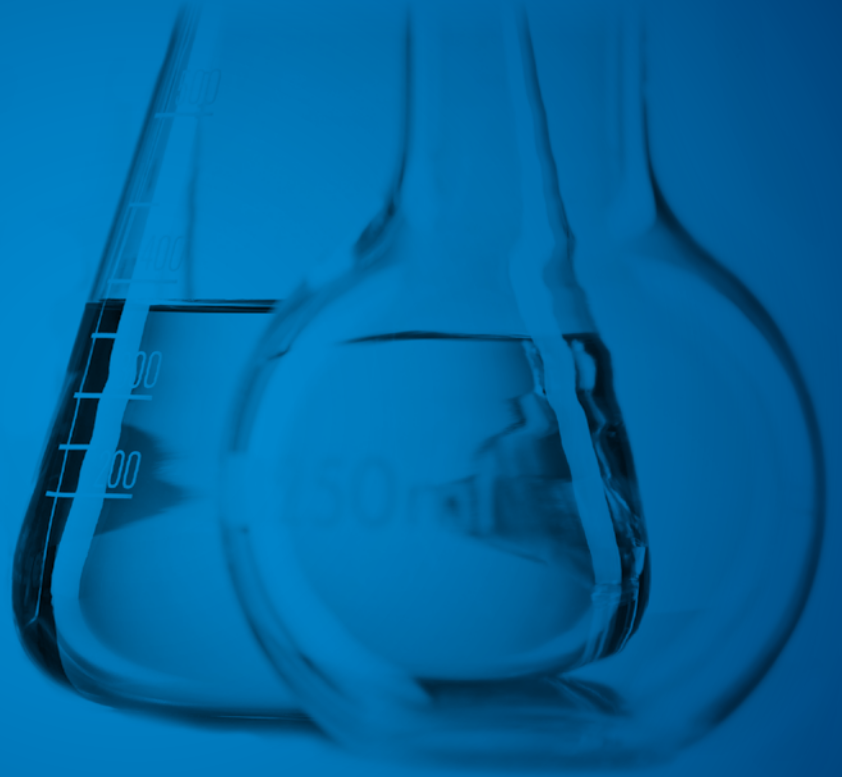




Prostate Cancer
Foundation
of Australia

2009/2010
Collaborative
Research
Update



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MESSAGE FROM THE CEO



PCFA is proud of its ongoing commitment to funding world-class Australian research into the cause, prevention and treatment of prostate cancer. Through its research funding and initiatives, PCFA hopes to dramatically reduce the impact of prostate cancer on the Australian community.

In Australia, we are fortunate to have an extensive pool of world-class research talent working in the health arena. As well as funding the work of established and internationally recognised researchers, PCFA's Young Investigator and Concept Grants actively encourage new talent into the field. It is hoped this will bring new and fresh ideas to the issue, as well as helping ensure the long-term future of prostate cancer research in Australia.

PCFA's Young Investigator Grants support young scientists, regardless of their degree, who have demonstrated research ability and are now ready to become independent investigators. Concept Grants support senior investigators who are not currently studying prostate cancer, but can bring innovative research proposals or new technology to the field.

At PCFA, we strongly believe international collaboration between prostate cancer researchers and funding bodies is vital to expediting research and trials that will improve patient outcomes. PCFA's Research Program encourages collaboration between PCFA-funded researchers on a national level, while PCFA's involvement with Cancer Australia ensures a sharing of information with other Australian funding organisations.

On an international level, PCFA is a founding member of the World Wide Prostate Cancer Coalition (WPCC). A coalition of prostate cancer interest groups from around the world, WPCC seeks to share information, ideas, visions and dreams that will ultimately minimise the impact of prostate cancer globally.

PCFA's ability to undertake such a large grant program is due to the incredible support it has received from The Movember Foundation. Since 2004, PCFA has been delighted to be a beneficiary of this hugely successful fundraising and awareness event. With this support, we can make a difference to the lives of the almost 20,000 Australian men and their families diagnosed with prostate cancer each year.

I hope this Collaborative Research Update offers insight into PCFA's research funding and initiatives, and some of the progress being made by PCFA-funded researchers around Australia.

While the battle is far from over, PCFA is proud to be leading the fight.

A handwritten signature in blue ink that reads "Andrew Giles". The signature is stylized and fluid.

ANDREW GILES
Chief Executive Officer

MESSAGES OF SUPPORT FOR PCFA'S RESEARCH FUNDING

The Hon. Wayne Swan MP

Treasurer of the Commonwealth of Australia

"I am pleased to be associated with the Prostate Cancer Foundation of Australia (PCFA). As a prostate cancer survivor, I appreciate PCFA's important work providing support, raising awareness and funding world-class Australian research. Each year, it is estimated that almost 20,000 Australian men and their loved ones will be affected by a diagnosis of prostate cancer. It is my hope that research carried out today will significantly reduce the impact of this disease on the Australian community."

Professor Marie Bashir AC, CVO,

Governor of NSW

"As the NSW Patron for the Prostate Cancer Foundation of Australia, I applaud the Foundation's commitment to funding research into the cause, prevention and treatment of prostate cancer. Considering that each year in NSW, more than 6,150 men will be diagnosed with prostate cancer, and approximately 980 men will lose their life to this disease, it is clear that significant breakthroughs in prostate cancer research are urgently needed. The Prostate Cancer Foundation of Australia's research funding program is helping to expedite significant advances that will ultimately benefit Australian men affected by this disease."

Professor David de Kretser

Governor of Victoria

"It is my privilege to be the Victorian Patron for the Prostate Cancer Foundation of Australia. I am particularly impressed with PCFA's leadership in the area of prostate cancer research. While it's reputation for funding world-class Australian research is well established, the important role of PCFA in stimulating collaboration and cooperation within the prostate cancer research community is not often acknowledged. I am grateful to PCFA for it's work around Australia, and particularly in Victoria where more than 4,200 men are diagnosed with prostate cancer each year."

Sue Murray

CEO, National Breast Cancer Foundation

"Research is the key to unlocking the important answers in prostate cancer. The National Breast Cancer Foundation has found that funding Australia's outstanding researchers and nurturing collaboration is the key to accelerating research. Congratulations to PCFA on leading the way and ensuring Australia stays at the forefront of prostate cancer research."

MESSAGE FROM PCFA'S RESEARCH COMMITTEE CHAIR



In Australia and internationally, prostate cancer funding is severely lacking, especially when compared with some other cancers that cause equivalent morbidity and mortality (e.g. breast or colon cancer). As a result, the number of prostate cancer investigators is relatively small, as is their research output. This manpower and funding deficit means that advances in diagnosis and treatment of prostate cancer, which are urgently needed, are taking longer to be discovered and developed.

PCFA's structured research program has the following aims:

- 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.

PROFESSOR JOHN MILLS
PCFA Chair, Research Committee

**To provide a logical,
consistent and
transparent framework
for submission, review
and selection of research
applications for funding.**

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.

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

Professor John Mills (Chair)

A specialist physician, medical scientist and businessman, Professor John Mills holds 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 has 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 actively involved in research review and administration.

Since 1992, Professor Mills has been involved in biomedical business, and is currently an Executive Director of TissuPath P/L, a specialist cytogenetics and histopathology practice with a special interest in uropathology and prostate cancer. He is also a Director of PCFA.

Associate Professor Howard Gurney

Director of the Department of Medical Oncology at Westmead Hospital in Sydney, Associate Professor Howard Gurney is a medical oncologist with sub-specialty interests in genitourinary and upper gastrointestinal tract cancers. 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 and novel methods for dose calculation. He has been an investigator on more than 50 clinical trials and has more than 50 peer-reviewed publications.

Associate Professor Susan Henshall

Group Leader of the Prostate Cancer Group in the Cancer Research Program at the Garvan Institute of Medical Research, Sydney, Associate Professor Henshall was one of the first recipients of a PCFA Young Investigator grant. She is currently a Cancer Institute NSW Fellow, and holds conjoint academic appointments with the University of New South Wales and Georgetown University in the United States.

Associate Professor Henshall's main research focus is 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.

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.

PCFA Research Committee - continued

Professor Suzanne Chambers

Director of Research at the Cancer Council Queensland since December 2006, Professor Suzanne Chambers is responsible for the strategic direction, development and management of research program activity. 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.

PCFA funding allowed Professor Chambers and the Australian Prostate Cancer Collaboration to undertake a project that examined views about support groups from support group leaders and clinicians, and also from men who attend these groups. In a national survey published in 2005 in the *British Journal of Urology International*, most men (88 per cent) indicated that the best time for men to be referred to a support group is at diagnosis; and most men found the group a positive and helpful experience.

In 2005, Professor Chambers 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 Newton

Director of the Vario Health Institute and Professor of Exercise and Sports Science at Edith Cowan University, Perth, Professor Robert Newton is also an accredited exercise physiologist. He directs the "Cancer Survivors Program" at the Institute, providing lifestyle support to people with cancer.

Professor Newton leads a research 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 Robert Alexander ('Frank') Gardiner

An Academic Urologist with the University of Queensland, Professor 'Frank' Gardiner is based at Royal Brisbane and Women's Hospital where he is a Consultant Urologist. He has academic appointments locally at the Queensland Institute of Medical Research, Queensland University of Technology and Cancer Council Queensland. Professor Gardiner collaborates widely in his research interests, which are centered on prostate cancer.

Professor Gardiner also holds a number of senior positions in national and international professional organisations.

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 held a dual appointment at Monash University. She 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, 2004-2008) and a member of Professor Sharon Lewin's laboratory at the Alfred Hospital, 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, Andrew Giles also sits as an ex officio member of the Committee.

PCFA

RESEARCH MILESTONES

PCFA has a long history of funding world-class Australian researchers working in the fight against prostate cancer.

In 1999, the Australian Prostate Cancer Collaboration identified the establishment of a national prostate cancer tissue bank as the number one priority for furthering Australian research into the diagnosis and treatment of prostate cancer. Such a tissue bank would allow researchers from all over Australia easy access to supplies of fresh prostate tissue essential for their research. The Collaboration approached PCFA to help source funds for this project. Here began PCFA's commitment to funding Australian prostate cancer research.

Through initial PCFA, Commonwealth Bank and Andrology Australia support, and subsequent government (NHMRC) Enabling Grant funding (2004-2009, and recently renewed 2010-2014), the Australian Prostate Cancer BioResource (APCB) is now established and operational.

A national tissue bank with four major nodes in Brisbane, Sydney, Melbourne and Adelaide, APCB is progressively acquiring a tissue and blood collection. At the end of December 2009 (collection over a period of four years and two months), the APCB had accrued samples from 2,375 Australian men treated for early stage prostate cancer by radical surgery.

APCB samples are used for genetic and other studies to discover or validate better biomarkers and/or therapeutic targets for prostate cancer. Since its inception, APCB has built 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 Society for Biological and Environmental Repositories.

Other key dates in the history of PCFA's commitment to research include:

- In 2002, PCFA awarded its first two Prostate Cancer Research Fellowships to Dr Susan Henshall and Dr Lisa Butler.
- In 2005, PCFA, with support from the Mazda Foundation, awarded its third Fellowship to Dr Annika Antonsson.
- In 2005, PCFA, with support from BHP Billiton, undertook a review of all the research currently underway in Australia. The results of this national survey enabled PCFA to establish its annual grant program in 2007, as well as develop its priority areas.

The current Research Committee was established in 2007 when Professor John Mills was appointed Chairman. The committee is made up of an outstanding group of scientists, and aims to provide a transparent, well-organised and academically rigorous venue for the funding of worthwhile research projects focused on prostate cancer.

PCFA now supports 53 research grants nationwide and has been acknowledged in more than 60 publications by its grantees. Three of the young scientists supported by PCFA's Research Scheme are now independent investigators and have established their own group, while two senior investigators attracted through the Concept Grant Scheme have now joined the army of prostate cancer researchers.

Since its establishment, PCFA's Research Committee has approved \$17 million of funding for research projects that will ultimately benefit the almost 20,000 Australian men and their families that are impacted by a diagnosis of prostate cancer each year.



**PCFA now supports 53
research grants nationwide
and has been acknowledged
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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. Proceeds from Movember Australia go to PCFA and beyondblue – the national depression initiative.

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. To give an idea of growth, at the time of publication, it is estimated that the latest campaign (2009) has raised more than \$20 million, thanks to the 128,000 Australian Mo Bros, Sistas and their supporters.

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.

Today, Movember takes place around the world. Motivated by what was happening in Australia, a further five countries now embrace the Mo in an official capacity each November - New Zealand, USA, Canada, UK and Ireland. In addition, Movember is aware of Mo Bros and Sistas supporting the cause right across the globe: from Russia to Dubai, Hong Kong to Finland and everywhere in between.

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, email info@movember.com, or call 1 300 47 69 66.

PCFA RESEARCH

FUNDING AROUND AUSTRALIA

PCFA Active Grants
Australia Wide
2007-2010



WHERE ARE THEY NOW?

Dr Lisa Butler and Associate Professor Susan Henshall were two of PCFA's first research grant recipients. Here they provide updates on their research and insights into the importance of PCFA's research funding program.



Dr Lisa M Butler

Dame Roma Mitchell Cancer Research Laboratories, University of Adelaide and Hanson Institute

PCFA Postdoctoral Fellowship: Development of a novel androgen receptor-based strategy

for the treatment of prostate cancer

The aim of my Postdoctoral Fellowship, funded by PCFA from 2002-2004, was to develop new, more specific strategies for treatment of advanced prostate cancers. Growth of prostate cancer cells is initially dependent upon hormones called androgens. Androgen ablation therapy is used to reduce androgen levels in patients with advanced prostate cancer in order to arrest tumour growth. Unfortunately, despite an initial response, resistance to androgen ablation inevitably occurs and there is an urgent need for better treatments for advanced prostate cancer.

My Fellowship project focused on developing new ways of blocking androgen action in prostate cancer cells. I utilised a series of inhibitors developed in our laboratory, which specifically blocked the function of the androgen receptor:

I showed that these inhibitors were effective regardless of the level of expression, function or activity of the androgen receptor in the cancer cell. Importantly, inhibition of the androgen receptor using these new agents, in turn, effectively suppressed the growth of prostate cancer cells. These studies provided strong evidence that specific targeting of the androgen receptor would be an effective approach to the management of metastatic prostate cancer.

Since completing the PCFA Fellowship, I extended this concept further to investigate a panel of clinical agents that also target the androgen receptor. I have demonstrated that combining low doses of different agents results in markedly more effective killing of prostate cancer cells than higher doses of the agents used alone. In addition to the potential for an increased clinical response in men with advanced prostate cancer, this approach, using considerably lower drug concentrations could result in fewer side effects. Ongoing studies will investigate the biological mechanism of this enhanced effectiveness using combinations of androgen receptor-targeted agents. I am also currently developing protocols to test these drug combinations in preclinical and clinical trials for patients with advanced prostate cancer.

The PCFA Fellowship has been invaluable for the development of my research career. The scientific outcomes from the research project provided a strong basis for establishing my research program in prostate cancer and led to the subsequent award of Florey and Cancer Council Research Fellowships, and funding for the project by the Cancer Council and NHMRC.

In 2009, I was awarded a three-year research grant from Cancer Australia/Prostate Cancer Foundation of Australia Priority-Driven Research scheme to further develop the combinatorial therapeutic approach. The research that has come out of this Fellowship has significantly increased our understanding of the role of androgen signalling in prostate cancer, and has strong potential for translation into clinical studies in the short term.



Associate Professor Susan Henshall
Prostate Cancer Foundation of Australia
Fellow 2002-2004

In 2002, I was awarded the inaugural Prostate Cancer Foundation of Australia Research Fellowship. This provided essential funding to pursue the discovery of biological markers that indicate poor outcome in prostate cancer patients.

As a result, the Prostate Cancer Group at Garvan undertook a genome-wide study to identify genes that are associated with aggressive prostate cancer. This study discovered that men who have low levels of a gene called AZGPI in the prostate at the time of surgery (radical prostatectomy) have a greatly increased risk of developing metastatic cancer. This means that these men could benefit from more aggressive treatment such as radiotherapy or chemotherapy around the time of surgery when they still have potentially curable cancer. Conversely, patients with a low risk of developing metastatic disease could have the option of deferring treatments that have a negative impact on quality of life.

At the completion of the PCFA Research Fellowship in 2004, I received funding from the Cancer Institute NSW and the E.J. Whitten Foundation. This allowed me to build on my earlier research to confirm the accuracy of AZGPI as a tissue biomarker for prostate cancer outcome in a prospective trial. This trial is currently underway in four hospitals in Sydney. If successful, the adoption of an AZGPI test into clinical practice will represent a major advance in the treatment of prostate cancer patients. In addition, my group's research into the underlying biology of aggressive prostate cancer has identified another gene, GATA-2, that might cooperate with AZGPI to drive the progression of this cancer.

The work originally funded by PCFA highlighted to me the importance of providing effective tailored treatment for cancer patients. In my current role at the Garvan Institute of Medical Research, Sydney, as part of the Garvan St Vincent's Cancer Centre Project Team, we are establishing a dedicated space for cancer researchers to work alongside cancer clinicians with facilities and infrastructure designed specifically to support patient focused research outcomes.

I am also a member of PCFA's Research Committee, supporting PCFA's Research Program. This program provides key funding for innovative prostate cancer research in Australia and continues to encourage young investigators to undertake research into prostate cancer.

RESEARCH UPDATES

Dr Kristen Radford and Dr Patrick Humbert are PCFA-funded researchers highlighted in the 2008/2009 Collaborative Research Update. Here they provide further insight into their research, and progress updates.



Dr Kristen Radford
Mater Medical Research Institute

The potential of Human Kallikrein 4 as a novel target for prostate cancer immunotherapy.

Prostate cancer is the second leading cause of cancer-related deaths in Australian men and there are currently no effective treatments for metastatic disease. Therefore, there is an urgent need for the development of effective, non-toxic treatments for metastatic prostate cancer.

We set out to use the body's own immune system to target the disease. The theory is, if we can 'train' the cells of the immune system (killer T cells) to recognise targets (or antigens) on the tumour cell surface, then these T cells will be able to kill the tumour cells. However, tumour cells are very good at hiding their antigens from the immune system, or using antigens that are similar to those present in healthy tissue, so the immune system will 'ignore' them. One of the main problems facing scientists is finding an antigen to teach the immune system to target. We identified a protein called human Kallikrein 4 (hK4), which was

expressed significantly more strongly by prostate cancer cells compared to healthy cells. This meant that hK4 was a good antigen against which to try and raise killer T cells. If the immune system could be taught to recognise this antigen, it would hopefully go on to kill tumour cells.

Rather than use the whole hK4 protein, we used information from computer programs to look for the parts most likely to raise an immune response. Based on the results of these programs, we identified five peptides (antigens) within hK4 that looked likely to be able to raise an immune response. Using blood samples from prostate cancer patients, we tested to see if killer T cells could be taught to recognise and target these peptides. For one out of the five peptides, we generated killer T cells in almost every donor. Next we took the killer T cells and put them in a flask with some prostate cancer cells. Our killer T cells were able to kill the prostate cancer cells.

After these exciting results with one peptide, we wanted to see if we could find more peptides from hK4 that the immune system could target. The idea was that if we had lots of different killer T cells, all trained to attack parts of the tumour cell, it would give the body's immune system an even better chance to fight the prostate cancer. We used computer programs to identify more peptides that would make good targets, and came up with a total of 105. We tested all of these peptides in an assay to see which of these the killer T cells would be most likely to bind and target. Of the 105 peptides, 19 were considered to make good targets. We are currently in the process of testing all of these peptides using blood samples from prostate cancer patients, to see if we can make killer T cells that will target them.



Dr Patrick Humbert
Peter MacCallum Cancer Centre

Every cell in our body has an intrinsic orientation that is controlled by a universal set of genes known as polarity genes. Loss of this orientation is a common and early

feature of prostate cancer.

At the outset of the project, we identified the gene Scribble as a new human polarity gene that controls cell orientation and whose levels appeared reduced in prostate tumours. This predicted Scribble may play an important role in protecting humans from prostate cancer.

In work supported by Australia Post/PCFA, in the last 12 months we have shown that this gene Scribble appears essential to prevent the development of prostate cancer. Lowering levels of Scribble in normal prostate cells increases the risk of prostate cancer by disorganising the prostate tissue and by increasing the speed at which cells grow within the prostate.

We are now trying to identify how this is achieved and which molecules might be involved. By identifying this mechanism, we should be able to design drugs that will keep prostate tissue growth in check and return the cancerous prostate back to a normal organised tissue.

Our observations in the human population indicate that alterations in the appearance of Scribble in prostate tumours is also associated with high grade tumours in these patients. We are now carrying out experiments to determine whether this observation can be used to better predict outcome for prostate cancer patients.

Ultimately, we hope our research will provide a better understanding as to how the incorrect positioning of prostate cells can occur, and its impact on prostate cancer progression. This may lead to the discovery of new prognosis factors, new chemotherapeutic targets, as well as a better understanding of prostate biology and cancer progression.

EXAMPLES OF PCFA-FUNDED RESEARCH 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.

Prof 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*.

Prof Des Richardson, Dr Steve Assinder and Associate Prof 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.

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.

Prof Peter Leedman

Laboratory for Cancer Medicine, Western Australian Institute for Medical Research

This research team has identified a novel regulator of androgen (testosterone) signaling in the prostate, termed SLIRP. It is proposed that SLIRP could present opportunities as a prostate cancer biomarker, helping to predict patient outcome in human prostate cancer.

Associate Prof 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.

Dr Jeff Holst

Origins of Cancer Lab, Centenary Institute

'Cell surface protein pumps' regulate the amount of nutrients a cell receives. Dr Holst is examining a particular 'pump' that is dramatically increased in prostate cancer, and might be responsible for increasing nutrient uptake in cancer cells. Dr Holst is also examining how 'pumps' might cooperate to regulate cancer growth, and the affect of diet on the disease. Understanding the role of these protein pumps may provide clues for entirely new dietary or drug therapies designed to 'starve' cancer.

Prof Pamela Russell AM

Director of Oncology Research Centre,
Prince of Wales Hospital

This team aims to understand why prostate cancer cells spread to and grow in other organs, forming secondary lesions (metastases), particularly in the bone. These studies will confirm the importance of new and potential therapeutic targets involved in prostate cancer, and help provide a strong platform for preclinical evaluation of novel drugs.

Prof Ronald J. Quinn, Prof Colleen Nelson and Dr David Camp

Eskitis Institute for Cell and Molecular Therapies, Brisbane
Innovation Park, Griffith University

This multidisciplinary research effort will identify synergistic combinations of novel small molecules and antisense molecules that inhibit or disrupt gene networks critical to prostate cancer

progression. The team will use the Automated Liquid Handler to screen small molecule libraries in combination with antisense molecules in cell-based assays. This will identify possibilities for new combination therapies, using a small molecule in conjunction with an antisense.

Dr Paul de Souza

Prostate Cancer Institute, St George Hospital

Dr de Souza and his team have developed and tested two compounds, cF and c2, that target a protein called Group IIA secreted Phospholipase A2 (sPLA2). Initial studies show that both c2 and cF slow or even stop tumour growth. Future studies might lead to the development of an effective and well-tolerated treatment for hormone refractory prostate cancer.

Dr Matthew J. Naylor

NHMRC Career Development Award and NBCF Fellow,
Conjoint Lecturer, UNSW and Group Leader, Cancer
Research Program Garvan Institute of Medical Research

Integrins are cell receptors that control a range of cell activities such as growth, survival, migration and detachment from the local tissue, which are altered during metastasis. This team will use gene deletion and alteration of integrin signalling in prostate cancer cells to determine the role of beta-1 integrin in the regulation of prostate cell function, cancer progression and metastasis. This project aims to develop new models to investigate prostate cancer and may identify new genes that control tumour growth and metastatic spread, providing new avenues for therapeutic intervention in prostate cancer.

Examples of PCFA-funded research to date - continued

Dr Patrick Humbert

Group Leader, Cell Cycle and Cancer Genetics Laboratory,
Peter MacCallum Cancer Centre

Studies show that prostate tumours in men who carry a mutation in a gene, BRCA2 (Breast Cancer 2), represent a highly aggressive subtype of prostate cancer. This project aims to generate a pre-clinical model for BRCA2 human patients, allowing testing of new therapies and providing molecular insight into the disease. These experiments will not only give greater insight into the molecular development of prostate cancer; they will also complement ongoing human studies and may yield new biomarkers for diagnosis, and open new avenues of therapy using drugs targeted at cells lacking BRCA2 function.

Associate Prof Ian Davis

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

This project evaluates how useful PET scanning is in the treatment of localised prostate cancer; compared to other standard assessments; whether it helps in making treatment decisions; and whether it can be used to monitor the results of treatment. The project involves two clinical trials focused on men whose cancer is thought not to have spread outside the prostate.

Associate Prof Ygal Haupt

Peter MacCallum Cancer Institute

The promyelocytic leukemia protein, PML, prevents the development of cancer. However, another protein, E6AP, reduces levels of PML in cells. This project aims to discover if the link between PML and E6AP is important in the development of prostate cancer, and how useful these two proteins are as diagnostic and predictive markers. If blocking the action of E6AP protects PML, it could be restored to pre-cancerous levels, potentially stopping the development of prostate cancer.

Prof Pamela Russell AM

Director of Oncology Research Centre,
Prince of Wales Hospital

While imaging techniques such as CT scans, MRI and radioisotopes can detect the spread of prostate cancer; they are not sensitive enough to determine if lymph nodes are involved. This team aims to develop new, more sensitive imaging technologies that will not only improve the ability to detect the cancer; but whether it has spread to other organs, in particular, lymph nodes. This additional information will help distinguish the stage of cancer and hence the treatment options.

Associate Prof 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.

Associate Prof 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.

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 Gianluca Severi

Deputy Director, Cancer Epidemiology Centre, Cancer Council Victoria

Recent studies on *Propionibacterium acnes* (*P.acnes*) suggest that this bacterium is prevalent in the prostate and that *P.acnes* is associated with acute and chronic prostatic inflammation, and perhaps prostate cancer. The aim of this project is to test whether *P.acnes* is a risk factor for prostate cancer and whether *P.acnes* infection influences survival after diagnosis.

Dr Benjamin Thierry

Senior Research Fellow, Ian Wark Research Institute, University of South Australia

This program aims to develop innovative and clinically relevant cancer diagnostic, prognostic and therapeutic applications of functional nanoparticles and nanomaterials. Nanotechnology is the creation and utilisation of materials, devices, and systems through the control of matter on the nanometer-length scale, i.e. at the level of atoms, molecules, and supramolecular structures. The design of advanced nanoprobe would allow more accurate diagnosis, imaging and ablation of prostate cancer.

Dr Gillian Mitchell

Familial Cancer Institute, Peter MacCallum Cancer Centre

The IMPACT study aims to assess the value of yearly PSA testing as a screening method for prostate cancer detection in men with a high risk due to BRCA gene alteration. Additionally, the study explores other compounds in the blood and urine that might prove to be a better diagnostic marker for detecting prostate cancer in all men.



PCFA-FUNDED RESEARCH: 2009 AND BEYOND

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

The PCFA 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.

The grants currently available include:

- Young Investigator grants of up to \$125,000 per annum for up to four years. These grants support scientists (regardless of their degree) who have demonstrated research ability and who are now ready to become independent investigators;
- Concept Grants of up to \$150,000 per annum for up to two years to support senior investigators not currently studying prostate cancer, but who can bring innovative research proposals or new technology to the field.
- Project Grants of up to \$125,000 per annum for up to three years. These grants encourage rigorous proposals for research that will provide direct, tangible benefits to patients with prostate cancer in a relatively short timeframe.
- Equipment Grants of up to \$100,000 to be allocated to investigators currently working in the prostate cancer field, with preference given to proposals with matching funding.

In 2009/2010, PCFA's priority areas for research are:

- Discovery of the genetic and cellular factors which initiate and/or perpetuate prostate cancer;
- Discovery, development and clinical validation of:
 - new tests to detect prostate cancer; and/or to determine whether a patient's cancer is curable;
 - new biomarkers that predict the future clinical course of prostate cancer and/or the response to future chemotherapy.
- Discovery, development and preclinical and clinical validation of novel molecular targets for chemotherapy of locally-invasive or metastatic prostate cancer; including androgen-independent cancers;
- Development of new treatment strategies for prostate cancer; especially locally-invasive or metastatic cancers;
- Projects which, if successful, are likely to provide immediate improvements to the quality of life of prostate cancer patients.

The grant round is launched in April each year for funding starting the following January. Full details about the program, grant categories and deadlines are on PCFA's website, www.prostate.org.au

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
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