Prostate Cancer Foundation of Australia

COLLABORATIVE RESEARCH UPDATE

2010/2011

CONTENTS

Message from the CEO 1

Message from PCFA's Research Committee Chair 2

PCFA Research Committee 3

PCFA research milestones 8

Finding a cure – one 'Mo' at a time 12

PCFA research program updates 14

Other important projects funded to date 24

PCFA research program 2011 and beyond 34

Interested in helping PCFA? 36

MESSAGE
FROM THE CEO

DR ANTHONY LOWE
Chief Executive Officer

I am extremely proud of PCFA's truly world class research program. To date we have funded more than 113 excellent projects in five states across Australia.

The ultimate aim of the program is to find a cure for prostate cancer - one of the biggest killers of Australian men. In the meantime, we need to discover better diagnostic markers, better treatments and better preventive measures.

PCFA is proud to acknowledge the generous support of Movember, the biggest funding partner of PCFA's research program. Since 2005 Movember has donated more than $27M to the program.

The research showcased includes efforts to identify new biomarkers in order to diagnose the disease earlier; efforts to identify better and more efficient treatments that will prolong the life of men with advanced prostate cancer; and nationwide initiatives in partnership with NHMRC and Cancer Australia to ensure that men with high risk prostate cancer, initially treated with surgery, will receive appropriate evidence-based cancer care.

Preserving the quality of life of Australian men with prostate cancer is high on our agenda. PCFA is committed to working collaboratively with Australia's leading health service researchers, cancer epidemiologists, urologists, radiation oncologists; and policy makers to find solutions that embed evidence-based care into routine practice.

As well as funding projects through our established research program, PCFA is working tirelessly to identify gaps and fund areas that are currently under-researched; and contribute to projects that concern under-represented areas of the community. To achieve this, we rely on the wealth of knowledge of experts in the field of prostate cancer research in Australia. Initiatives such as the Young Investigator Award, the Concept Grant and the newly launched New Directions Development Award, will ensure that funds are awarded to the best researchers in the country.

MESSAGE FROM PCFA'S RESEARCH COMMITTEE CHAIR

PROFESSOR JOHN MILLS
PCFA Chair, Research Committee

"PCFA's research program aims to support the very best Australian research into prostate cancer, and to ensure that allocation of PCFA grant funds is guided by a clear strategic focus and a set of specific research priorities, based on deficits in existing research."

In Australia and internationally, prostate cancer has lagged behind many other cancers that cause equivalent morbidity and mortality (e.g. breast or colon cancer). The limited research funding for prostate cancer has meant limited research manpower and outcomes, which has in turn has resulted in diagnostic and treatment options which are suboptimal.

PCFA's structured research program aims to correct this imbalance between prostate cancer and other important cancers:

- To provide a logical, consistent and transparent framework for submission, review and selection of research applications for funding.
- To support the very best Australian research into prostate cancer, and to ensure that allocation of PCFA grant funds is guided by a clear strategic focus and a set of specific research priorities, based on deficits in existing research.
- To play a catalytic role in expanding the number of distinguished, senior Australian scientists working on prostate cancer, whilst ensuring that promising young investigators have the funding required to allow them to mature into independent prostate cancer researchers.

PCFA
RESEARCH COMMITTEE

Since 1999, PCFA has been committed to providing a transparent, well-organised and academically rigorous venue for the funding of worthwhile research projects focused on prostate cancer.

In 1999, PCFA's Peer Review Committee (as the Research Committee was then known) was chaired by Professor Roger Reddell (1999 -2003), followed by Professor Robert Baxter (2003-2006). The current Chairman, Professor John Mills, was appointed in 2007 at a time when, due to the ongoing success of Movember, PCFA was able to establish its annual grant program.

With Board input, oversight and approval the Research Committee is responsible for:

- Developing the broad goals of the PCFA Research Program (the Research Strategy), developing its specific aims, assisting in the implementation of that Program, and reviewing the Research Strategy on at least an annual basis
- Reviewing applications tendered as part of the Research Program, in a rigorous, transparent and fair process, and identifying and ranking applications that should be funded for the Board's review
- Identifying areas of prostate cancer research which are felt to be under-investigated (especially in the case where there are insufficient applications) and developing strategies to correct that imbalance.

An outstanding group of scientists bring their experience and expertise to PCFA's Research Committee.

PROFESSOR JOHN MILLS

Professor John Mills has been the Chair of PCFA's Research Committee since its establishment in 2007. A specialist physician, medical scientist and businessman, Professor John Mills received a BS (Hons) from the University of Chicago and an MD (Hons, with specialisation in microbiology) from Harvard Medical School. He holds Fellowships in the American College of Physicians, the Royal Australian College of Physicians and is an Associate Fellow of the Royal College of Pathology of Australasia. Professor Mills has been actively involved in patient care since 1966, and retains a small clinical practice at the Alfred Hospital. He holds professorial appointments at UCSF, Monash University and RMIT. Conducting medical research since 1961, Professor Mills has more than 200 peer-reviewed publications reporting original research, plus numerous reviews, book chapters and edited texts. He has been on the editorial board of several journals, the recipient of a number of prestigious awards, and is currently actively involved in research review and administration. Since 1992, Professor Mills has been involved in biomedical business, and is currently a Director of TissuPath P/L, a specialist histopathology practice with a special interest in uropathology and prostate cancer, Chairman of Swedish biotechnology company Cavidi AB, and non-executive director of GBS Venture Partners Pty Ltd. He is also a Director of PCFA.

PCFA
RESEARCH COMMITTEE

MR. BRUCE KYNASTON (Consumer Representative)

Bruce Kynaston initially graduated as Medical Officer and eventually became Director of The Queensland Radium Institute. Later in his career he worked for an extended period of time as a Radiation Oncologist and in his role as consultant to Princess Alexandra Hospital in Brisbane, Bruce treated many men for prostate cancer in the pre PSA era. In addition, he acquired a qualification in medical administration and served on the NH&MRC ('76-'84), and its Medicine Advisory Committee and Radiation Health (Standing) Committee. Bruce was later appointed to the Ionizing Radiation Advisory Committee that reported to the federal Minister for the Environment where he served for 3 years. In 1985, two years post his retirement, Bruce had a refresher course in radiotherapy as a patient for prostate cancer. Since his prostate cancer diagnosis, he has been actively involved as a member of Brisbane, Gold Coast and Sunshine Coast support groups and has helped with his advice and opinion related to prostate cancer testing issues and consumer involvement whenever needed.

Bruce is currently symptoms free of PCa and plans to help us along in the area of support to other men for years to come.

PROFESSOR SUZANNE CHAMBERS

Professor Suzanne Chambers heads the Department of Preventative Health at Griffith Health Institute, Griffith University, Queensland. Prof. Chambers has been the Director of Research at the Cancer Council Queensland from 2006 to early 2011. In this role, she was responsible for the strategic direction, development and management of research program activity, the broad aim of which is to undertake psycho-oncology and epidemiology research that translates into improved and effective clinical practice, public health interventions and policy, and optimal individual behaviour. This includes six defined research areas: Descriptive Epidemiology; Lifestyle and Cancer; Prostate Cancer; Skin Cancer; Community and Applied Psycho-Oncology; Cancer Aetiology; as well as the Queensland Cancer Registry and Cancer Counselling Service. In 2005 she received an academic appointment from the Griffith University School of Psychology and since 2006 has been a member of the Griffith Psychology Health Research Centre. Her particular area of interest is in adjustment to prostate cancer and she is currently leading two large scale NHMRC funded trials into psycho-education/ decision support and couples based interventions for men with localised prostate cancer. Professor Chambers also holds an NHMRC Career Development Award.

PROFESSOR ROBERT ALEXANDER GARDINER

Professor Robert Alexander ('Frank') Gardiner (AM, MBBS, MD, FRCS, FRACS) is an Academic Urologist with the University of Queensland at the UQ Centre of Clinical Research and is a Consultant Urologists at the Royal Brisbane and Women's Hospital. He also has senior adjunct academic appointments at the Queensland Institute of Medical Research and Queensland University of Technology.

In addition to being a member of PCFA's Research Committee, he is Chairman of the MSAC of Cancer Council Queensland, Chairman and member of the Executive of the Viertel Centre for Research in Cancer Control, Queensland and is Chairman of the Pathology subcommittee of the Royal Australasian College of Surgeons. In addition to membership of the Board of Directors, Cancer Council Australia, the Advisory Board of Andrology Australia and the Advisory Board of the Asian Pacific Prostate Society, he has an appointments on the editorial boards of 5 international journals. He holds the position of a Web-page editor, BJU International journal and is Section editor, FingerTip Urology, BJU International, which he initiated and instigated. He has a long history in prostate cancer research and is an author on over 130 peer-reviewed publications in urology and urological research and the recipient of many competitively won research grants. He is a Fellow of the Urological Research Society which is limited to 75 members elected internationally.

ASSOCIATE PROFESSOR HOWARD GURNEY

Director of Clinical Research, Medical Oncology at Westmead Hospital in Sydney, Associate Professor Howard Gurney is a medical oncologist with sub-specialty interest in prostate and genitourinary cancer. He helped establish a large multidisciplinary prostate cancer management team in Western Sydney involving urologists, radiation oncologists and medical oncologists. Associate Professor Gurney has a strong track record in clinical and translational research, particularly in anti-cancer drug disposition, novel methods for dose calculation and new therapies for prostate and genitourinary malignancies. He has been an investigator on more than 70 clinical trials and has more than 60 peer-reviewed publications.

ASSOCIATE PROFESSOR SUSAN HENSHALL

A/Professor Susan Henshall has been the Group Leader of the Prostate Cancer Group in the Cancer Research Program at the Garvan Institute of Medical Research, Sydney for more than one decade. She is a past PCFA Young Investigator and is currently a Cancer Institute NSW Fellow. She holds conjoint academic appointments with the University of New South Wales and Georgetown University in the United States. Her main research focus over the years has been the identification of genes and pathways whose expression changes can predict the development of aggressive life-threatening prostate cancer or resistance to chemotherapy used for the treatment of advanced stage prostate cancer. Recently, Sue has accepted a new position with Cancer Council Australia. She is now the Union for International Cancer Control (UICC) Advocacy Director at CCA.

PROFESSOR ROBERT NEWTON

Professor Robert Newton is Director of the Vario Health Institute and Professor of Exercise and Sports Science at Edith Cowan University. He leads a research

PCFA
RESEARCH COMMITTEE

team investigating the impact of exercise, nutrition and psychological interventions on symptom experience, fatigue, body fat, muscle mass, bone density, physical performance, quality of life and psychological wellness of prostate cancer patients. Professor Newton is an accredited exercise physiologist and directs the "Cancer Survivors Program" at the Institute which provides lifestyle support to people with cancer.

ASSOCIATE PROFESSOR RICHARD PEARSON

Following three years as a Human Frontiers of Science Fellow at the Friedrich Miescher Institute in Basel, Switzerland, Associate Professor Pearson was appointed Head of the Protein Chemistry Laboratory at the Peter MacCallum Cancer Centre in 1995. He is also Co-Head of the Cell Growth and Differentiation Program at Peter Mac, and is a NHMRC Senior Research Fellow and Principal Fellow in the Department of Biochemistry and Molecular Biology at the University of Melbourne.

Associate Professor Pearson's research focuses on understanding the molecular basis of the regulation of ribosome biogenesis, protein synthesis and cell growth, and using this knowledge to address how deregulation of these processes contributes to malignant transformation. He currently receives project grant support from NHMRC and Cancer Council Victoria and has co-authored more than 55 peer-reviewed articles. He served on NHMRC Grant Review Panels between 2006 and 2008.

ASSOCIATE PROFESSOR LISA HORVATH

Dr Lisa Horvath is the Head of the Department of Medical Oncology (Royal Prince Alfred Hospital) at the Sydney Cancer Centre and a Visiting Post-doctoral Scientist at the Garvan Institute for Medical Research. She is also a senior lecturer at both the University of Sydney and the University of New South Wales. She has an active clinical practice, is involved with a large number of clinical trials in prostate, lung and colorectal cancers in addition to phase I trial work. Dr Horvath has published 24 original research papers published in peer-reviewed journals in the last 10 years. She has presented extensively at national and international meetings both peer-reviewed and invited presentations.

Dr Horvath's research interest is predominantly on tissue biomarkers of prognosis in localized prostate cancer but since returning to clinical practice, her research has focused more on drug resistance in hormone-refractory prostate cancer.

PROFESSOR PETER LEEDMAN

Dr Leedman completed medicine at the University of Western Australia (UWA), then trained in endocrinology at Royal Melbourne Hospital in the mid-1980s. He completed his PhD at the Walter and Eliza Hall Institute in Melbourne with Len Harrison on autoimmune thyroid disease from 1987-1991. From 1991-1994 he was a Lucille P Markey Fellow with Bill Chin, a Howard Hughes Investigator in the Division of Genetics, Brigham and Women's hospital,

Harvard Medical School in Boston where he worked on the molecular mechanisms of thyroid hormone action. His laboratory is focused on applying advances in understanding these molecular mechanisms to the development of novel therapeutics. The team's discovery of several novel transcriptional nuclear receptor coregulators, including SLIRP, has generated much interest in the role of RNA-binding coregulators in hormone action. Professor Leedman is Head of the Laboratory for Cancer Medicine and Deputy Director of WAIMR. He is also an endocrinologist and Director of Research at Royal Perth Hospital.

DR MIRANDA XHILAGA

PCFA's National Research Committee is coordinated by Dr Miranda Xhilaga (PCFA National Manager – Research Programs)

Miranda is a physician and Adjunct Senior Lecturer in the Department of Medicine, Monash University. In addition to her medical qualifications, she holds a Diploma in Immunology and a PhD in Molecular Biology from Monash University. Prior to joining PCFA as National Manager, Research Programs, Dr Xhilaga was a member of Professor David de Kretser's research group at the former Institute of Reproduction and Development (now Monash Institute for Medical Research) focusing on viral latency in the prostate, testis, epididymis and seminal vesicles, and the role of these organs in viral transmission. Dr Xhilaga has published more than 16 peer reviewed papers, most in high impact journals such as Journal of Virology, Nature Microbiology, Blood and has served as a reviewer for several journals including the Asian Journal of Andrology. She has received many prestigious postgraduate and postdoctoral awards including a NHMRC CJ Martin Postdoctoral Fellowship and the US National Institutes of Health Fellows Award for Research Excellence. Dr Xhilaga is a member of the Society for Reproductive Biology and the Australian Society for Medical Research.

PCFA's CEO, Dr Anthony Lowe, also sits as an ex officio member of the Committee.

PCFA
RESEARCH MILESTONES

PCFA has a long history of funding world-class Australian researchers into accelerating finding a cure for prostate cancer.

PCFA's structured Research Program is indeed a new program compared to other programs run by not-for-profit organizations such as Cancer Councils and the National Breast Council Foundation. PCFA has however been supporting prostate cancer since 1999.

One of PCFA's first initiatives was to stand behind the first national biobank in Queensland, now a major success. In 2002, PCFA awarded its first two Fellowships to Dr Lisa Butler and Dr Susan Henshall followed by the third Fellowship awarded to Dr Anika Antonsson with the support of the Mazda Foundation.

Funding from BHP Billiton in 2005 enabled PCFA to conduct a review of prostate cancer activities in Australia. This audit underpinned our strategy for research funding. Based on the information gathered, Prof. John Mills, with the full support of the Research Committee, developed the current strategy of the structured PCFA Program, which was further refined through presentations to the PCFA National Board of Directors. The whole program is based on a strategy that has been developed taking into account needs for research funding in the most important areas of this research field. As indicated by the name, PCFA's Research Program operates mainly in a targeted mode. Proposals are submitted in response to a targeted funding mechanism and our call for proposals is characterised by opening and closing dates and defined eligibility criteria. Proposals are invited from PCa researchers and those whom aspire to join the PCa research workforce based on tight criteria and set funding categories.

RESEARCH PROGRAM MILESTONES	TIMELINES
PCFA appoints its first Research Committee headed by Prof. Roger Reddell followed by Prof. Robert Baxter	1999-2003 2003-2006
PCFA commissions Health Technology Analysis to conduct gap analysis pertaining to the PCa research activities in Australia	2006
PCFA appoints a new Director of Research to the National Board, Prof. John Mills and due to the ongoing success of Movember, establishes its annual funding program now known as PCFA's Research Program	JAN 2007
Prof. Mills develops grant program and documentation and appoints new Research Committee	APR 2007
Opening of the first funding round	JUN 2007
Results of first funding round announced	NOV 2007
PCFA partners with Cancer Australia in the PdCCRS	NOV 2007
National Manager for Research Programs recruited	JUL 2009
Listed in the competitive grants register– secures infrastructure funding for our researchers	JAN 2010
First Scientific PCFA Forum	AUG 2010
First Think Tank meeting to review strategy and impact of the research program	AUG 2010
PCFA awards the first prizes for the best senior and best young investigator in PCa research	AUG 2010
Movember signs a new 3 year agreement with PCFA	DEC 2010

PCFA
RESEARCH MILESTONES

Since its establishment in 2007 PCFA's Research Program's total expenditure has reached nearly $27M, an investment in PCa almost equal to the average funding invested in PCa research by NH&MRC (i.e. total NH&MRC expenditure 2000-2010 was $69M, an average of $6.9M/year whereas the total PCFA expenditure in the last 4 years is $27M with an average of approximately $6.5M/year). This is an impressive investment that has doubled the overall funding available to researchers in the field, and which has clearly increased the "labor pool" for prostate cancer research.

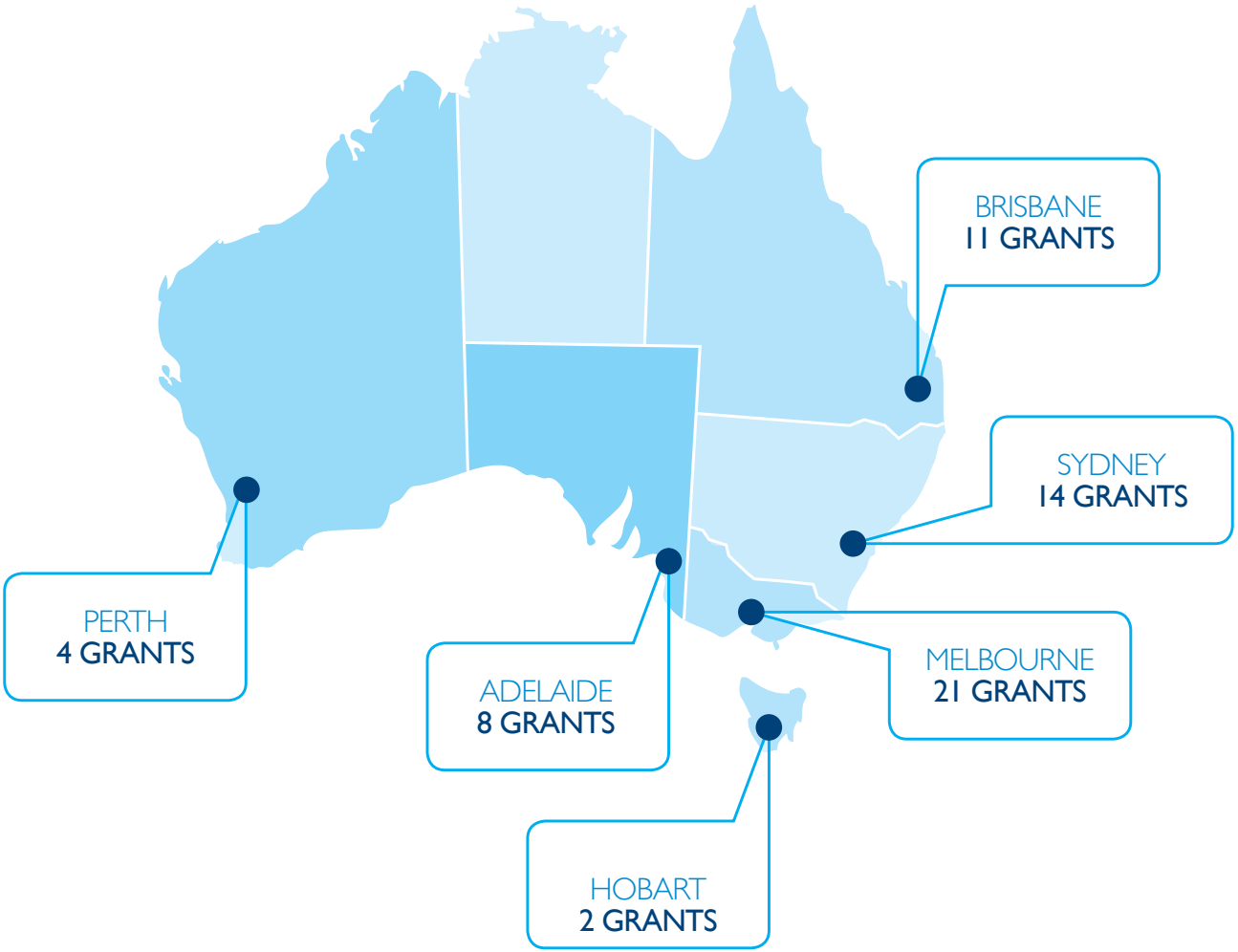
From 2007-2011, PCFA Research Program has approved funding to 50 projects, 16 equipment projects, 15 concept grants and has funded 18 young investigators. Since 2008, PCFA grantees have published more than 60 peer review papers in highly ranked journals, have lodged four patents pertaining to major discoveries in the field and have constantly taken their findings to international and national forums and have been awarded major awards and prizes.

From 2008-2010 PCFA grantees have secured up to $5.5M in leveraged funding from other agencies, a return of approximately 20% of our total investment for that period.

Furthermore, through the Concept Grant scheme, the program has recruited 10 new investigators into PCa research. Three of these investigators have already secured funding form the NH&MRC and Cancer Councils to be able to continue to work in this new field of research in their laboratories; we expect more in the future. Of 11 Young Investigators funded from 2007-2010, 9 are now independent researchers and run their own laboratories.

PCFA funded research has been presented and acknowledged in more than 200 international and national conferences and media sources. Our funded research projects will ultimately benefit the almost 20,000 Australian men and their families that are impacted by a diagnosis of prostate cancer each year.

PCFA ACTIVE GRANTS 2011
STATE DISTRIBUTION



FINDING A CURE
ONE 'MO' AT A TIME

Movember is an annual, month-long celebration of the moustache that highlights men's health issues, specifically prostate cancer and depression in men.

In November each year, moustaches are grown by Mo Bros with the aim of prompting public and private conversation around the topic of men's health. The funds raised in Australia support equally two of the biggest health issues men face – prostate cancer and depression. Funds are directed to programs run directly by Movember and its men's health partners, the Prostate Cancer Foundation of Australia and *beyondblue: the national depression initiative*. Together, the three channels work together to ensure that Movember funds are supporting a broad range of innovative, world-class programs in line with their strategic goals, in the areas of awareness and education, survivorship and research.

Movember was conceived back in 2003, with the first official fundraising campaign held in 2004. The goal was to build an event that promoted the growth of moustaches, while raising a small amount of money for charity and having fun.

Inspired by the women's health movement, it was acknowledged that men needed a way to become engaged and actively involved in their own health. Prostate cancer and later depression, were identified as illnesses that needed a stronger voice at the time.

In 2004, 450 Mo Bros took part, and by getting their mates, families and colleagues to sponsor the growth of their Mo's, raised $55,000 – it was the largest single donation PCFA received that year.

Motivated by what was happening in Australia, Movember is today embraced by countries around the world and become a truly global movement. Outside of Australia, significant campaigns run in the UK, the US, New Zealand, Ireland, South Africa, Finland, the Netherlands, Spain and the Czech Republic. Together these countries and ex-pats spread across the globe had 447,779 registered Mo Bros and Sistas that garnered 1.8 million individual donations raising $72 Million (AUD).

This success has enabled Movember to identify an opportunity to accelerate research outcomes. The Movember Foundation's vision is to have an everlasting impact on the state of men's health. To this end Movember has established the Movember Global Action Plan (GAP), which aims to accelerate prostate cancer outcomes through global research collaboration.

Working with its prostate cancer partners in each country over the last few years, Movember identified an opportunity to accelerate research outcomes that benefit men by providing researchers around the world the ability to work together to address critical research challenges. Given Movember's presence internationally, Movember is uniquely

MOVEMBER
PROUDLY FUNDED

placed to address this challenge by facilitating and funding a new and bold approach to prostate cancer research collaboration that fast tracks outcomes.

As well as funding important Australian prostate cancer research, Movember also plays a vital role in raising awareness about this disease. Recent research carried out by the Movember Foundation revealed that 82 per cent of Mo Bros talked about men's health with friends, family or work, and that 55 per cent of Mo Bros did some of their own research into Movember supported causes. These are vital first steps in helping to raise further awareness about prostate cancer.

Going forward, Movember will continue to work towards helping to change established habits and attitudes and make men aware of the risks they face, thereby increasing early detection, diagnosis and effective treatment.

The Prostate Cancer Foundation of Australia sincerely thanks everyone who has participated in Movember over the years by either growing a Mo or sponsoring the growth of a Mo.

For further information about Movember check out www.movember.com or email info@movember.com, or call 1300 47 69 66.

PCFA RESEARCH PROGRAM UPDATES

In search for better biomarkers.

Dr Luke Selth, Movember Young Investigator, Dame Roma Mitchell Laboratories, Hanson Institute.

Each year, over 20,000 men are diagnosed with prostate cancer in Australia and it is estimated that more than 3,300 men will die from the disease in 2011.

After being diagnosed with prostate cancer, patients can have very different outcomes. Whereas many men have insignificant cancers that will not affect life expectancy, others may have an aggressive form of cancer that is not treatable by surgery or radiation therapy and likely to progress rapidly. Unfortunately, it is very difficult to distinguish between these insignificant and aggressive cancers. This creates two major problems: first, there is extensive over-treatment of men with insignificant cancer, resulting in unnecessary health problems for the men and an avoidable burden on our health system; and second, men with aggressive cancer are at risk of being sub-optimally treated. Therefore, the development of new tests that are able to distinguish between these men is desperately needed.

The primary goal of the proposed study is to identify new molecules in the blood that are able to distinguish between aggressive and insignificant disease. Moreover, Dr Selth will test whether these "markers" influence prostate cancer development and progression, which may lead to the identification of new drug targets. The researchers believe that achieving these goals will have a rapid and significant impact on the management and treatment of this devastating disease.

With the support of Movember, in 2010 Dr Selth was awarded a Young Investigator grant that will allow him to pursue this very important research. To date, Luke and his team have made good progress on this research program. They have discovered a group of molecules in the blood, termed microRNAs that are key regulators of cancer. They are now assessing whether these microRNAs can be used as biomarkers to predict an individual man's risk of dying from prostate cancer.

A combinatorial approach targeting androgen signalling for treatment of prostate cancer.

Dr Lisa M Butler, Dame Roma Mitchell Research Laboratories, University of Adelaide and Hanson Institute.

The use of new clinically-available agents that block androgen receptor expression and/or activity will enable Dr Butler to translate her preclinical studies into Phase I/II clinical trials. In addition, they will determine whether a therapeutic response to the combinatorial AR-targeting therapy can be predicted by a specific gene signature

in human tumour cells. This has the potential to directly improve patient treatment and reduce mortality associated with prostate cancer by ensuring that patients who are unlikely to respond to our AR-targeting therapy can be identified prior to commencing therapy.

Dr Lisa Butler, a Senior research Fellow at the Dame Roma Mitchell Cancer Research Laboratories in Adelaide strongly believes that the data they will obtain in these studies have the potential to improve the design of subsequent clinical trials based on this combination approach, and to provide us with new therapy targets for prostate cancer. Both of these outcomes would have long-term benefits for people affected by prostate cancer.

The prostate cancer patients who will most benefit from the research in this proposal are patients with metastatic disease who are progressing on androgen deprivation therapy and are destined to die of their disease. In this group of patients, treatment strategies are limited to second-line hormone manipulations and chemotherapy, both of which achieve only modest increases in patient survival. Dr Butler's novel combinatorial approach will enhance the efficacy and specificity of targeting AR signalling in prostate cancer patients, which will improve overall survival in a group of men with disease associated with a very poor outcome. Lisa's project was funded through Cancer Australia's Priority Driven Collaborative Cancer Research Scheme.

PCFA RESEARCH PROGRAM UPDATES

Improving evidence based care for locally advanced prostate cancer: A randomised phased trial of clinical guideline implementation through a clinical network.

Associate Professor Mary Haines, Sax Institute and University of Sydney.

Prostate cancer is the most common cancer registered in Australia and is the second most common cause of cancer death in males. There is an urgent need to improve care for men with advanced prostate cancer if we wish to improve their survival. A national strategy to improve prostate cancer services and thereby improve patients' quality of life and survival recently identified the provision of evidence based care for "high risk" men with prostate cancer as a high priority.

Compelling new evidence suggests we need to alter current practice by offering radiotherapy to high risk men with prostate cancer– but will clinicians change their practice? This study will assess whether a clinician-led and tailored intervention in nine hospitals within the NSW Agency for Clinical Innovation's Urology Network (with urology multidisciplinary teams) increases evidence based care for high risk patients after surgery. The study will identify reasons why the intervention did or did not result in greater referral to radiation oncology services. The results of this study will be of immediate use to the PCFA to ensure men with high risk prostate cancer, initially treated with surgery, will more quickly receive appropriate evidence based cancer care.

Prof. Haines and her team aim to trial a strategy that harnesses the Agency for Clinical Innovation's Urology Network within NSW hospitals to:

Phase 1. Assess whether a clinician-led and tailored intervention in nine hospitals within the Urology Network (with urology multidisciplinary teams) increases evidence based care for high risk patients after surgery - i.e. referral to radiation oncology services.

Phase 2. Identify reasons why the intervention did or did not result in greater referral to radiation oncology services.

This project is funded by the NHMRC and PCFA's Research Program through the Partnership Scheme. It showcases PCFA's committed to working collaboratively with the nation's leading health service researchers, cancer epidemiologists, urologists, radio-oncologists and policy makers to find solutions as to how we can embed evidence based care into routine practice.

Can novel imaging technologies and a different type of PET scanning help doctors to better diagnose and treat localized prostate cancer?

A/Prof Ian Davis, Team Leader, Uro Oncology Laboratory, Ludwig Institute for Cancer Research, Austin Hospital.

A PET scan is a type of scan that can give information about what is happening inside tissues, such as how quickly they are using sugar or other building block materials to grow. Many areas of the body normally have high rates of metabolism (including many internal organs). Cancer metastases (areas of cancer spread) can often be distinguished from non-cancerous tissues using a PET scan. Until recently, conventional PET scanning has been of limited use in prostate cancer.

A/Prof. Ian Davis and his team have conducted preclinical and clinical evaluations of novel imaging technologies including a different type of PET scan in trials of prostate cancer detection and progression.

The project will evaluate how useful PET scanning is when compared to other standard assessments; whether it helps in making treatment decisions; and whether it can be used to monitor the results of treatment.

Co-funded by Cancer Australia, PCFA and Radiation Oncology through the pDCCRS, the project involves two clinical trials for men with prostate cancer that is not thought to have spread outside the prostate. One study involves men planned for surgery and the other involves men planned for radiotherapy. To date the team has had excellent support from colleagues in all professional disciplines involved in the project. Both trials have successfully recruited the planned 30 patients each. Preliminary data indicate that 11C-choline PET scanning identifies the dominant intraprostatic lesion, correlating with conventional imaging and histopathology; and that data from the PET scans can be used for radiotherapy treatment planning. Analyses regarding the effects of PET on decision making are in progress. An additional research project has been approved by the Austin Health Human Research Ethics Committee (HREC), allowing use of the PET data for patients undergoing radical prostatectomy to be used to model theoretical radiotherapy treatment planning.

PCFA RESEARCH PROGRAM UPDATES

Immunotherapy for Prostate Cancer.

Dr Kristen Radford, Cancer Immunotherapies Groups Leader, Biological Therapies Program, Mater Medical Research Institute.

Immunotherapy using dendritic cells is a promising treatment for prostate cancer but this type of vaccine is currently expensive, difficult to produce and not suitable or effective for many patients.

Dr Radford's project aims to overcome these limitations by developing a new vaccine that will directly target the "cancer fighting" dendritic cell directly without first needing to remove them from the patient.

A recently FDA approved vaccine (Provenge) is a preparation that contains many different cell types, including different types of dendritic cells that are specialised in stimulating the immune system. These are isolated from the patient, loaded with a prostate-cancer target in the lab and reinfused back into the patient. The procedure is costly and the vaccine needs to be individually tailored for each patient.

Dr Radford's and her team have identified a subtype of dendritic cells that they believe is the key subtype involved in inducing cancer-specific immune responses. The vaccine they are developing will directly stimulate these cells in vivo without having to first remove them from the patient. Such vaccine will be more efficacious, practical, cost effective and applicable to treat a wider range of patients. Additionally, with the support of a previous grant received from PCFA, Kristen has identified a new prostate cancer specific target against which potent immune responses can be generated. They aim to incorporate this new target into the new vaccine, potentially with other known prostate cancer targets to maximise the immune responses that can be generated.

Clinical trial of a novel, orally active, secreted phospholipase A2 inhibitor for the treatment of prostate cancer.

Dr Paul De Souza, Prostate Cancer Institute, St George Hospital.

With the number of hospital admissions for men with prostate cancer on the rise (i.e. 13,715 cases in 2000–01 to 25,429 in 2005–06) and the cost to the Australian health system of CaP soaring (i.e. in 2000–01 was $201M, a 93% increase over 1993–94), there is a desperate need, to find an effective, and preferably well–tolerated treatment for hormone refractory prostate cancer (HRPC).

Dr De Souza and his colleagues have developed and tested two compounds, cF and c2, that target a protein called Group IIA secreted Phospholipase A2 (sPLA2), that can be taken orally. Their studies on the growth of human tumours in mice have shown that both c2 and cF significantly slowed the growth of tumours relative to control–treated animals and in the case of c2 completely stopped tumour growth.

These data indicate that clinical studies to determine the benefit of these compounds for prostate cancer are warranted.

With the support of a new Movember grant Dr De Souza and his colleagues plan to complete their experiments in mice, define the dose response of these drugs in these small animals and prepare for single dose pharmacokinetic and pharmacodynamic study to study drug behaviour in man.

Exercise for prostate cancer patients on the RADAR.

Associate Professor David Galvao, Movember Young Investigator, Group Leader, Vario Institute.

Men with prostate cancer are often given hormones to slow down the growth of the cancer, but there are many side-effects such as loss of muscle and strength, increased fat around the waist, increased risk of heart disease and diabetes, and reduced physical abilities. Researchers think that exercise might reduce these side-effects, but there has been no large study to test this in prostate cancer patients who are taking or finishing hormone treatment.

With the support of a Movember Young Investigator Award, A/Prof. Galvao is looking at the effects of supervised exercise in 370 prostate cancer patients in Australia and New Zealand who are already part of this study on hormone treatment and radiotherapy.

The aim of the project is to determine the effects, efficacy, retention and compliance of physical exercise interventions in a large established cohort of prostate cancer patients from the Randomised Androgen Deprivation and Radiotherapy (RADAR) study. Specifically, David's team aims to compare a prostate cancer-specific supervised exercise program against a standard public health physical activity strategy utilizing printed resources. They will assess both in the short and long term, the following risk factors for metabolic syndrome: 1) cardiorespiratory capacity, 2) abdominal obesity, 3) lipid and glycemic control, and 4) self-reported physical activity, quality of life and mental health.

Some of the outcome measures undertaken are: aerobic walking capacity, anthropometric measures/abdominal obesity, blood markers (testosterone, prostate specific antigen (PSA), insulin, lipid profile, glucose and HbA1c levels), self-reported physical activity, overall physical function using the SF-36 physical function sub-scale, pedometer for seven days for quantitative measure of steps per day as well as a health history questionnaire etc.

To date in WA, of the 255 eligible participants, 208 have been screened and 57 completed baseline testing listed above; in the NSW site, 68 participants have been screened and 15 completed baseline testing listed above; in the NZ site, 50 participants have been screened and 28 completed baseline testing listed above; in all sites (WA, NSW, NZ) 305 participants have been screened and 100 participants have completed baseline testing listed above. Seven exercise training sites in Western Australia and 3 in NSW and 3 in New Zealand are

PCFA RESEARCH PROGRAM UPDATES

receiving participants. 51 participants have completed the initial 6-month phase tested successfully on the outcomes listed above. These men will be asked if they want to be part of this study as well, and then a local exercise specialist will contact them. Some of the men will be part of a supervised exercise group for six months and some will only receive printed information about exercise. The study protocol has now been published in the journal of BMC Cancer.

Researchers hope that this study will help to reduce complications from hormone treatment, like muscle loss, heart disease and diabetes, and improve the survival rates and quality of life of prostate cancer patients.

Men teaching men's health- toward better diagnosis and prevention of prostate cancer.

Professor Richard Turner, Professor of Surgery, School of Medicine, University of Tasmania.

Dr Christine Fairbank, Director, Clinical Teaching Associates Program, Melbourne Medical School, University of Melbourne.

Leading causes of death and disease burden in men in Australia include prostate cancer, tumours of the male genitalia and bladder cancers.

All of these conditions depend on early diagnosis and treatment to minimise morbidity and mortality. While in some cases accurate screening tests are available, physical examination still plays a major role in diagnosis in the Primary Care setting. It is therefore imperative that doctors-in-training be comfortable and adequately skilled in performing these examinations.

This project is aimed at better educating medical students so that they are both confident and competent in their ability and approach within men's health. One of the aims of this important project is to teach students a "patient centred" model of performing a rectal examination – an essential skill for them to have if the morbidity and mortality from prostate cancer is to improve.

Dr Fairbank and Dr Turner are piloting a new method of teaching the skills needed in the men's health area, including hernia examination, genital examination and rectal examination. Their program, the Urological Teaching Associate program, aims to give students individual tuition in the technical and interpersonal skills required for these examinations so that they become both self-assured and proficient in these areas. They recruit men from the community and teach these volunteers, the Urological Teaching Associates (UTAs), the technical skill and the interpersonal skills required for these examinations as well as feedback skills. These trained volunteers then teach the students whilst being examined themselves. Each student receives feedback on their performance.

The results so far show a dramatic increase in the students' confidence to perform each of these examinations after the tutorial. They state that the tutorials help both their technical and their communication skills and they very much appreciate and value this method of learning.

Australian Prostate Cancer BioResource (APCB), a national tissue bank that aims to facilitate efficient access to samples, encourages collaboration between researchers and enhances research productivity.

In 2004, PCFA, Commonwealth Bank and Andrology Australia co-funded the establishment of the Australian Prostate Cancer BioResource (APCB).

Professor Judith Clements, Chair, Australian Prostate Cancer Bioresource Management Committee.

The Prostate Cancer BioResource is a "virtual tissue bank" comprising 4 physically separate tissue collection nodes (Brisbane, Sydney, Melbourne and Adelaide), each with its own database for collection of tissue-associated clinical and pathological data, which will be linked by a web-based central database, containing minimum clinical and pathological datasets downloaded by the individual nodes and which can be interrogated to assemble specific research cohorts.

The initial support led to the first 5 year NH&MRC Enabling Grant of the centre and further development to its current level of activity. This was a significant leverage of PCFA funds that has led to a resource now used by many of the prostate cancer researchers funded more recently by PCFA. It constitutes the largest bank of PCa specimens and other critical samples used in research and fosters collaborations nationwide in the field of PCa research.

A tissue and blood collection is being progressively acquired by the APCB nodes. At the end of December 2009 (4 years 2 months of collection), the APCB had accrued samples from 2375 Australian men treated for early stage prostate cancer by radical surgery. The APCB samples are used for genetic and other studies to discover or validate better biomarkers and/or therapeutic targets for prostate cancer. Over the last 4 years since its inception, the APCB has built up a national and international reputation as a first-class biobanking facility, and has numerous links with international prostate and other cancer tissue banks around the world through its involvement with the international biobanking society, ISBER (International Society for Biological and Environmental Repositories).

In early 2010 the NH&MRC announced the continuation of funding under the Enabling Grant Scheme of $2M for the APCB for 5 years (2010-2014). This outcome was affirmation of the quality resource we have helped establish and recognition of the clear need for this resource to continue to underpin prostate cancer research in Australia. To allow the centre to maintain its activities and serve the

PCFA RESEARCH PROGRAM UPDATES

PCa research community. PCFA's National Board approved an additional support of $1M over 4 years (2010-2014).

This level of funding will allow APCB to sustainably fund their program of prospective tissue and clinico-pathology data acquisition from men with early stage prostate cancer. It is well recognized that the natural history of prostate cancer necessitates long term clinical follow-up to generate meaningful clinical and molecular correlates of disease progression and outcome.

A collaborative Prostate Cancer Centre for Researchers in South Australia.

With support from Movember funding, in 2010, PCFA partnered with the University of Adelaide to fund the establishment of the Adelaide Prostate Cancer Research Centre (APCRC) comprising a multidisciplinary team of medical researchers with expertise in prostate cancer spanning basic science, translation, advanced clinical practice and education and evaluation programs.

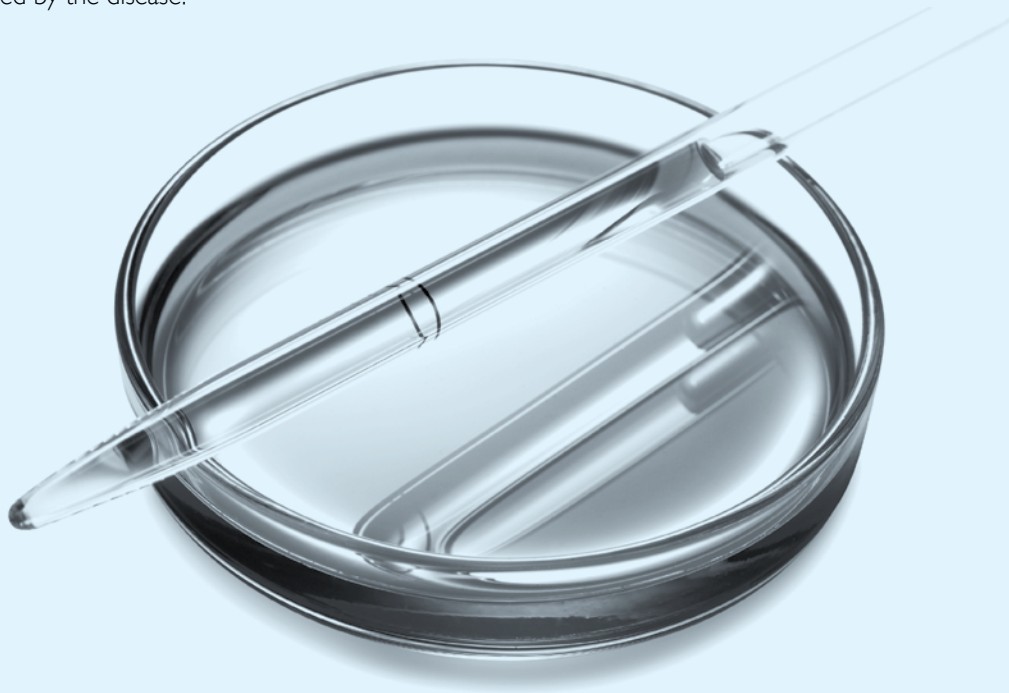
The centre comprises members from the Dame Roma Mitchell Cancer Research Laboratories and the Freemasons Foundation Centre for Men's Health and is led by the Centre Director Prof. Wayne Tilley and Management Group, advised by a Scientific Advisory Committee and supported by a Board of Patrons.

The objective of APCRC is to pursue a multidisciplinary, innovative research program utilising novel approaches and new technologies to address important clinical issues. Through well-established clinical linkages, the centre will rapidly and effectively translate its research findings into clinical and general practice, health education and health policy. Collaborations and synergies with other local, national and international scientists and research organizations will maximise research outputs, research outcomes and research impacts. APCRC is committed to developing effective treatments and preventive measures.

Members of the APCRC have developed an internationally recognised research program focused on prostate cancer, breast cancer, hormones and other factors involved in ageing and cancer. Particular research interests include mechanisms of resistance to cancer therapies, and the development of new therapeutic strategies and prostate cancer biomarkers. These laboratories comprise approximately 50 staff including

senior scientists, clinical affiliates, postdoctoral fellows, research assistants and students.

The Centre's overarching mission is the pursuit of new knowledge pertaining to the development and progression of prostate cancer, biomarkers for predicting indolent versus aggressive disease and treatment response, mechanisms of treatment resistance, new treatment strategies and translation of research findings into clinical and general practice, health education and policy to improve the quality of life of those directly and indirectly affected by the disease.



OTHER IMPORTANT PROJECTS
FUNDED TO DATE

DR JONATHAN HARRIS

Senior Lecturer in Protein Chemistry and Molecular Simulation Group Leader, Institute of Biomedical Innovation.

The dominant strategy in chemotherapy for prostate cancer is to prevent testosterone from reaching the prostate tumour and stimulating its growth, a scheme known as androgen blockade. This research is directed at providing a complementary approach to androgen blockade without the side effects.

PROFESSOR DIETMAR HUTMACHER

QUT Chair in Regenerative Medicine, Institute of Health and Biomedical Innovation, Queensland University of Technology.

Professor Hutmacher and his team aim to explore the potential of bone-engineering technology platforms, with an initial focus on unlocking some of the mechanisms of bone metastases developing from prostate cancer. This work has been published in high impact journals including Nature Materials and Trends in Biotechnology.

PROFESSOR DES RICHARDSON, DR STEVE ASSINDER AND ASSOCIATE PROFESSOR QIHAN DONG

The Bosch Prostate Cancer Focus Group.

This research team has identified potentially important cellular pathway interactions that vary between prostate cancer patients. These interactions provide targets for novel drug development and an array of markers that could inform individualised treatment options and allow monitoring of treatment response.

ASSOCIATE PROFESSOR MARTIN LACKMANN

Department of Biochemistry and Molecular Biology, Monash University.

In previous work, Professor Lackmann and his team developed an antibody that binds to 'EphA3', a type of cell surface protein that controls whether cells adhere to, or are repelled from each other. Trials have shown that the antibody effectively stopped the growth of prostate tumours in mice. Human clinical trials are planned for 2010.

ASSOCIATE PROFESSOR ANDREW BROWN

School of Biotechnology and Biomolecular Sciences, University of NSW.

Cholesterol is known as a risk factor for heart disease. However, evidence shows links between cholesterol and cancer, particularly prostate cancer. While drugs that affect cholesterol levels may prove useful in the treatment of prostate cancer, this research aims to understand how cholesterol metabolism occurs in prostate cancer cells. This information might inform the design of future drug therapies for prostate cancer.

ASSOCIATE PROFESSOR JARAD MARTIN

Radiation Oncologist, Senior Lecturer, Department of Medicine, University of Queensland. Honorary Associate Prof, Faculty of Science, University of Southern Queensland and Principal Australian Investigator for 'PROFIT'.

PROFIT is a study asking if external beam radiotherapy treatment for prostate cancer can safely be compressed from the current eight-week regimen into four weeks. If so, prostate cancer patients from regional areas would require less time away from home, treatment waiting times would be reduced, as would the overall cost of treatment.

DR CAROLINE GARGETT

RD Wright Fellow and Senior Scientist, Centre for Women's Health Research, Monash Institute of Medical Research and Monash University Department of Obstetrics and Gynaecology.

Tumour cells are surrounded by another cell type, fibroblasts, that also undergo cancer-specific changes. Carcinoma-associated fibroblasts (CAFs) have been shown to promote prostate cancer progression. This project aims to isolate and characterise stem cell-like CAFs and test if they can stimulate benign prostate cells to form tumours.

DR STUART ELLEM

Research Fellow, Prostate and Breast Cancer Research Group, Faculty of Medicine, Nursing and Health Sciences, Monash University.

This study examines the influence of estrogen on mast cells, as well as their role in the prostate, the development of prostatitis and prostate cancer. Increased insight into the cause of prostatic inflammation might identify mast cells as a novel target for future diagnostics and treatments for prostatitis, thereby reducing the risk and incidence of prostate cancer.

PROFESSOR ROBERT PIKE

Head of Department, Department of Biochemistry & Molecular Biology, Monash University.

The fibroblasts associated with cancer (CAFs) stimulate cancer due the unique complement of proteins they express. In particular protease proteins can concurrently affect many processes in tumour formation including blood coagulation, inflammation, and breakdown of the tissue surrounding the prostate glands. This grant assesses if protease inhibitors identified in breast are effective in decreasing the tumour stimulating ability of CAFs and so prostate cancer growth.

OTHER IMPORTANT PROJECTS
FUNDED TO DATE

PROFESSOR PATRICK HUMBERT

Head, Peter MacCallum Institute, Melbourne, Victoria.

Recent studies have shown that prostate tumours arising in men carrying a mutation in a specific gene, BRCA2 (Breast Cancer 2), a gene involved in the faithful repair of DNA, represent a specific highly aggressive subtype of prostate cancer with the vast majority of patients showing advanced metastatic disease as they are first diagnosed. In this project we aim to generate a pre-clinical model for BRCA2 human patients that will allow testing of new therapies as well as provide molecular insight into these patient's disease. These studies will complement ongoing human studies and may yield new biomarkers for the diagnosis of prostate cancer, and open new avenues of therapy using drugs targeted at cells that lack BRCA2 function.

DR ADDIE WOOTTEN

Psychologist, Department of Urology, Royal Melbourne Hospital, Parkville, Victoria.

Men are not routinely offered psycho-social support despite strong evidence that being diagnosed with prostate cancer poses significant quality of life concerns for men and their partners and consequently significant potential of developing a range of mental health disorders, including major depression and anxiety disorders. This is in part due to lack of available resources. This project aims to develop and assess an online psychological intervention for men with prostate cancer.

DR LUC FURIC

Research Fellow, Monash University, Department of Anatomy and Developmental Biology.

Prostate cancer cells have accumulated multiple mutations resulting in the hyperactivation of some key pathways (PI3K, MAPK) governing their survival and resistance to common therapeutical approaches. Specifically, we want to test the efficacy of new combination therapy in mouse models of prostate cancer and human prostate tissue samples in order to validate new potential treatments and translate these findings to clinical trials.

DR MICHELE TENG

NH&MRC Peter Doherty Postdoctoral Fellow, Peter MacCallum Cancer Centre, Cancer Immunology Program.

Tumor-induced immune suppression represents a major obstacle to effective treatment of established prostate cancer. My project aims to investigate the immunosuppressive role of regulatory T cells (Tregs), T cell anergy, and the cytokine IL-23 in the local prostate tumor microenvironment. Understanding these processes will allow the design of more effective cancer therapies.

PROFESSOR PAMELA J SYKES

Professor Preventive Cancer Biology, Haematology and Genetic Pathology, Flinders University and Medical Centre.

Low doses of radiation have been demonstrated to slow cancer growth in some blood cancers in animal studies. In this project we aim to use low doses of radiation to prevent, or at least slow cancer formation, in animals prone to prostate cancer. Identification of the key molecules involved in this low dose radiation induced protective mechanism could provide novel anti-tumour drugs for prevention of prostate cancer.

ASSOCIATE PROFESSOR ANNETTE HAWORTH

Clinical Research Physicist, Department of Physical Sciences, Peter MacCallum Cancer Centre.

Treatment of low risk prostate cancer with tiny radioactive seeds has been shown to be highly effective in controlling the cancer, but may leave the patient with undesirable side effects. In this project we aim to demonstrate that a non-uniform distribution of radioactive seeds through the prostate may still achieve high cure rates but minimise side effects. To achieve this we will be using radiobiological and mathematical modelling with advanced imaging techniques to develop a novel approach to this treatment.

ASSOCIATE PROFESSOR IAN DAVIS

The Ludwig Institute for Cancer Research, Uro Oncology Laboratory, Austin Hospital.

Prostate cancer (PC) causes significant health problems and deaths in Australian men. Abiraterone is a new treatment being tested for PC but it does not work in everyone or can stop working. This project will study why PC becomes resistant to abiraterone, by testing samples of PC tissues from men who have or have not received abiraterone treatment. This might allow us to predict men who need abiraterone or who should have other treatments for PC.

ASSOCIATE PROFESSOR JOHN HOOPER

Leader – Cancer Biology Team, Mater Medical Research Institute.

Drugs currently used to treat aggressive prostate cancer initially cause tumour regression. Unfortunately, over time the tumour cells that are not killed by these drugs are able to regrow the tumour and this ultimately results in the death of the patient. Our project aims to identify the genetic characteristics that are unique to the cells that survive drug treatment – the so-called "tumour initiating cells". From this information our goal is to develop drugs that selectively kill these tumour initiating cells and thereby prolong the life of the patient.

OTHER IMPORTANT PROJECTS
FUNDED TO DATE

DR MICHELLE M HILL

Research Fellow, Epithelial Cancer Cluster, The University of Queensland Diamantina Institute.

Caveolin-1 is over-expressed in high grade prostate cancer and has been associated with cancer spreading (metastasis). In this project, we use a systems biology approach to examine how cancer-associated caveolin-1 increases metastasis ability of prostate cancer cells. Better understanding of the cellular function will allow design of drugs that specifically target caveolin-1-associated prostate cancer, and new drugs that could potentially prevent prostate cancer spreading.

ASSOCIATE PROFESSOR YGAL HAUPT

Head, Tumor Suppression Laboratory, Research Division, Peter MacCallum Cancer Centre.

The function of proteins that protect our body from cancer, called tumour suppressors, is often compromised in cancer cells. We have recently identified a new pathway by which tumour suppressors are destroyed. Our project aims to establish the involvement of this novel pathway in prostate cancer, and to test the efficacy of the protection of tumour suppressors as a new treatment for prostate cancer. We will test our hypothesis in prostate cancer cells, in mouse models for prostate cancer, and in human prostate cancer samples.

DR NICHOLAS J FERRIS

Director of MRI, Department of Cancer Imaging, Peter MacCallum Cancer Centre.

In some patients whose prostate cancer has been removed surgically, the cancer can return at the edges of the space left behind by the operation. This 'recurrent' cancer is often treated with radiation, but it is important to avoid irradiating nearby normal organs, such as the bowel and the bladder. Our study is mapping how far these organs, and the prostate bed, can move with normal breathing and bowel activity. This will help radiotherapists to better target the recurrent cancer, while minimizing side-effects due to irradiation of normal tissues.

DR JEFF HOLST

Head, Immunity and Cancer Laboratory, The Centenary Institute.

We are studying the role of pumps that control the amount of nutrients taken into and out of cancer cells. We have discovered that two of these nutrient pumps are increased in prostate cancer. Since these pumps are present on the outside of cells, they are excellent candidates for drug targeting. These drugs could be designed to inhibit the function of these pumps, 'starving the cancer' by restricting nutrient uptake.

ASSOCIATE PROFESSOR GILDA TACHEDJIAN

NHMRC Senior Research Fellow, Head Retroviral Biology and Antivirals Laboratory, Centre for Virology, Burnet Institute.

Xenotropic murine leukemia virus-related virus (XMRV) is a virus that has been associated with prostate cancer. However, the reported XMRV prevalence in prostate cancer tissue is highly variable (0 - 27%) suggesting geographical differences in the presence of XMRV, sequence variation of strains or laboratory contamination of tissue samples. To date there have been no published studies to examine the presence of XMRV in Australia. In this project we aim to use molecular and serological techniques to determine whether XMRV is present in prostate tissue and white blood cells of prostate cancer patients and whether the presence of XMRV is associated with aggressive prostate cancer. Identification of XMRV could provide a biomarker for aggressive prostate cancer.

ASSOCIATE PROFESSOR LISA HORVATH

Head of the Department of Medical Oncology (RPAH), Sydney Cancer Centre.

Advanced prostate cancer is the second leading cause of cancer death in Australian men. Chemotherapy (Docetaxel) is effective in only 50% of patients with this disease. A molecule, MIC-1, is a potential predictive blood marker and mediator of Docetaxel resistance . We will identify how MIC-1 causes Docetaxel resistance and what other new drugs can be given with Docetaxel to overcome this resistance. A clinical trial will also be run to develop the MIC-1 blood test as a predictor of resistance.

PROFESSOR PAMELA J RUSSELL

Australian Prostate Cancer Research Centre, Queensland, and Institute of Health and Biomedical Innovation, Queensland University of Technology.

Knowing whether prostate cancer has spread from the prostate to local lymph nodes would alter the management of patients with this disease. We aim to develop new imaging techniques based on the use of nanoparticles or multi-branched polymers which have been joined to an antibody that targets prostate cancer cells to increase the sensitivity of standard or functional magnetic resonance imaging (MRI). We hope that using these particles will allow sufficient sensitivity to enable lymph node involvement to be detected. By modifying these agents so that they can also deliver drugs locally to targeted prostate cancer deposits would enable targeted therapy to reduce side effects and imaging of the response to treatment in "real time."

OTHER IMPORTANT PROJECTS
FUNDED TO DATE

PROFESSOR COLLEEN NELSON

Executive Director, Australian Prostate Cancer Research Centre – Queensland & Professor and Chair Prostate Cancer Research, Institute of Health and Biomedical Innovation, Queensland University of Technology.

When prostate cancer no longer responds to blocking the production of male sex steroids which feed the cancer and the cancer continues to grow, other therapies such as chemotherapy, aimed at treating or slowing the progression of symptoms, can be provided. However, these therapies do not work for all patients or stop working as cancer cells become "resistant" to treatment, allowing cancer to survive in large part to the stress response in the cancer cells that make them more resilient. Two stress-activated proteins, YB-1 and G3BPs are good indicators of poor prognosis in prostate cancer. This project aims to investigate the function of these two proteins and their downstream pathways with respect to mechanisms of cancer cell survival and progression. This will help to identify novel therapeutic targets for advanced prostate cancer.

PROFESSOR JUDITH A CLEMENTS

Scientific Director, Australian Prostate Cancer Research Centre-Queensland (APCRC-Q), Professor, Cell & Molecular Bioscience (CMB) Discipline & Institute of Health and Biomedical Innovation (IHBI), Queensland University of Technology.

Prostate-specific antigen or PSA is the current serum test for prostate cancer and is especially useful to detect tumour recurrence, but we still do not understand the precise functional role of PSA in prostate cancer progression. PSA has been used in the past to direct immunotherapy and gene therapy and help deliver cytotoxic drugs to prostate tumours but no-one has developed drugs to specifically inhibit the proteolytic activity of PSA. This project aims to determine what PSA specifically does in the tumour environment and identify the pool of proteins that PSA interacts with and how this action then regulates the genes in the tumour cell. The findings from this study will provide key information that will determine the potential of PSA as a new therapeutic intervention target.

PROFESSOR ANDREW BOYD

Division of Cancer and Cell Biology, Queensland Institute of Medical Research.

Advanced prostate cancer is characterised by the spread of cancer cells from the prostate into neighbouring tissues and to other sites in the body. This process requires an alteration in cell movement. In this project we aim to explore the role of two protein families which control cell movement and position, the Ephs and ephrins. Understanding how these proteins affect prostate cancer cells may lead to new therapies for advanced cancer.

DR XUE QIN YU

Senior Research Fellow, Cancer Epidemiology Research Unit, Cancer Council NSW.

Accurate estimates of the numbers of men in the community at the different stages of their cancer journey now and in the future are required to plan for and provide adequate cancer care services. Moreover, the resources needed to treat newly diagnosed patients are very different from those for supporting long-term survivors or those nearing the end-of-life. Therefore, estimates of cancer prevalence for each of the relevant stages of care are required to provide a more meaningful and useful measure for health care planning purposes. In this study, we will develop statistical methods to predict the future prevalence of prostate cancer by stage of clinical care.

ASSOCIATE PROFESSOR NIGEL WATERHOUSE

Group leader, Apoptosis and Cytotoxicity Laboratory, Mater Medical Research Institute.

One promising new approach for prostate cancer treatment is to use a person's own immune system to treat their cancer. The team will achieve this by taking a sample of blood from the patient with cancer, isolating the cancer-fighting immune cells from the blood, stimulating those immune cells in the laboratory to fight prostate cancer cells and then giving back the now 'supercancer-fighting' immune cells back to the patient. Studies like this have been carried out in the past, and unfortunately researchers found that the prostate cancer cells were not being killed effectively. Dr Waterhouse's team will try to understand why some prostate cancer cells are killed by the patient's immune system and why some are not. Results of the research will enable the design of drugs that can be given to the patient along with the immunotherapy that should improve the effectiveness of the treatment.

PROFESSOR TREVOR HAMBLEY

Director or Research, Faculties of Science, University of Sydney.

A primary cause of cancer deaths is relapse following treatment, with the disease then typically being resistant to chemotherapy. In part, this comes about because the toxicity of most drugs limits the dose that can be used in the initial treatment and because the drugs are unable to penetrate to all parts of the tumour. In this project Prof. Hambley's team will develop strategies for modifying anticancer agents so that they are better able to penetrate into all parts of the tumour and have toxicities low enough to enable sufficient doses to be used. This will be achieved by preventing the drugs from entering cells, tumour or healthy, until they are processed and activated by PSA, a protease that is present at much higher levels in the prostate tumour environment than in the rest of the body.

OTHER IMPORTANT PROJECTS
FUNDED TO DATE

DR RENEA TAYLOR

Senior Research Fellow, Prostate & Breast Cancer Research Program, Monash University.

Prostate cancer patients are commonly given drugs to reduce the action of androgens in their bodies. Although in many men initially the tumour shrinks, the cancer can re-grow. This advanced stage of the disease is known as "castrate-resistant prostate cancer". There are currently limited options for treating castrate-resistant prostate cancer, and this is the focus of this grant application. Dr Taylor and her team believe that the cells surrounding the cancer cells, known as the stromal cells, respond to hormonal (androgen) withdrawal in a way that may actually help the tumour grow. By improving their understanding of the biological events that lead to the development of castrate-resistant prostate cancer, scientists may be better placed to design hormone therapies that treat prostate cancer more effectively.

DR GRANT BUCHANAN

Senior Research fellow, Dame Roma Mitchell Research Laboratories.

Dr Buchanan's team has found that fibroblasts surrounding the cancerous epithelial cells begin to secrete signaling molecules called chemokines that stimulate the proliferation of the cancer cells and allow them to spread to other parts of the body. His objectives are to first investigate whether chemokines produced by cancerous fibroblasts can tell us if the cancer will or has already spread. This will improve our ability to classify aggressive from benign cancers. Second, Dr Buchanan's team will test if the effects of these chemokines in promoting progression can be halted by the active ingredient of turmeric, curcumin. Specifically, they will test if curcumin can prevent prostate cancer in an animal model, and if it can work in combination with androgen ablation to better treat existing disease. As curcumin is not toxic in human studies, this has the potential for rapid translation into clinical prostate cancer management within a short time frame.

DR MIKA JORMAKKA

Senior Post-doctoral fellow, Department of Structural Biology, Centenary Institute.

Dr Jormakka and his colleagues are studying the role of protein pumps that control the amount of nutrients taken into and out of cancer cells. They have discovered that two of these protein pumps, LAT1 and LAT3 are very important in controlling such process. To enable drugs to be designed against these two proteins, scientists need to know exactly what these proteins look like. Dr Jormakka will first study how these protein pumps function, manufacture large amounts of the purified protein pumps and make crystals. These crystals will then be studied using a very powerful X-ray machine to determine their structure (i.e. what they look like). Once we know what these pumps look like, they can then design drugs specific to these pumps, like designing a key to fit a lock.

These drugs could be designed to inhibit the function of these pumps, in essence 'starving the cancer' by restricting nutrient uptake.

PROFESSOR SUSAN CLARK

Head, Cancer Research Program – Epigenetics Group, Garvan Institute of Medical Research.

Cancer is a disease of the DNA with both genetic and epigenetic lesions contributing to changes in gene expression. It is now widely accepted that epigenetic changes play a critical role in the

initiation and progression of a wide range of cancer types. This project will define in detail the role of a gene known as H2A.Z in prostate cancer using two different approaches. Firstly, it will determine if H2A.Z is able to deregulate key genes in prostate cancer. Secondly, it will determine the biological consequences of decreased or increased H2A.Z expression in both in vitro and in vivo cancer models. These expected results would characterise H2A.Z as a potential target and/or molecular marker for prostate cancer diagnosis, prognosis and therapy.

PROFESSOR LEONIE ASHMAN

Department of Medical Biochemistry, University of Newcastle.

Two molecules known as tetraspanin (CD151 and CD9) participate either in enhancing (CD151) or suppressing (CD9) metastasis in cancer. To effectively use these proteins as therapeutic targets or prognostic markers it is vital to understand what controls the level of expression of CD151 and CD9 in prostate cancer. In addition it is essential to determine how the altered expression of CD151 and CD9 contributes to prostate cancer progression. How these proteins contribute to prostate cancer will be identified through determining the proteins they interact with. Prof. Ashman and her team believe that identifying how the expression of the tetraspanins is altered in cancer and how this contributes to cancer progression will greatly advance the development of these proteins as therapeutic targets and prognostic indicators.

PCFA RESEARCH PROGRAM
2011 AND BEYOND

With the dramatic increases in scientific knowledge in the prostate cancer (PCa) research field as well as the significant changes in diagnosis, treatment, prevention, translation, and delivery of care, researchers must continue to meet future challenges.

PCFA's Research program aims to provide the much needed funds that will help researchers to accelerate the pace of discovery and apply its research results in a timely manner.

PCFA's Research Program has made a significant impact on prostate cancer research in Australia.

PCFA's program helps to bridge the existing funding gap between prostate cancer and other areas of cancer research. It aims to fund only the best grants and investigators in the field, with a focus on translational research that will directly benefit the consumer.

There is a long way to go in the fight against prostate cancer, however PCFA is delighted to be leading the battle through its national grant program. To maintain momentum in prostate cancer research, PCFA is committed to funding new projects annually.

Grants currently available include:

Young Investigator Grants: To support young scientists beginning a career in prostate cancer research. Up to $150K/pa over 4 years.

Concept Grants: For senior scientists not currently working in prostate cancer who have an innovative proposal and are seeking startup funding. Up to $125K/pa over 2 years.

New Directions development Grants: For proposals submitted by senior investigators in PCa research that are aimed at exploring novel ideas in established prostate cancer laboratories, including support for innovative clinical trials. Up to $150K/pa over 2 years.

Equipment Grants: For significant items of equipment needed to progress ongoing prostate cancer research. Up to $100K in any given year.

In 2011-2012 PCFA invites applications in its priority areas for funding, specifically, projects seeking to:

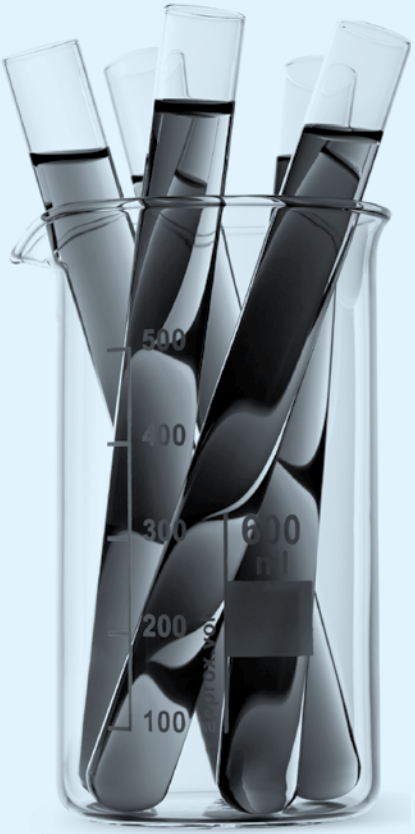
- Discover the genetic and cellular factors which initiate and/or perpetuate prostate cancer
- Discover, develop and clinically validate new, non-invasive tests to detect prostate cancer, and/or to determine whether a patient's cancer is surgically curable.
- Discover, develop and clinically validate new biomarkers that predict the future clinical course of prostate cancer and/or the response to future chemotherapy
- Discover, and validate through preclinical and clinical trials, novel molecular targets for chemotherapy of locally-invasive or metastatic prostate cancer, including androgen-independent cancers
- Develop new treatment strategies for prostate cancer, especially locally-invasive or metastatic cancers
- Provide immediate improvements in the quality of life of patients with prostate cancer

INTERESTED
IN HELPING PCFA?

If you are interested in helping PCFA to continue funding world-class prostate cancer research, please contact us:

Phone toll free on 1800 22 00 99

Visit us online at www.pcfa.org.au



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