, we will develop novel models of Prostate Cancer metastasis, assemble world-class clinical cohorts of dormant and overt bone metastases, and interrogate these platforms by bringing to bear our new technologies, including single cell genomics/transcriptomics, high resolution genome mapping and single cell intravital imaging of dormant cancer cells, to the challenge.

Successful completion of our goals will deliver near-term transformative insights into the biology and heterogeneity of Prostate Cancer dormancy in bone and metastatic growth and a new era of Prostate Cancer therapeutics.

Proudly funded by:

Prostate Cancer Foundation of Australia

Movember
Prostate cancer is the second most common cancer in men and causes 3300 deaths in Australia and 250,000 deaths per annum, world-wide. Although treatments are available for localised disease, 40% of patients will eventually develop metastases, specifically metastases to the skeleton. While patients with metastatic prostate cancer may be responsive to initial therapy, the mechanisms responsible for metastatic prostate cancer are unknown and as a result metastatic disease remains incurable and is invariably lethal.

**THE CHALLENGE OF PROSTATE CANCER BONE METASTASIS**

With no cure, understanding how prostate cancers develop in the skeleton, particularly what controls prostate cancer cell dormancy and the transition from dormancy to active prostate metastasis growth, is critical if we are to develop new approaches to treatment. This will depend on being able to find, and study, the individual prostate cancer cells that initiate the development of cancers that grow in bone. Until now, addressing these questions has not been technically possible. However, **ProMis** (Prostate Cancer Metastasis) uniquely brings together researchers from different backgrounds, each with diverse skills and proven track records in their areas of expertise, to tackle this problem. Our Team has now developed unique clinical cohorts and animal models of disease, new single cell imaging techniques that allow us for the first time to identify individual dormant cancer cells in the skeleton, and new single cell genetic techniques that will allow us to study the cells that cause prostate cancer bone metastasis.

**THE PROMIS RESEARCH PROGRAM**

**ProMis** will use our unique skills, novel technologies and resources to test the hypothesis that ‘Prostate cancer cells are retained in a dormant state in the skeleton through interaction with a specific microenvironment and can be released from dormancy to form overt bone metastases by cell autonomous changes (‘intrinsic’) and/or microenvironment (‘extrinsic’) changes. These interactions represent new opportunities for therapeutic intervention’.

**ProMis** will focus on four interconnected areas with the specific aims of:

1. Defining the cellular and molecular mechanisms that control the transition from prostate dormancy to active tumour growth in bone.
2. Determining the impact of existing therapies on the mechanisms controlling the transition from dormancy to growth.
3. Targeting new mechanisms to prevent and treat prostate bone metastasis.
4. Developing approaches to widening awareness of prostate bone metastasis.

**The ProMis Team**

To address these challenges **ProMis** has assembled a world-class team of researchers, each with unique skills and expertise, from some of the most prestigious Institutes from across the world. **ProMis** is led by three centres in Australia – the Garvan Institute of Medical Research, the Department of Surgery at the University of Melbourne and the Department of Biochemistry at La Trobe University, Melbourne. We have three key partners from the United States – the Institute of Precision Medicine, Weill Medical College, New York, the J. Craig Venter Institute, San Diego and the Department of Surgery, University of California San Diego, and key partners in Europe, the Mellanby Centre for Bone Research, University of Sheffield, UK, the Nuffield Department of Surgery, University of Oxford, UK and Institute of Molecular Medicine, Hospital de Santa Maria, Lisbon. **ProMis** will also capitalise on a number of unique research facilities within partner institutes, including the Centre for Clinical Genomics and the Small Animal Imaging Facility at the Garvan Institute of Medical Research.

**ProMis** is led by eight Team Leaders each responsible for a key element of the Program. Team Leaders each coordinate a group consisting of early career researchers and research students as well as more experienced researchers who individually are leaders in their own field. A critical element of **ProMis** is the commitment to train a new generation of researchers in the skills required to tackle prostate cancer metastasis. Integrated within ProMis are basic scientists and clinical researchers, which ensures both clinical relevance and the rapid translation of our discoveries for patient benefit.
PARTNER INSTITUTES

J. CRAIG VENTER INSTITUTE, SAN DIEGO

UNIVERSITY OF CALIFORNIA (UC) SAN DIEGO MOORES CANCER CENTER, SAN DIEGO

INSTITUTE FOR PRECISION MEDICINE OF NEW YORK — PRESBYTERIAN HOSPITAL AND WEILL CORNELL MEDICAL COLLEGE, NEW YORK

NUFFIELD DEPARTMENT OF SURGERY, OXFORD UNIVERSITY, OXFORD

INSTITUTE OF MOLECULAR MEDICINE, HOSPITAL DE SANTA MARIA, LISBON

THE MELLANBY CENTRE FOR BONE RESEARCH, UNIVERSITY OF SHEFFIELD, SHEFFIELD
THE TEAM

TEAM LEADERS

PROF PETER CROUCHER
A/PROF HIMISHA BELTRAN
DR NIALL CORCORAN
PROF TONY COSTELLO

TEAM MEMBERS

DR NIKOLA BASCHUK
DR EVA CHAN
PROF SUSAN CLARK
PROF LUÍS COSTA
DR COLBY EATON

A/PROF CHRISTINA JAMIESON
PROF ROGER LASKEN
PROF JOHN MATTICK
DR RADHIKA NAIR
DR KATE PATTERSON
THE TEAM

PROF VANESSA HAYES
DR BELINDA PARKER
PROF MIKE ROGERS
DR ALEX SWARBRICK

DR CLAIRE EDWARDS
DR BEN ELSWORTH
A/PROF RUTA GUPTA
PROF FREDDIE HAMDY
A/PROF CHRIS HOVENS

DR DESIERE PETERSEN
DR TRI GIANG PHAN
PROF MARK RUBIN
The Garvan Institute of Medical Research (GIMR) is one of the largest independent medical research institutes in Australia, and forms part of the St Vincent’s Research Precinct in Darlinghurst, Sydney. The Institute was incorporated as an autonomous, non-profit research institute by the NSW Garvan Institute of Medical Research Act in 1984, and is academically affiliated with the University of New South Wales.

The Garvan Institute has over 500 research staff organised around five Research Divisions – Cancer, Diabetes & Obesity, Immunology, Neuroscience, and Bone Biology. Of particular relevance to ProMis is an ongoing collaboration between the Cancer, Immunology and Bone Biology Divisions in the area of bone metastasis. The Institute’s scientific activities are focussed on basic discovery-orientated research into molecular processes underpinning development and disease, and its translation into health applications. Its research expertise includes genomics, epigenomics and bioinformatics, molecular and population genetics, molecular and cellular biology, immunology, physiology, endocrinology, biochemistry, and cell imaging. Emerging areas of strength, which reflect an evolution towards holistic and translational research activities, include major initiatives in clinical genomics, monoclonal antibody development, advanced molecular / cellular imaging technologies and systems biology.

A central theme of the institute’s research philosophy is the elucidation of the basic molecular events underlying human disease. Researchers at the Institute recognise the importance of overlapping involvement of different systems and processes in biological functions. This includes in areas such as cancer and bone homeostasis, and interactions between researchers in these disciplines are resulting in major breakthroughs in the understanding of both normal and disease processes in human biology. It is our vision that basic mechanistic discoveries underpin new insights into important biological problems, and that from this will flow a real understanding of the basis of human disease and development of new therapies that are more targeted and more specific than those currently available.
focusing on translational research and personalised cancer care, our mission is to align world-class cancer research with rapid translation to the clinic to improve outcomes for cancer patients by:
- building world-class facilities and strategic collaborations to enhance advances in science that translate into improved cancer diagnosis, treatment and prevention
- developing integrated, multi-disciplinary, multi-institutional approaches to cancer research and patient care to reduce the impact of cancer in the community
- providing a holistic, compassionate approach to cancer care throughout the entire cancer journey, from diagnosis to full recovery where cure is possible, and supportive care and information to all, with preservation of patient dignity
- establishing world-class educational and training programs to develop high quality researchers and clinicians to optimise translational outcomes.

The Kinghorn Cancer Centre is placed as a major centre in Australia focused on the translation of research breakthroughs into novel diagnostic, prognostic, treatment and prevention options for a number of key National Health Priority cancers including: breast, prostate, GI (pancreas and colorectal) and non-Hodgkins lymphoma. The Kinghorn Cancer Centre will build on its unique strengths to deliver targeted, cost effective, personalised therapies suitable for integration into larger nationwide cancer treatment services.

Bringing together researchers and clinicians onto a single site, TKCC is fostering laboratory research directly driven by clinical challenges, “a bedside to bench” model, and enable research findings to be rapidly translated into clinical application for the diagnosis, treatment and prevention of cancer, with the prospect of improving cancer outcomes for all Australians.

DEPARTMENT OF SURGERY, UNIVERSITY OF MELBOURNE, ROYAL MELBOURNE HOSPITAL | MELBOURNE, AUSTRALIA

The Department of Surgery at The Royal Melbourne Hospital forms the focus for academic activities in surgery for The University of Melbourne and The Royal Melbourne Hospital. Members of the department are involved in research and in both undergraduate and postgraduate teaching in surgery. These activities are undertaken both within the department, and more broadly on the hospital campuses. Research in the department is focused on a number of areas including cardiovascular research, photodynamic therapy, cell signalling and tumour biology. There is a focus on prostate cancer, particularly in the development of advance disease and metastasis.

In addition, the Royal Melbourne Hospital Academic Centre comprises the Departments of Medicine, Surgery, Psychiatry and Radiology at The Royal Melbourne Hospital, as well as the Clinical School. The aims of the Academic Centre as an organisation are to optimise the academic activities involving both teaching and research, and enhance our interactions with the Faculty and University, as well as with the host hospital, The Royal Melbourne Hospital.

DEPARTMENT OF BIOCHEMISTRY
LA TROBE UNIVERSITY | MELBOURNE, AUSTRALIA

The new LIMS institute has established La Trobe University as an international leader in the fields of molecular science and biotechnology. The biochemistry department at LIMS has a strong reputation for research excellence, and continues to be ranked as one of the leading universities in Australia for research in biochemistry and cell biology. A major focus of LIMS is understanding the molecular pathogenesis of disease and the institute is unique in its multidisciplinary approach to studying cancer, including projects spanning immunology, cancer cell biology, invasion and inflammation, epigenetics, therapeutics and proteomics, along with strong structural biology and molecular modelling groups to allow progression from target discovery to drug design. To give researchers an international edge, LIMS houses world-class core research facilities equipped with the latest state-of-the-art equipment including mass spectrometry and proteomics, flow cytomtery, histology, microscopy and imaging, biomolecular interactions, genomics, bioinformatics and models of disease and in vivo imaging.
**J. CRAIG VENTER INSTITUTE | SAN DIEGO, USA**

The J. Craig Venter Institute (JCVI) is a world leader in genomic research fuelled by a team-centred, multidisciplinary approach to large research initiatives. JCVI has a long track-record of creative and interdisciplinary approaches to genomics and has been a leader in large-scale DNA sequence generation and analysis since its founding in 1992 as The Institute for Genomic Research (TIGR). From its inception, JCVI faculty and staff created a dynamic infrastructure and scientific atmosphere that allows for the development and application of state-of-the-art high-throughput methods for generating and analysing biological data in the areas of genomic medicine, infectious disease, microbial and environmental genomics, plant genomics, synthetic biology and bioenergy, and informatics. JCVI published the first complete genome sequence of a free-living organism, that of Haemophilus influenzae in 1995, the first diploid sequence of a human in 2007, and the first synthetic bacterial cell in 2010. With more than 200 scientists and staff located in Maryland and California, the JCVI is one of the largest independent, not-for-profit research institutes in the United States.

**INSTITUTE FOR PRECISION MEDICINE OF NEW YORK – PRESBYTERIAN HOSPITAL AND WEILL CORNELL MEDICAL COLLEGE | NEW YORK, USA**

In January 2013, New York-Presbyterian Hospital and Weill Cornell Medical College created the Institute for Precision Medicine (IPM), a translational research hub to promote molecular diagnostics and therapeutics. Prof Mark Rubin was named as the Institute’s first Director. Relevant to ProMis, patients with metastatic prostate cancer are referred to the Precision Medicine Clinic, led by Himisha Beltran, MD. After informed consent through an IRB approved protocol, metastatic tumour biopsy is performed and both tumour and germline sequencing are performed. Through an integrative sequencing strategy, clinically relevant targets for treatment are identified and reviewed by a multi-disciplinary Precision Medicine Tumour Board. Clinically relevant results are disclosed to the patient and referring clinician, patients are followed prospectively for response to therapy and clinical outcomes, and data is captured in a clinical database.

The state-of-the art IPM Biobank uses novel techniques developed at Weill Cornell to expertly prepare tissue samples, and it provides qualified investigators access to well-annotated human biospecimens in a regulatory compliant manner. Annually, approximately 800 prostate cancer patients are diagnosed and treated at Weill Cornell, and within the past four years, more than 2,000 prostate samples have been collected and stored. Protocols for collection and processing of metastatic samples, particularly sclerotic metastasis, have been developed to ensure that high quality samples are obtained and processed with consideration of patient safety, time to sample preparation, and maximised tumour density. This is an iterative process, and genomic results are monitored and benchmarked to ensure that the processing pipeline is optimal for this activity.

IPM sequencing core equipment includes Illumina 2500 and MiSeq sequencers, Agilent 2100 Bioanalyzer, Nanodrop, Qubit fluorometer, Taqman 7900HT real-time PCR machine, Affymetrix GeneChip platform, GenePix 4000B array reader, Covaris S2 High Performance Ultrasonicator, and Ion Torrent Personal Genome Machine (PGM). Notable assets include several
large-memory, multi-CPU systems (including several 32 core nodes with 384 GB of memory and Infiniband networking) and over 2 TFlops and nearly 600 processor cores of cluster computing power, much of it backed by a high-speed, low latency fiber-optic interconnect. This computational power is backed by a large, 1 Petabyte pool of managed storage. Users’ home directories and most systems are backed-up daily. Additionally, local mirrors of commonly used biological datasets (such as sequence databases, COSMIC, and the Protein Data Bank) are maintained and continuously updated. The IPM computational data analysis pipeline is built on many years of experience in the area of cancer genomics and includes applications for mathematical and statistical modeling, graphics and data visualisation, molecular and systems modeling packages, and many others. The Institute has also implemented visualization tools including a customised cBio cancer genomics portal from Memorial Sloan Kettering for use by laboratory-based investigators, which will facilitate data sharing with other team members as part of this application.
NUFFIELD DEPT. OF SURGICAL SCIENCES & NUFFIELD DEPT. OF ORTHOPAEDICS, RHEUMATOLOGY AND SURGICAL SCIENCES | OXFORD, UK

The Bone Oncology Research Group is jointly appointed between NDS & NDORMS, and is located within the Botnar Research Centre, University of Oxford Institute of Musculoskeletal Research Sciences. The Botnar Research Centre is on the grounds of the Nuffield Orthopaedic Centre, enabling basic researchers to work alongside clinicians to facilitate the translation of basic research from bench to bedside. The Bone Oncology Group is headed by Dr Claire Edwards and incorporates cell and molecular approaches, murine models of cancer-induced bone disease and translational research utilising clinical samples. Research is focused predominantly on multiple myeloma and prostate cancer bone metastases. Within NDS are many clinical cancer specialties, including urology, providing excellent interactions with urologists, and facilitating acquisition of clinical samples. Prof Freddie Hamdy is the Chief Investigator of many studies, including the ProtecT (Prostate testing for cancer and Treatment) and the ProMPT study (Prostate Mechanisms of Progression and Treatment), providing and invaluable source of sequential samples from men with prostate cancer.

INSTITUTE OF MOLECULAR MEDICINE, HOSPITAL DE SANTA MARIA | LISBON, PORTUGAL

The Oncology Division at Hospital de Santa Maria has focused on bone metastases since 1995 and has been involved in 12 clinical trials (breast, colon, prostate cancer and other solid tumours, and bone metastases), and is currently active in 17 international clinical studies. Research focuses on the role of collagen fragments as growth/survival factors for cancer cells and the hypothesis that matrix metalloproteases have a central role in bone metastasis progression and resistance to bisphosphonates. Since 2007 the Division has developed a program of biobanking bone metastases, with serum and urine samples from the same patients. It has also been involved in the discovery of bone metastasis gene signatures in human samples and participated in phase 2 and phase 3 trials with new bone-target agents to treat bone metastases.
KINGHORN CENTRE FOR CLINICAL GENOMICS (KCCG) GARVAN INSTITUTE OF MEDICAL RESEARCH | SYDNEY, AUSTRALIA

KCCG was established within the Kinghorn Cancer Centre in October 2012 as an initiative of the Garvan Institute. KCCG is a purpose-built facility for undertaking state-of-the-art clinical-grade genomic sequencing. It contains two Illumina HiSeq 2500s, that combined are capable of sequencing 175 clinical-grade exomes (>200X mean coverage) or 10 clinical-grade whole genomes (>40X mean coverage) per week. KCCG is also equipped with ultra-high performance computing that has been tailor-designed for genome informatics. The system, which is housed within the Garvan IT data-centre, comprises 1400 CPU cores, 10 TB of memory and 1 PB of storage. KCCG undertakes collaborative research projects with scientists at the Garvan Institute as well as external partners, in all areas of medical research. As well as sequencing and high performance computing, KCCG also undertakes genome-based research to improve the interpretation of genomes and genome variants with the overall aim to further the use of genomic information in patient care.

GARVAN INSTITUTE SMALL ANIMAL IMAGING FACILITY | SYDNEY, AUSTRALIA

The Small Animal Imaging Facility is a state-of-the-art Pathogen Containment level 2 (PC2) facility specifically designed for minimally-invasive longitudinal multimodal imaging and is ideally set up for studying tumour development in the long bones of live mice from the microscopic to macroscopic level. The facility is located within the Biological Testing Facility where experimental animals are housed and is supported by core funded in-house veterinarian, a small animal imaging technician and veterinary staff. In addition to standard imaging technologies the Facility has three unique technologies that place us at the leading edge of the field, these include:

- **IVIS Spectrum and Quantum FX microCT Pre-clinical In Vivo Imaging System.** This multimodal imaging system combines high resolution (up to 20nm) optical imaging of bioluminescent or multispectral fluorescent signals from the tumour cells with microCT scanning of the whole mouse to localise tumours to skeletal and non-skeletal sites, quantify tumour progression and assess the impact of the tumour on bone over time.

- **Zeiss LSM 7MP multi-photon system.** This two-photon microscope is purpose-built to enable deep tissue imaging at subcellular resolution (300nm) in live animals by interrogation with an ultrafast femtosecond-pulsed infra-red laser. The system has been optimised for longitudinal intravital imaging of long bones and makes it possible to directly visualise the steps involved in bony metastases from the initial seeding by single cancer cells to their expansion into colonies. Importantly, it also enables the identification of dormant tumour cells within their niche and the cellular interactions that maintain this dormant state.

- **Leica SP8 compact OPO multiphoton system.** This state-of-the-art dual colour multiphoton microscope enables simultaneous high-resolution imaging of subcellular molecular events to be monitored from deep within live disease tissue. The optical parametric oscillator (OPO) allows dual imaging of simultaneous events to be imaged in real-time while the inbuilt FLIM-FRET system allows us to apply molecular biosensor FRET imaging to disease tissue. The SP8 is also set up to allow intravital imaging through optical windows to monitor longitudinal molecular changes in response to drug treatment and combination therapy.
The Australian Prostate Cancer Research Centre New South Wales (APCRC NSW) is a newly established and funded centre and is part of the national APCRC initiative that includes centres within Victoria and Queensland. The multi-institutional NSW centre brings together both clinical and basic prostate cancer researchers from St Vincent’s Clinic and Hospital, St Vincent’s Prostate Cancer Centre, The Kinghorn Cancer Centre, The Garvan Institute of Medical Research, Royal Prince Alfred, Concord and Royal North Shore Hospitals and the Chris O’Brien Lifehouse. The APCRC NSW is led by the Director Prof Phillip Stricker (urologist, St Vincent’s Prostate Cancer Centre) and committee members Prof Susan Clark (scientist, The Garvan Institute of Medical Research/The Kinghorn Cancer Centre), Prof Vanessa Hayes (scientist, The Garvan Institute of Medical Research/The Kinghorn Cancer Centre and the University of Sydney Medical School), A/Prof Lisa Horvath (medical oncologist, Royal Prince Alfred Hospital/Chris O’Brien Lifehouse and The Garvan Institute of Medical Research/The Kinghorn Cancer Centre), Prof James Kench (pathologist, Royal Prince Alfred Hospital and The Garvan Institute of Medical Research/The Kinghorn Cancer Centre) and Dr Kris Rasiah (urologist, Royal North Shore Hospital and The Garvan Institute of Medical Research/The Kinghorn Cancer Centre). The central core of the APCRC NSW includes a biobank and database with over >12,000 cases of men diagnosed with prostate cancer and initiated in the 1990s with almost 20 years of follow-up.

The Federal Government established and funded the Australian Prostate Cancer Research Centre at Epworth Healthcare in Victoria in 2008. Since this time the APCRC Victoria has led a number of exciting advancements in prostate cancer research including:

- **Development of novel risk stratification tests for detection of high risk disease in the early stages of the disease:** Determining the potential lethality of prostate cancer at an early stage would have a significant impact upon disease outcome. We are using both unbiased screens and hypothesis driven approaches a number of different biological specimens for potential markers of clinical outcome. We have identified 2 lead candidates that have the potential to identify the presence of high-risk disease through the identification of an associated field effect, which now require translation into a more clinically useful platform, and then analytic and clinical validation. To do this we have engaged with a number of research groups (i.e. University of Western Australia, University of Melbourne) for access to independent validation cohorts, as well as having preliminary discussions with prospective commercial partners. In addition, within the next 12 months we anticipate that our lethal program will deliver a tissue based metastatic signature that may be similarly translated into a clinically useful test.

- **Lethal Sequencing Program:** The multidimensional analysis of paired primary and metastatic prostate samples, including bone metastasis, is a unique program worldwide, and has attracted significant interest and collaboration from major groups worldwide (i.e. Sanger Centre, Cancer Research UK, University of British Columbia). The unique datasets generated have formed the basis of formal collaborations going forward, with both national and international groups.

- **Engagement of public and private practitioners not usually associated with research:** Prostate cancer research in Victoria has traditionally taken the form of commercially driven phase 3 studies in stand-alone urology or medical oncology units. As a significant proportion of prostate cancer patients are diagnosed and treated in the private sector, this traditional model of research delivery may exclude insured patients access to potentially beneficial new treatments, while limiting research capacity by decreasing the potential pool of recruitable patients. Through our advanced prostate cancer clinic we have been able to engage large numbers of urologists and medical oncologists from both the public and private sector, across multiple catchments, with our investigator-initiated trials. This engagement facilitates large-scale validation pipeline opportunities for the key areas of need we have identified in patient care, as well as the real therapeutic opportunity offered by our trials.
Prof Croucher graduated with a BSc in Zoology from University College Cardiff in 1987 and completed a PhD at the University of Wales, College of Medicine, Cardiff, in 1990. Prof Croucher’s postdoctoral training was in the Department of Medicine at the University of Cambridge and in the Department of Human Metabolism and Clinical Biochemistry, University of Sheffield. In 1997, Peter was awarded a prestigious five-year Bennett Senior Fellowship by the Leukaemia Research Fund. He relocated to the University of Oxford, Institute of Musculoskeletal Sciences as a Senior Research Fellow in 2001 and then returned to the School of Medicine and Biomedical Sciences at the University of Sheffield in 2003 as Professor of Bone Biology. In 2009 he was appointed Head of the Department of Human Metabolism and Director of the Mellanby Centre for Bone Research. In 2011, Prof Croucher moved to the Garvan Institute of Medical Research where he is now Head of the Bone Biology Division.

Prof Croucher’s principal research interest is in understanding how tumours grow in bone and cause bone disease, particularly the haematological malignancy multiple myeloma, and breast and prostate cancer bone metastasis. This has been based on the development of some of the most robust experimental models available of cancers that grow in bone, particular models of tumour cell dormancy and activation. This has been underpinned by ‘state of the art’ imaging technology, including two-photon intra-vital imaging, three-dimensional bioluminescence imaging and ex vivo and in vivo micro-CT imaging, along with detailed dynamic bone histomorphometric techniques. Prof Croucher’s early research focused upon the role of the RANKL pathway in mediating the destructive osteolytic bone disease seen in multiple myeloma and has seen new drugs targeting this pathway move into the final stages of clinical development. More recently the focus has been on determining the role of the Wnt pathway in regulating osteoblast suppression, which has also resulted in the development of new agents to stimulate bone repair. However, most recently his research has switched to investigate the role of the local bone microenvironment in regulating the critical events associated with tumour cell colonisation of the skeleton, engagement in the ‘bone metastasis niche’ and in regulating tumour cell dormancy and activation. This has led to entirely new ways of thinking about how bone cells control bone metastasis. Prof Croucher’s research is currently funded by the Cancer Council, Cancer Research UK, the Wellcome Trust and the European Union.
After receiving her medical degree from New York Medical College in 2004, Dr Beltran completed her residency training in Internal Medicine at the University of Pennsylvania and fellowship in Hematology and Medical Oncology at Weill Cornell Medical College. She joined faculty at Weill Cornell Medical College in 2011 as Assistant Professor in Medical Oncology and is Director of the Precision Medicine Clinic of the Institute for Precision Medicine of NewYork Presbyterian-Weill Cornell since its inception in February 2013. She is actively involved in both laboratory-based and clinical research, and she serves as the liaison for several bench-to-bedside translational research efforts at Weill Cornell and with external collaborators.

Dr Beltran’s clinical specialty is in caring for patients with genitourinary malignancies. She has been particularly focused on utilising next generation genomic sequencing and integrative molecular analysis of advanced metastatic prostate tumours towards developing precision cancer care and biomarker driven clinical trials. As Director of the Precision Medicine Clinic, Dr Beltran developed an Institutional Review Board approved protocol to perform sequencing and follow patients prospectively while on systemic therapies. She has worked with a multidisciplinary team to develop effective precision medicine biopsy protocols to enhance tissue collection and quality for sequencing and integrate data with clinical follow-up including response to targeted therapies and survival endpoints. Dr Beltran has a strong track record of clinical translation and has used the science she generated in her laboratory to develop novel biomarkers and a multi-institutional Phase 2 trial of a targeted therapy for patients with neuroendocrine prostate cancer. Her research has also brought increased attention to identifying and targeting androgen receptor (AR) negative prostate cancer as a late stage phenotype in prostate cancer.

Dr Beltran’s research is currently funded by the United States National Institute of Health, United States Department of Defense, Prostate Cancer Foundation, Starr Cancer Foundation, and Damon Runyon Cancer Research Foundation.

Dr Beltran’s research has also brought increased attention to identifying and targeting androgen receptor (AR) negative prostate cancer as a late stage phenotype in prostate cancer.
**ADVANCES IN THE CLINICAL MANAGEMENT OF PROSTATE CANCER**

**DR NIALL CORCORAN**  
**PHD, FRACS (UROL)**

Senior Lecturer, Department of Surgery,  
University of Melbourne  
Director of Translational Research,  
APCRC Epworth

Dr Corcoran is an Australian trained urologist and research scientist with clinical appointments at Royal Melbourne and Geelong Hospitals. He is a senior lecturer in the Department of Surgery, University of Melbourne, where he holds the prestigious David Bickart Clinician Research Fellowship and he is also the Director of Translational Research at the Australian Prostate Cancer Centre Epworth. His clinical interest is in the surgical and multimodal management of high-risk prostate and bladder cancers. His clinical research interests are risk stratification for early prostate cancer, neo-adjuvant and adjuvant trials for high-risk disease and early phase clinical studies for castration-resistant disease. His basic research interest lies in the molecular events underlying the development and progression of lethal prostate cancer, the discovery and development of new agents for high-risk disease.

Dr Corcoran graduated MB BCh BAO (First Class Honours) from the University College Dublin in 1998, and undertook his basic surgical training through the Royal College of Surgeons in Ireland, gaining admission as an associate fellow in 2001. In 2002 he immigrated to Australia and enrolled in a PhD in the molecular biology of prostate cancer through the University of Melbourne under the supervision of Dr Hovens and Prof Costello, graduating in 2006. During his studies he discovered that one particular form of selenium (sodium selenate) is a specific activator of the protein phosphatase PP2A, which downregulates PI3K/Akt signalling in prostate cancer cells. On the basis of these discoveries, a number of patent applications were filed, and he co-founded a University of Melbourne spin-off company, Velacor Therapeutics, to commercially develop this novel technology. He successfully raised $1.5 million in venture capital to fund a Phase I trial in patients with castration-resistant prostate cancer, which he designed and recently reported. He also extended these findings to Alzheimer’s disease, where PP2A is implicated in pathological tau hyperphosphorylation and accumulation. Recently he was involved in the design of a Phase II study of sodium selenate in patients with Alzheimer’s disease/Fronto-temporal dementia, which is currently ongoing at the Royal Melbourne Hospital (funded by Velacor).

His clinical research interests are risk stratification for early prostate cancer, neo-adjuvant and adjuvant trials for high-risk disease and early phase clinical studies for castration-resistant disease.
Prof Costello is Professorial Fellow & Head Department of Urology, The Royal Melbourne Hospital, affiliated with Department of Surgery, University of Melbourne. His major interest is prostatic cancer – localised therapy and emerging treatments for advanced metastatic prostate cancer.

In 1998 he completed his Doctorate in Medicine by thesis on Laser tissue interaction and application of lasers in prostatic surgery. He was the first urologist to use lasers to treat benign prostatic hyperplasia and has had international recognition in this field.

Prof Costello was trained in surgery in Melbourne and then subsequently completed fellowship training at the University of Texas, MD Anderson Hospital & Cancer Centre, and the London Hospital in the University of London.

His current interest is in the development of drug treatment for metastatic prostate cancer and in clinical application of robotics in prostate cancer surgery. He heads the largest robotic surgery program in Australia and has been invited to teach the technique of robotic prostatectomy for prostate cancer surgery at the American Association of Urological Surgery Annual General Meeting on several occasions.

Prof Costello was elected to membership of the American Association of Genitourinary Surgeons in 2004. He is also an invited member of the International Advisory Board of the Cleveland Clinic Urological Department.

In 2005 he attracted grants from the Victorian Government, University of Melbourne, and the University of Queensland for $1.8 million for development of a novel biological treatment of hormonal refractory prostate cancer. This substance is now being trialled in phase I treatment for men with hormonal refractory prostate cancer.

Prof Costello has an established international urologic oncology fellowship program commencing in 1991 and there have been over 45 fellows from all parts of the world come for periods of one year and beyond to learn postgraduate urologic oncology surgery.

In 2007 Prof Costello initiated the establishment of the Victorian Prostate Cancer Research Collaborative, a network of research institutes interested in prostate cancer research housed at The Royal Melbourne Hospital. This is a Victorian State Government $1.5 million supported initiative.

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**DEVELOPING NEW TREATMENT STRATEGIES IN LOCALISED AND ADVANCED PROSTATE CANCER**

**PROF TONY COSTELLO**

MD, FRACS, FRCSI (HON), MBBS

Director of Urology, The Royal Melbourne Hospital

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**IN 2007 PROF COSTELLO INITIATED THE ESTABLISHMENT OF THE VICTORIAN PROSTATE CANCER RESEARCH COLLABORATIVE...**
Prof Vanessa Hayes BSc, BSc Hons, MSc, PhD
Professor, Head of Laboratory for Human Comparative and Prostate Cancer Genomics, Garvan Institute of Medical Research
Petre Chair of Prostate Cancer, University of Sydney

Prof Hayes graduated with a BSc (1992), BSc Honours (1993) and MSc degrees (1996) from the University of Stellenbosch in South Africa, where she started her research career in human and cancer genetics. She completed a PhD at the University of Groningen, The Netherlands in 1999, defining the genetic landscape of key regulator genes driving common human cancers. Returning to South Africa briefly, she headed a Genetics Laboratory focused on genetic risk factors associated with HIV/AIDS, while initiating her interest in prostate cancer. In 2003 she was recruited to the Garvan Institute of Medical Research in Sydney where she led a Cancer Genetics group with a major focus defining prostate cancer genetic risk factors in Australian men. During this time she was awarded the Cancer Institute of New South Wales Premier’s Award for Cancer Research Fellow (2007), an Australian Young Tall Poppy Award for Science (2008) and the Australian Academy of Science Inaugural Ruth Stephens Gani Medal for Human Genetics (2008). In 2008 she moved to the Children’s Cancer Institute of Australia to establish a research laboratory in genomics, acquiring one of the countries first next generation sequencers. This technology was used to drive two large efforts, namely the Southern African Genome Project (Nature 2010) and the Tasmanian Devil Genome Project (PNAS 2011). During this period she was awarded a Fulbright Professional Scholarship to Penn State University, Pennsylvania (2009) and ultimately resulted in her recruitment to the J. Craig Venter Institute, San Diego, in 2010 as Professor of Genomic Medicine. She has recently returned to Australia and the Garvan Institute of Medical Research in a part-time capacity and will return full-time in 2014 to take up the position of Petre Chair of Prostate Cancer, a conjoint Professorship between the Garvan Institute (The Kinghorn Cancer Centre) and the University of Sydney, and expand the newly established Human Comparative and Prostate Cancer Genomics Laboratory. Additional affiliations include Conjoint, Honorary or Membership Professorship positions at the University of New South Wales (since 2010), University of Limpopo, South Africa (since 2012), and the Cancer Disparities Program, University of California San Diego Moores Cancer Centre (since 2012). Prof Hayes has significant expertise in genomics (whole nuclear and mitochondrial, and targeted genome), genomic technologies (high-throughput to bench-top), genetic variation and classification (in particular human cancer), genome-wide genotyping, epidemiology, bioinformatics, statistics, and prostate cancer genetics. Prof Hayes’s research is currently funded by the United States National Institute of Health.

Hayes has significant expertise in genomics, genomic technologies, genetic variation and classification...
Dr Parker graduated with a PhD (Biochemistry) from La Trobe University in 2002. Her postdoctoral training began in 2001 in the Breast Cancer Program, Department of Oncology at Johns Hopkins University in the field of breast cancer biology and invasion. In 2003, she returned to Australia on a US Army Department of Defense BCRP Postdoctoral Fellowship to join the Metastasis Research Laboratory at the Peter MacCallum Cancer Centre and initiate studies into cell specific mechanisms of metastasis using immunocompetent models. This work initiated new projects in the laboratory that saw Dr Parker attract competitive funding internationally (DOD BCRP Concept Award) and nationally (NHMRC and CCV project grants, NHMRC Career Development Fellowship) and a promotion to Team Leader in 2012. In early 2013, Dr Parker moved to the new La Trobe Institute for Molecular Science at La Trobe University where she is currently Head of the Cancer Microenvironment and Immunology Laboratory.

Dr Parker’s research focuses on the interactions between tumour cells and surrounding “normal cells” that promote cancer invasion and metastasis. She has a particular interest in bone metastasis, including the mechanisms of cancer dormancy and outgrowth in the bone microenvironment. Through use of syngeneic mouse models of cancer, Dr Parker’s laboratory has identified key molecular pathways that are altered in the tumour microenvironment to promote bone metastasis. A focus of the lab is assessing the prognostic and therapeutic potential of targeting such pathways in metastatic disease. Her research is multidisciplinary, crossing cancer biology, metastasis, immunology and therapy. Expertise of the lab includes in vitro and in vivo assessment of metastatic phenotype, immune response and bone degradation, along with visualisation of metastases and protein targets by histopathology and in vivo imaging. One key aspect of research in her laboratory is the tumour-induced suppression of anti-tumour immunity (via altered type I interferon signalling). Her recent publications in this area suggest that apart from co-opting bone cells such as osteoclasts and osteoblasts, tumour cells also need to suppress anti-tumour immunity to survive in the bone environment.

Dr Parker is currently an NHMRC Career Development Fellow and recently received an ARC Future Fellowship to commence in 2014. She also currently holds two NHMRC project grants as CIA.
Prof Mike Rogers graduated from the University of Sheffield (UK) in 1989 with a first class honours in Biochemistry and in 1994 with a PhD in bone pharmacology. Mike moved to the University of Aberdeen in 1997 as a Lecturer, becoming Senior Lecturer in 1999 and Professor of Musculoskeletal Pharmacology in 2003. From 2005-2010, Prof Rogers led the Musculoskeletal Research Programme, a large, multi-disciplinary team that was recognised as a Centre of Excellence by the European League Against Rheumatism. Prof Rogers served on several European Grant and Fellowship Committees, was a member of the Board of Directors of the International Bone & Mineral Society (IBMS), and a member of four Editorial Boards. He was awarded more than $10.7M in funding (a 5-year program grant, 37 project and equipment grants, 17 grants from 9 different pharmaceutical companies). Prof Rogers was twice the first recipient of international young investigator awards – the Iain T Boyle Award from the European Calcified Tissue Society and the Herbert Fleisch Award from the IBMS. Prof Rogers relocated to the Garvan Institute in 2012 to establish a Bone Therapeutics Laboratory within the expanding Bone Biology Division.

Prof Rogers is internationally recognised as an authority on bone cell biology and world leader in the molecular pharmacology of bisphosphonates, a blockbuster class of drugs used worldwide for common bone disorders including post-menopausal osteoporosis and cancer-associated bone disease. Prof Rogers’s team discovered two distinct molecular mechanisms of action of bisphosphonates that involve either the formation of toxic metabolites or inhibition of the cholesterol biosynthetic pathway in osteoclasts. These discoveries had a major impact in the field of bone biology, providing insights into the mode of action of these blockbuster drugs and their side-effects, and guiding efforts of the pharmaceutical industry in the design of potential new therapeutic agents and treatment strategies. Additionally, his research has also provided important insights into mechanisms regulating bone cell function and the causes of human bone diseases such as osteopetrosis. Prof Rogers’s research currently seeks to identify the mechanisms underlying the additional beneficial effects of bisphosphonate drugs, particularly their anti-tumour actions and ability to increase survival of patients with multiple myeloma and breast cancer.
Dr Swarbrick graduated with a Bsc (Hons I) in Molecular and Cellular Biology from the University of New South Wales in 1995. After obtaining his PhD in 2003 Dr Swarbrick undertook postdoctoral training with J. Michael Bishop at the University of California, San Francisco, supported by a CJ Martin Travelling Fellowship from the National Health and Medical Research Council (NH&MRC). In 2008 he established the Tumour Progression Laboratory in the Garvan Institute and in 2012 was appointed co-Head of the Breast Translational Oncology Program in the newly commissioned Kinghorn Cancer Centre. Dr Swarbrick is a Career Development Fellow of the NH&MRC.

Dr Swarbrick’s primary research interests are the mechanisms driving inter- and intra-tumoural heterogeneity and the implications for neoplastic progression, metastasis and therapeutic response. Dr Swarbrick has focused on gene regulation by transcriptional networks and microRNAs, with a disease focus on breast and prostate carcinoma and the childhood cancer neuroblastoma. His laboratory combines fundamental discovery techniques including single cell transcriptomics to deconvolute transcriptional heterogeneity with genome-scale functional genomics to functionally annotate new regulatory networks in malignancy. He also has a strong track record in the discovery, development and preclinical validation of novel therapeutic targets and molecular biomarkers, using ‘state of the art’ patient-derived xenograft and transgenic models of disease in collaboration with clinical partners. Dr Swarbrick was the first to demonstrate therapeutic benefit from systemic delivery of a drug-like microRNA inhibitor in vivo, and his laboratory was the first to demonstrate paracrine Hedgehog signaling as a novel therapeutic target for high-risk basal breast cancer. Dr Swarbrick’s research is currently supported by the NH&MRC, National Breast Cancer Foundation, ANZ Breast Cancer Clinical Trials Group, Kids Cancer Project, Prostate Cancer Foundation of Australia and Cancer Council NSW.

Dr Swarbrick was the first to demonstrate therapeutic benefit from systemic delivery of a drug-like microRNA inhibitor in vivo, and his laboratory was the first to demonstrate paracrine Hedgehog signalling as a novel therapeutic target for high-risk basal breast cancer.
Tumour colony and dormant cancer cells
Dr Nikola Baschuk received her PhD from the University of Cologne, Germany in 2009 in the field of cancer immune surveillance. Her postdoctoral studies began in the Department of Cancer Immunology at the Peter MacCallum Cancer Centre, where she joined the Cellular Immunology laboratory, headed by Prof Mark Smyth from 2010-2012 followed by the Cancer Cell Death group of Prof Joe Trapani in 2013. During her time at Peter Mac, she developed strong expertise in innate immunity, infection and cancer. In early 2014, she was recruited to the Cancer Microenvironment and Immunology laboratory of Dr Belinda Parker at the La Trobe Institute of Molecular Science where she is currently a Research Fellow. Dr Baschuk's main research interest is to understand the dynamics and complexity of immune responses during infection and cancer, with a particular interest in immunoregulation of metastasis. Her current research focuses on the interaction between prostate cancer cells and the immune system specifically within the bone microenvironment, and how such interactions impact metastatic spread and the potential of immunostimulatory therapies. This includes dissecting the specific immune signals and immune cells that control metastatic outgrowth from dormancy and can be targeted as novel therapies to prevent metastatic outgrowth in bone.

Dr Baschuk’s main research interest is to understand the dynamics and complexity of immune responses during infection and cancer, with a particular interest in immunoregulation of metastasis.
Dr Chan graduated with a BSc (Honours) in Bioinformatics in 2002 and completed a PhD in Computational Genetics and Genomics at the University of New South Wales in 2007. Dr Chan’s postdoctoral training was in the Department of Livestock Industries at the Commonwealth Scientific and Industrial Research Organisation (QLD, Australia) and in the Department of Plant Sciences at the University of California, Davis (CA, USA). In 2009, Eva took up a position as the Statistical Genetics Lead at the Vegetable Seeds Division of Monsanto Company, in California. In 2013, Eva returned to Sydney where she is now a Senior Research Scientist at the Garvan Institute of Medical Research.

Dr Chan’s principal research interest is in developing and applying statistical and bioinformatics approaches to better understand genetic and genomic variation. This has largely been driven by continued rapid advancements in high-throughput data generation technologies; the -omics era. Dr Chan’s early research focused on understanding the genetic architecture, and quantifying the natural diversity, of the transcriptome and metabolome. More recently the focus has been on linking measurable traits (phenotypes) with both the genotypes of individuals as well as genomic profiles of subpopulations. However, most recently her research has switched to investigating the diversity of human kind at the level of whole genomes and mitochondrial genomes, with aimed emphasis on elucidating the extent of variation within and between cell types, such as “normal” and cancer cells.

**DR CHAN’S PRINCIPAL RESEARCH INTEREST IS IN DEVELOPING AND APPLYING STATISTICAL AND BIOINFORMATICS APPROACHES TO BETTER UNDERSTAND GENETIC AND GENOMIC VARIATION.**
Prof Susan Clark BSc (Hons 1), PhD
Professor, Head of Laboratory for Epigenetics Research
Acting Head, Cancer Research Division, The Kinghorn Cancer Centre

Prof Clark has a highly acclaimed international reputation for her work in cancer epigenetics. Prof Clark is currently Acting Director, Cancer Division, The Kinghorn Cancer Centre and also heads the Cancer Epigenetics Program at the Garvan Institute of Medical Research in Sydney, Australia. She graduated in 1982 with a PhD in Biochemistry, University of Adelaide and then spent ten years in Genetic Technology before returning to basic research in gene regulation in 1992. Her studies over the last twenty years have initiated profound questions about the importance of epigenetics in early development and in disease, especially in cancer. She has made ground-breaking discoveries relating to DNA methylation patterns in normal and cancer genomes, that have led to the commercialisation of new methylation-based tests for early cancer detection. The techniques she pioneered in the early 1990s, including bisulphite sequencing, have revolutionised and now underpin a new era in epigen“omic” research. She was founding member of IHEC (International Human Epigenome Consortium) and led the formation of the AEpiA (Australian Epigenetics Alliance). She has a number of awards including the RPAH Research Medal in 2002, Julian Wells Medal in 2003, “Biochemisch Analytik Preis” for outstanding contribution for Methylation analysis in 2004. In 2006 was elected a Fellow of the World Technology Network for Biotechnology, in 2009 was awarded one of Australia’s “Top Ten” National Health and Medical Research (NH&MRC) Project Scientists and the Rotary Award for Vocational Excellence in 2012.

Prof Clark’s research is now focused on the development of next generation epigenome sequencing technologies and development of bioinformatics tools to analyse and integrate epigenetic landscapes in both normal and prostate cancer cells. Epigenetic information determines the structure of DNA, that is how DNA is organised in the cell and determines which genes or noncoding RNAs are expressed in normal development but it can also be influenced by environmental factors and potentially inherited between generations providing risk factors for development of cancer. Prof Clark’s current work is aimed at understanding how the pattern of spatial and temporal epigenetic processes are controlled, and how disruption of these processes contributes to cancer and other diseases; to mediate the translation of this knowledge into the clinical setting to improve health outcomes, through development of epigenetic-based biomarkers and potential therapeutic targets; and to foster opportunities for talented researchers to build their careers in cancer epigenomic research in Australia.
Prof Costa is Professor of Medicine at the Lisbon Medical School – University of Lisbon, Portugal and he has been the head of the Clinical Translational Oncology Research Unit at the Institute of Molecular Medicine (IMM) since 2007. Prof Costa serves also as director of Oncology Division at Hospital de Santa Maria in Lisbon since 2005. At the School of Medicine he is the Coordinator Professor of “Oncobiologia” a new teaching unit that aims to teach the understanding of clinical oncology through molecular medicine, and he acts as member of the Editorial board of Harvard Medical School Portugal Program.

Prof Costa is the IMM Portuguese representative of the Global Cancer Genomics Consortium.

Prof Costa acts also as an expert for grant reviews at the European Research Council, the Cancer Research UK, and CAIBER (Spanish Clinical Research Network), and the French National Cancer Institute. Prof Costa’s clinical research, publications and scientific presentations have primarily focused on bone metastases, related to breast cancer, and other solid tumours. He has published various peer-reviewed papers discussing these topics.
Dr Eaton graduated with a BSc in Anatomy and Experimental Pathology from the University of St Andrews, Fife, Scotland in 1978. He subsequently studied at the Tenovus Institute for Cancer Research in Cardiff and completed a PhD at the University of Wales, College of Medicine in 1984. Dr Eaton undertook postdoctoral studies at the Tenovus Institute until his appointment as lecturer in the Department of Surgery, University of Sheffield in 1994. In 1998 he moved to the Department of Human Metabolism and Clinical Biochemistry, University of Sheffield and later joined Professor Freddie Hamdy in the Department of Academic Urology in 2000. He became a Senior Lecturer in 2004 and moved to the Academic Unit of Bone Biology in 2008.

Throughout his research career, Dr Eaton’s research has centred on prostate cancer. He has developed a number of novel in vitro and in vivo model systems to study the regulation of growth and survival of prostatic cancer cells and their cellular interactions with other cell populations. His recent interests are focused on defining the populations of prostatic cancer cells that act as the ‘seed’ for the initiation of bone metastases and identifying the mechanisms by which these cells survive and proliferate in the bone microenvironment. In particular, his studies using human prostate cancer models have recently shown that even in cell lines that proliferate rapidly in vitro, the cells that arrive and initially take up residency in bone, when cells are injected into experimental animals, are mitotically dormant and remain so for extended periods. Only a small subset of these cells eventually form proliferating lesions. This is an important observation suggesting that the imperative for tumour cells is to survive in new environments and not necessarily to proliferate. Current studies are focused on the mechanisms controlling dormancy and on strategies to kill dormant tumour cells.

Dr Eaton’s research is currently funded by Cancer Research UK (CRUK): Programme grant: ‘Defining the metastatic niche’ and he has recent received extensive funding from the EU (FP6) on several programmes that have established collaborative networks across the EU (PRIMA, PROMET, P-Mark). In particular he has strong collaborations with the University of Leiden (Dr Gabri van der Pluijm) and the University of Bern (Dr Marco Cecchini).
Dr Edwards graduated from the University of Sheffield with a first class honours degree in Pharmacology in 1995. Her interest in bone oncology began with her PhD studies, and she completed a PhD at the University of Sheffield in 1999. She undertook postdoctoral studies at the University of Sheffield and the University of Oxford. Dr Edwards then relocated to the University of Texas Health Science Centre at San Antonio, and subsequently Vanderbilt University to work with the late Prof Gregory Mundy as an Assistant Professor. In 2010, she was recruited to the University of Oxford, where she is currently a University Lecturer in Bone Oncology.

Dr Edwards’ research is centred around the cellular and molecular mechanisms that mediate tumour growth within bone and the development of cancer-induced bone disease, with a particular focus on multiple myeloma and prostate cancer bone metastases. Dr Edwards’ early research investigated the role of anti-resorptive drugs such as bisphosphonates, and signalling mechanisms including the RANKL and Wnt signalling pathways. More recently, she has concentrated on the contributions from the host microenvironment, and has developed a murine model enabling the molecular investigation of the host microenvironment in vivo. Her studies have revealed novel roles for bone marrow stromal cells and adipokines in the pathogenesis of cancer-induced bone disease.

Dr Edwards is the recipient of a number of awards, including the European Calcified Tissue Society Iain T. Boyle Award, designed to acknowledge the contributions of the recipient to bone biology. Her research is currently funded by the National Institute of Health/National Cancer Institute, Leukaemia and Lymphoma Research, the Kay Kendall Leukaemia Foundation and the European Union.

Dr Edwards... has developed a murine model enabling the molecular investigation of the host microenvironment in vivo.
Dr Elsworth graduated from the University of Edinburgh with a BSc in Zoology in 2003, obtained a Bioinformatics MRes with distinction from the University of York in 2007 and completed his PhD at the Institute of Evolutionary Biology, University of Edinburgh in 2013. This latter project involved being the sole bioinformatician in the assembly and annotation of the first annelid genome using purely high throughput sequencing (HTS). His first postdoctoral position was working in conjunction with the University of Cambridge on a second genome project, that of a developmental model butterfly. Both genome projects involved implementing bleeding edge techniques and writing novel software solutions where necessary; many of which are used regularly by researchers worldwide.

A new role in the Tumour Progression group at the Garvan Institute will provide the opportunity to apply this experience and knowledge to a more focused biological problem.

With five years experience handling, storing, analysing and visualising HTS data, Dr Elsworth’s research interests lie firmly in the field of modern day sequencing-related bioinformatics. This involves being at the forefront of data generation technology, analytical methods and software design. Moreover, Dr Elsworth has demonstrated that combining all these facets, and bringing multiple data types together into a centralised resource provides an excellent environment to interrogate and analyse large and diverse volumes of data using complex queries. This approach not only provides the ability to observe the system as a whole, but also to delve into the hidden nuances within. Previous projects have demonstrated how this methodology can also allow project collaborators and ultimately the community to access the data in an instant and powerful way.

Key bioinformatics discoveries have included identifying the limitations of HTS with regards to genome and transcriptome studies. This led to the development of a novel algorithm to improve de novo HTS genome assemblies using transcriptome data and a new genome exploration environment. Biological insights within annelids have also been obtained, notably a plant cell wall degrading enzyme unique to earthworms and an expansion of P450 enzymes, which agrees with an observed adaptation to extreme environments.
A/Prof Ruta Gupta was admitted as a Fellow of the Royal College of Pathologists of Australasia in January 2011. Her initial training in pathology included completion of postgraduate training in pathology from Tata Memorial Hospital, India, followed by Fellowships in molecular and advanced diagnostic techniques at Cedars Sinai Medical Centre, United States of America. She holds a Fellowship in Genitourinary pathology from Cedars Sinai Medical Centre, Los Angeles, United States of America under the guidance of Dr Mahul B. Amin (Editor-in-Chief of AJCC Cancer Staging Manual’s eighth edition). She has also worked as an academic fellow in anatomic pathology at The Canberra Hospital and lecturer at the Australian National University, ACT, followed by training in neuropathology at the Royal Prince Alfred Hospital, University of Sydney.

A/Prof Gupta is currently working as a full time staff specialist in the Tissue Pathology and Diagnostic Oncology at the Royal Prince Alfred Hospital. In addition to the busy clinical service, she participates in the Genitourinary Multidisciplinary meetings and contributes to the Head and Neck Oncology and Thyroid Multidisciplinary meetings as a lead Pathologist.

A/Prof Gupta’s research interests principally include genitourinary pathology including renal and prostate cancers and head and neck pathology. Her research efforts are centred on identification of histopathologic prognostic factors and novel biomarkers using immunohistochemical techniques. Her research interests have generated 41 publications in international peer reviewed indexed journals, 50 publication abstracts (5 of which have won national and international awards) and 2 textbook chapters based on evidence based medicine and research methodology.

A/PROF RUTA GUPTA
MBBS, MD, FRCPA,
GRAD CERT IN HIGHER EDUCATION

Staff Specialist,
Royal Prince Alfred Hospital
Clinical Associate Professor,
University of Sydney
Visiting Scientist,
The Kinghorn Cancer Centre

A/Prof Gupta’s research efforts are centred on identification of histopathologic prognostic factors and novel biomarkers using immunohistochemical techniques.
Prof Hamdy joined Oxford in October 2008 as Nuffield Professor of Surgery and Head of the Nuffield Department of Surgical Sciences, Professor of Urology and Honorary Consultant Urological Surgeon at the Oxford University Hospitals, as well as Fellow of Balliol College. In November 2010, he was appointed Director of the Division of Surgery and Oncology at the Oxford University Hospitals NHS Trust. This is one of OUHTs largest Divisions with approximately 1400 staff, encompassing a range of surgical and oncological activities with additional specialties such as Haematology and Gastroenterology. He was previously founding Chair of Urology and Director of the Division of Clinical Sciences, then Head of Oncology at the University of Sheffield. He obtained his primary medical degree from the University of Alexandria, Egypt, and trained in Surgery and Urology at Liverpool, Sheffield and Newcastle.

His research activities encompass clinical, translational and basic science programmes on the biology of prostate and bladder cancer. He is Principal/Chief Investigator of many studies including ProtecT (Prostate testing for cancer and Treatment) – a study of case-finding and randomised controlled trial of treatment effectiveness in prostate cancer – the largest of its kind worldwide, funded by HTA NIHR. He was the first recipient of the Crystal Matula award from the European Association of Urology in 1996, the Golden Telescope award from the British Association of Urological Surgeons in 2002, and St Peter’s Medal from the same association in 2012. He was Chairman of the Scientific Committee at the European Association of Urology between 2004-2012, and was elected Fellow of the Academy of Medical Sciences in 2007. He has authored over 230 peer-reviewed articles, and raised to date over £50m in peer-reviewed grants. He leads the Surgical Innovation and Evaluation Theme of the Oxford NIHR Biomedical Research Centre, and is co-Director of the first Surgical Intervention Trials Unit in the UK.

He has introduced robot-assisted surgery to Oxford, and established various multidisciplinary research platforms. More recently, he has secured funding with colleagues to establish a new world-leading Precision Cancer Medicine Institute on the Old Road Campus site. This will take an all-encompassing approach to patients with early stage cancer, to develop, test and implement personalised minimally invasive treatments, combined with targeted diagnosis, imaging and therapy.
A/Prof Hovens is the Director of Scientific Research at the Australian Prostate Cancer Research Centre at Epworth Hospital and Royal Melbourne Hospital. He is a senior scientific investigator on a number of sponsored prostate cancer clinical research programs within the Department of Urology at the Royal Melbourne Hospital and the Department of Surgery at the University of Melbourne. He has served as Chief Scientific Officer and main scientific advisor for two start up, drug development companies he has co-founded, Velacor Therapeutics Pty Ltd and CCH Pharma Pty Ltd.

In 2001, A/Prof Hovens was promoted to Director of the Prostate Cancer Research Center in the Departments of Urology and Surgery, University of Melbourne. He has also worked on the functional characterisation of spread tumour suppressor proteins and made the discovery of a new, tissue-restricted member of the family, Eve-3. His recent work concerns the co-discovery of a small, water soluble inhibitor of the PI3K/Akt pathway which has been extensively characterised in in vitro and in vivo models of prostate and brain cancer.

A/Prof Hovens was awarded a PhD in 1992 for cloning and analysis of the Ryk Receptor Tyrosine Kinase performed at the Ludwig Institute for Cancer Research under the supervision of Drs Andrew Wilks and Ashley Dunn. In 1992, A/Prof Hovens took up a post doctoral position at the Institute for Molecular Biology in Zurich.

In 2008, he and Professor Costello have also received a project grant ($460,000) from the Prostate Cancer Foundation of Australia for their Circulating Cells as Biomarkers for Prostate Cancer study. He has more than 55 peer-reviewed articles and 2 Book Chapters.

A/Prof Hovens received $7.5m from the Federal Government with Professor Anthony Costello in 2008 to establish a Research Centre for Prostate Cancer (Australian Prostate Cancer Research Centre at the Epworth Hospital). In 2008, he and Professor Costello have also received a project grant ($460,000) from the Prostate Cancer Foundation of Australia for their Circulating Cells as Biomarkers for Prostate Cancer study. He has more than 55 peer-reviewed articles and 2 Book Chapters.

A/Prof Jamieson received her PhD in molecular immunology from Brandeis University, Boston, in 1993 and did her post-doctoral training at the University of California, San Francisco. A/Prof Jamieson then joined the University of California at Los Angeles as an Assistant Professor in the departments of Urology and Human Genetics, where she initiated her work on bone metastatic prostate cancer. In 2010 A/Prof Jamieson moved to the University of California, San Diego, to join the Department of Surgery, where she established new patient-derived xenograft (PDX) models of bone metastatic prostate cancer and a biorepository of surgical prostate cancer bone metastasis specimens.

Prostate cancer bone metastases are not often surgically removed and, thus, have been challenging to study. However, in cases in which the bone metastasis is causing a pathologic fracture, orthopaedic surgical repair is performed and the tumour tissue is removed. In collaboration with surgeons Drs Anna Kulidjian and Christopher Kane, A/Prof Jamieson has used this surgical bone metastasis tumour tissue to establish a new series of patient-derived xenograft (PDX) mouse models that closely recapitulate the bone metastatic disease seen in patients. These PDX models are being used to develop novel therapies for inhibiting prostate cancer growth in the bone-niche.

A/Prof Jamieson is the first to show that the bone niche supports castration resistant growth of bone metastatic prostate cancer. She identified gene networks associated with prostate cancer growth in the bone microenvironment and established a co-culture model system in which prostate cancer cells induced osteoblast differentiation of bone marrow stromal cells. These findings support the hypothesis that crosstalk with the bone microenvironment leads to therapy-resistant growth of cancers.

The biorepository that A/Prof Jamieson has established consists of patient surgical prostate cancer bone metastases from different stages of treatment within the same patients. The patient-derived primary samples and the PDX models derived from these patient specimens are being analysed in genome sequencing, transcriptome and proteasome studies. A/Prof Jamieson is further enhancing the PCSD (Prostate Cancer San Diego) models with human immune cell and human stromal cell reconstitution. The combined clinical and scientific expertise of the UCSD team is producing a deeper understanding of the bone effects and tumour growth properties in their new models and better identification of clinically relevant targets for inhibiting bone metastatic prostate cancer in the bone.

A/Prof Jamieson’s research funding is from Phi Beta Psi Charity Trust, Center for Therapeutic Innovation (CTI) Pfizer, California Institute for Regenerative Medicine (CIRM), National Institutes of Health (NIH) NIBIB and NCI, Leo and Anne Albert Charitable Foundation.
Prof Lasken completed a PhD in Myron Goodman’s laboratory at the University of Southern California, Department of Molecular Biology, in 1985. Prof Lasken’s postdoctoral training was at the Stanford University School of Medicine, Biochemistry Department, in the laboratory of Arthur Kornberg. In 1988, Prof Lasken joined the Cornell University Medical College, New York, as an assistant Professor. In 1990 he joined Life Technologies as a Principle Investigator developing DNA amplification and DNA sequencing technologies. He was Director of Genomics at Molecular Staging Inc from 1988-2004 where his group developed the MDA method. He joined JCVI in 2006.

The laboratory is focused on developing methods for single cell sequencing and transcriptomics. Prof Lasken has a unique track record in method development for genomic DNA sequencing and genotyping from limiting cells. The group was the first to sequence DNA from a single cell and is recognised for pioneering methods in single cell genomics (reviewed in Lasken, R.S., Genomic sequencing of uncultured microorganisms from single cells, Nature Reviews Microbiology, 2012, vol 10, 631-640). The MDA method of whole genome amplification was developed in the laboratory 11 years ago and is now the industry standard for sequencing from limiting specimens. MDA is distributed as GenomiPhi and TempliPhi (GE Healthcare) and Repli-g (Qiagen Inc).

Prof Lasken has published more than 20 research articles, reviews and book chapters on MDA. The group is also one of the first to conduct single cell gene expression studies with next generation sequencing technology. A publication currently in press at PNAS is the first to demonstrate whole transcriptome analysis by RNA-seq from single nuclei. An additional goal of the group has been to disseminate single cell methodology to the scientific community through seminars and invited conference talks and training of guest scientists at JCVI.
Prof Mattick graduated with a BSc(Hons) in Biochemistry from the University of Sydney in 1972 and completed a PhD on mitochondrial DNA replication and mutation at Monash University, graduating in 1978. Prof Mattick’s postdoctoral training was in the Department of Biochemistry at Baylor College of Medicine in Houston, where he cloned the genes and determined the functional architecture of the multifunctional fatty acid synthase complex, now featured in major biochemistry textbooks. In 1982, he joined the CSIRO Division of Molecular Biology in Sydney, where he developed one of the first genetically engineered vaccines (against ovine footrot), and elucidated the molecular genetics of the protective antigen involved in host colonization by a wide variety of bacterial pathogens. In 1988 Prof Mattick was appointed the Foundation Professor of Molecular Biology and Foundation Director of the Centre for Molecular Biology and Biotechnology at the University of Queensland, which later became the Institute for Molecular Bioscience, which he directed from 2000-2005. He was also the Foundation Director of the Australian Genome Research Facility (1996-2002) and the ARC Special Research Centre for Functional and Applied Genomics (2000-2002). In 2006 he was awarded an ARC Federation Fellowship, followed by an NHMRC Australia Fellowship in 2010, and pioneered studies on the function of non-coding RNA. He was appointed Executive Director of the Garvan Institute of Medical Research in 2012.

Prof Mattick’s principal research interest is in understanding the role of non-coding RNA in human development, brain function and disease. He was the first to posit that most of the human genome specifies an RNA-based regulatory system. He was a member of the international consortia that discovered the expression of large numbers of long noncoding RNAs (IncRNAs) from mammalian genomes. He discovered ultraconserved elements in the human genome, and was the first to show cell- and stage-specific differential expression and subcellular localization of IncRNAs, their association with chromatin and chromatin-modifying complexes, and their perturbation in cancer and neurological diseases. Prof Mattick also discovered nuclear tiny RNAs associated with transcription start sites and splice junctions, and other classes of small RNAs. He showed that nucleosomes are preferentially positioned at exons, and that alternatively spliced exons are associated with promoters, revealing the dynamic organization of the transcription-splicing complex.

Prof Mattick has received many awards, most recently the Julian Wells Medal (2009) of the Lorne Genome Society, Fellowship of the Australian Academy of Science (2008), the inaugural Gutenberg Professorship of the University of Strasbourg (2008), the International Union of Biochemistry and Molecular Biology Medal (2011), and the Human Genome Organisation’s Chen Award for Distinguished Achievement in Human Genetic and Genomic Research (2012).
Dr Nair completed her PhD from the National Institute of Immunology after being awarded two fellowships from the Department of Biotechnology (India) in 2003. After a career break, she was awarded the prestigious international Career Development Fellowship by the Medical Research Council for her post-doctoral work at Hutchison/MRC Cancer Centre, Cambridge UK in 2005. She then relocated to Australia to work with Dr Swarbrick at the Garvan Institute of Medical Research. She is currently a Senior Research Officer in the Cancer Research Division at the Kinghorn Cancer Centre.

Dr Nair’s primary research interests lie in investigating heterogeneity in cancer with a focus on transcriptional networks controlling metastasis. The aim of her work is to discover the mechanisms underlying the metastatic phenotype by integrating genomic, epigenetic and proteomic data. This will allow us to understand the transcriptional and proteomic control of tumour cells which are critical for tumourigenesis and metastasis, with the ultimate aim of identifying and targeting these cells in a therapeutic context. She has been instrumental in developing cutting edge in vitro and in vivo models of breast cancer. More recently, she has been applying single cell gene expression and RNA-Seq technology to identify metastatic tumour populations in patient derived xenograft models. Importantly, this work will also inform on the fundamental biology of metastasis applicable to a range of cancers. The natural therapeutic consequences of her work will be to identify metastatic “activators” and “suppressors” which may be new therapeutic targets in the treatment of metastatic disease.

THE AIM OF... DR NAIR’S... WORK IS TO DISCOVER THE MECHANISMS UNDERLYING THE METASTATIC PHENOTYPE BY INTEGRATING GENOMIC, EPIGENETIC AND PROTEOMIC DATA.
Dr Patterson graduated from the University of Sydney faculty of Veterinary Science in 2003. She worked full time as a small animal veterinarian until 2005 and then continued to work part time in clinical practice while completing her PhD in cancer biology, signal transduction at the Garvan Institute. Following her PhD, Dr Patterson worked with Prof Susan Clark in the Epigenetics research group at the Garvan Institute as a science writer and visual science communicator. She also worked part time as a freelance medical and scientific illustrator trading as MediPics and Prose, and as a science writer for the National Breast Cancer Foundation in 2011. Following maternity leave in 2012, Dr Patterson returned to the Garvan Institute as a full time biomedical animator and visual science communicator.

Dr Patterson’s work primarily focuses on using visual language to translate complex scientific discoveries for a general audience. She is a registered biomedical illustrator with the Australian Institute of Medical and Biomedical Illustrators and an active member of the Australian Science Communicators network with whom she directs the biennial Science-As-Art exhibition at the national conference. She uses state-of-the art animation software (Maya and After Effects) to create scientifically accurate, three-dimensional animations that are designed to be visually impressive. Aesthetically appealing awe-inspiring images have the ability to attract attention and engage a viewer such that an audience-appropriate scientific message can then be conveyed most effectively.

Dr Patterson’s work is co-funded by the Garvan Institute and the Australian Government’s Inspiring Australia Initiative.
Dr Desiree Petersen received a PhD in Human Genetics, Health Sciences from the University of Stellenbosch, South Africa in 2006. She also holds a BSc degree (1998) in Natural Sciences as well as a BSc (Hons) degree (1999) and MSc degree (2002) in Human Genetics, Medical Sciences from the University of Stellenbosch. During her postgraduate studies, she performed research at the University of Maastricht in The Netherlands, National Cancer Institute in Frederick, Maryland, USA and the Garvan Institute of Medical Research in Sydney, Australia. In 2006, she was awarded a postdoctoral fellowship from the Freedman Foundation, Australia and joined the Cancer Genetics group, Cancer Research program at the Garvan Institute of Medical Research. Her research focused on the genetic analysis of inflammatory cytokines and their role in predisposition to prostate cancer. She relocated with the Cancer Genetics group in 2008 to the Children’s Cancer Institute Australia where she was a Research Officer before joining the J. Craig Venter Institute, San Diego, USA in 2011 as a Staff Scientist in the Genomic Medicine group. Dr Petersen will return to the Garvan Institute of Medical Research in January 2014 as a Senior Research Officer in the laboratory to further establish the genetic basis of complex diseases such as prostate cancer. This includes a strong interest in advancing research and development of new genomic tools for generating data that validates genetic and structural variation amongst individuals. Previous contributions to technical development include assisting with establishing the first research laboratory in Australia to use Next Generation Sequencing with the Roche 454 GS FLX instrument and performing high-throughput genotyping on the Illumina platform.

Dr Petersen’s current research interest involves investigating genomic diversity within and between human populations for Human Comparative and Prostate Cancer Genomics and will be responsible for research and development of a new phase of genomic technology.

Her technical expertise was utilised to generate both sequencing and genotype data for international collaborative research efforts that included the analysis of genetic diversity in the Tasmanian Devil population and complete sequencing of Khoisan (Bushmen) and Bantu genomes from Southern Africa.
Dr Phan graduated from medicine at the University of Sydney with the University Medal and completed a double fellowship in Internal Medicine and Pathology under the guidance of Dr Stephen Adelstein and Dr Roger Garsia in the Department of Clinical Immunology at the Royal Prince Alfred Hospital, Sydney. He developed a B cell receptor knock-in mouse model to study in vivo B cell responses to foreign and self-antigen for his PhD under the supervision of Prof Antony Basten and A/Prof Robert Brink at the Centenary Institute, Sydney for which he received a New Investigator Award from the Australasian Society of Immunology. His interest in defining the in vivo contexts of B cell responses and resolving germinal centre selection events in space and time lead to post-doctoral studies as an NHMRC CJ Martin Fellow with Prof Jason Cyster at the Howard Hughes Medical Institute, University of California, San Francisco where he used intravital two-photon microscopy to investigate the initiation of B cell responses in the lymph node. Upon his return to Sydney, Dr Phan established an intravital two-photon microscope facility at the Garvan Institute in 2010.

A major goal in Dr Phan’s research program is to image tumour cells in their niche in the bone marrow. To achieve this goal he has developed breakthrough techniques to image the cells occupying the endosteal and perivascular niches in the bone marrow of live mice, something that was not possible until now. This has allowed him, in collaboration with Prof Mike Rogers, to visualise in real-time osteoclastic resorption of bone using fluorescently labelled bisphosphonates. More importantly, in collaboration with Prof Peter Croucher, he has been able to visualise the first steps involved in invasion of the bone by multiple myeloma cells. Furthermore, mice can be recovered from anaesthesia after an imaging session and this makes it possible to perform longitudinal imaging over several weeks to track the fate of these cells. The model systems and techniques to be used in the research are therefore already well established and will form the basis of our approach to investigating the steps involved prostate cancer micrometastases, the interactions between the prostate cancer cells and their niche and the factors that determine if the cancer cells remain dormant or become activated to proliferate and develop into overt bony metastases.

Dr Phan’s research is currently funded by the National Health and Medical Research Council, Australia Research Council and Cancer Institute NSW.

**A MAJOR GOAL IN DR PHAN’S RESEARCH PROGRAM IS TO IMAGE TUMOUR CELLS IN THEIR NICHE IN THE BONE MARROW.**
Prof Rubin is Vice Chair of Experimental Pathology at Weill Cornell Medical College, Director of the Institute for Precision Medicine, and Co-Director of the Prostate Cancer Research Program at New York Presbyterian-Weill Cornell. He completed medical school training at Mount Sinai Medical Center, training in anatomic pathology at Georgetown University Medical Center, and a fellowship in anatomic pathology at Johns Hopkins Hospital. His previous academic appointments include Assistant Professor of Pathology at Columbia University College of Physicians and Surgeons, followed by Associate Professor of Pathology with Tenure at the University of Michigan, then Associate Professor of Pathology at Brigham and Women’s Hospital of Harvard Medical School, before being recruited to Weill Cornell Medical College as Professor of Pathology and Laboratory Medicine in 2008.

Prof Rubin’s laboratory is dedicated to prostate cancer biomarker and genomic research and over the past thirteen years has been involved in some of the key prostate cancer biomarker discoveries, including the first expression profiling paper on prostate cancer (Nature 2001), the role of EZH2 in prostate cancer (Nature 2002), the first prostate cancer whole genomes in collaboration with the Broad Institute (Nature 2011, Nature Genetics 2012, Cell 2013). He is the co-discoverer of ETS rearrangements in prostate cancer with Dr Arul Chinnaiyan (Science 2005). He is the Chair the EDRN Prostate Cancer Collaborative Group and PI of a SU2C Prostate Cancer Foundation Dream Team Award. Prof Rubin is a board certified pathologist and an internationally recognised expert in prostate pathology.

Current funding sources include: United States National Institute of Health, National Cancer Institute and the Early Detection Research Network, Stand Up to Cancer, Prostate Cancer Foundation, Starr Cancer Consortium.

PROF RUBIN’S LABORATORY IS DEDICATED TO PROSTATE CANCER BIOMARKER AND GENOMIC RESEARCH AND OVER THE PAST THIRTEEN YEARS HAS BEEN INVOLVED IN SOME OF THE KEY PROSTATE CANCER BIOMARKER DISCOVERIES...
Single colonising cell – time lapses
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