





2008 NBCF Grant Recipients

NBCF would like to congratulate all our 2008 NBCF grant recipients and to wish them all the best on their exciting work!

If a grant is being undertaken by a team of researchers, the Chief Investigator's (who is nominated as the team leader) photos and details are listed below. If a grant involves a number of resources and individuals from multiple states, the state of the Chief Investigator is listed.

We want to acknowledge that a very large percentage of our grants are collaborative efforts. They are often comprised of many investigators and institutions around Australia. The intention of this document is to provide a very brief overview.

NBCF Project Grants

<p>Chief investigator: Dr Victoria White <i>Centre for Behavioural Research in Cancer The Cancer Council Victoria</i> Can a peer support program for cancer gene mutation carriers reduce distress? A randomized controlled trial <i>Victoria</i></p> <p>Lay description: Women with BRCA1/2 gene mutations have a very high lifetime risk of developing breast and ovarian cancer. Women with these mutations must make complex decisions regarding risk management options and learn how to cope with familial issues.</p> <p>Research has found a need for peer support among this group. This project examines whether a telephone-based peer support program actually helps to reduce psychological distress among women with BRCA1/2 mutations.</p>	
<p>Chief investigator: Associate Professor Kum Kum Khanna <i>Queensland Institute of Medical Research</i> Cep55 over-expression a potential mechanism for tumorigenesis <i>Queensland</i></p> <p>Lay description: Defects in cell division underlie a number of major diseases like cancer and understanding this process has enormous implications for cancer. We have recently identified a novel protein that is involved in the final stages of cell division. There is some evidence that the protein is over-expressed in cancer. Experiments are planned to study the level of expression of this protein in breast tumor samples and relate it to disease outcome.</p>	

Chief investigator:

Associate Professor Matthew Gillespie

Prince Henry's Institute

Role of Parathyroid Hormone-related Protein in DNA repair and breast cancer

Victoria

Lay description:

This project aims to investigate a protein (parathyroid hormone-related protein-PTHrP) that is expressed by breast cancers to influence cell growth and spread to bone. In our examination of clinical samples of breast cancer, we have determined that PTHrP expression in the primary cancer confers a more favourable patient outcome, but when expressed by a breast cancer cell in bone, PTHrP contributes to the bone destruction. We aim to define how PTHrP has these apparently different roles.



Picture: Mark Wilson
Leader Newspapers

Chief investigator: Dr Robin Anderson

The Peter MacCallum Cancer Centre

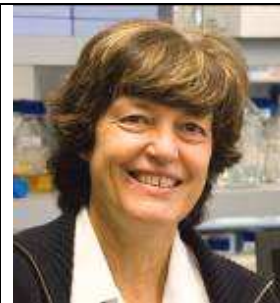
Functional genomic screen for metastasis suppressor genes controlling breast cancer metastasis to bone and lung

Victoria

Lay description:

When diagnosed early, breast cancer can be treated with a high degree of success. However, if the cancer spreads to other organs such as lungs and bone, the disease more likely leads to death, as well as severe pain and debilitating symptoms.

Therapies for patients with advanced disease are extremely limited. By identifying genes that control this process, we may identify the more susceptible patients earlier and treat them better. Furthermore, once we know which genes are critical to the spread of cancer cells, we may be able to develop therapies that target these genes and prevent the spread of breast cancer.



Chief investigator:

Associate Professor David Callen

Hanson Institute, Institute of Medical and Veterinary Science

The role of FBXO31 in a novel pathway of breast tumour suppression

South Australia

Lay description:

We aim to investigate a novel breast tumour suppressor called FBXO31 that we have identified. As levels of FBXO31 protein are abnormally low in breast tumours, we will quantify levels of FBXO31 in sections of breast tumours to determine if FBXO31 can be used as a prognostic marker of breast cancer. FBXO31 functions by degrading a critical unidentified protein that performs an important function in the cell. We will identify this protein as this may help to develop new drugs for breast cancer.



Chief investigator: Dr Carl Sprung

The Peter MacCallum Cancer Centre

Severe radiotherapy reactions: genome-wide exon array analysis and early radiation response

Victoria

Lay description:

This proposal will focus on determining which genes might be involved in predisposing occasional cancer patients to severe radiotherapy side effects. Such sensitive cases restrict the use of larger doses that would cure many more cancers. By elucidating the genetic causes of radiosensitivity, this project could allow individualisation of patient treatment by tailoring the best treatment to the patients' needs.



Doctoral Research Scholarships

Miss Kelly Betterman

Hanson Institute, Institute of Medical and Veterinary Science

The identification of genes important for lymphatic vascular remodelling during mammary gland development

South Australia

Lay description:

Lymphatic vessels are a critical route of transport for tumour cell metastasis. The stimulation of lymphatic vascular growth is one mechanism used by breast tumours to access the lymphatic vascular network and thereby spread to distant sites. Very little is currently understood regarding the identity of signals that regulate the growth, development and regression of the lymphatic vasculature, processes that normally occur in a highly regulated fashion during breast development.

This project aims to identify genes that control lymphatic vascular development in the breast, in order to understand how they are deregulated to facilitate tumour metastasis. Ultimately, the results of this project will identify targets for the design of new therapeutics to benefit breast cancer patients by preventing breast cancer metastasis.



Mr Steven Williams

Ludwig Institute for Cancer Research

Role of lymphatic endothelial cells in breast cancer metastasis

Victoria

Lay description:

Metastasis is the spread of cancer to other sites of the body. Breast cancer often spreads to the nearby lymph nodes, and on to other organs such as the liver, lungs or bones. This is the main cause of cancer death, and is therefore an important factor in diagnosis and treatment. Cancer cells can travel to the lymph nodes through the lymphatic vessels. It has been shown that some tumours actually encourage the growth of new lymphatic vessels around them, providing more opportunity to spread. We are now able to use a new technology called RNA interference to test the importance of every gene in lymphatic cells by 'knocking down' their expression, one at a time.

My project plans to study the events of metastasis such as attraction and adhesion of breast cancer cells to the lymphatic vessels, and identify the specific lymphatic genes required. This knowledge will be important to identify breast cancer patients with a high risk of the tumour spreading to other organs, and could aid development of therapeutics that prevent metastasis.



Ms Renata Zobalova

Griffith University

Ways to overcome resistance of breast cancer stem cells to treatment

Queensland

Lay description:

Over the last decade, improvements in breast cancer therapy has prolonged the lives of breast cancer patients. However, after successful initial therapy and recovery, there is often development of secondary tumours leading to the relapse of the disease. Recent studies have indicated that there is a small cell population within a tumour with stem cell characteristics and the ability to self-renew. These cells do not readily, if at all, respond to the current treatments of cancer. The cancer stem-like cells are characterized by increased expression of certain protein receptors, such as CD133, increased expression of ATP-binding cassette (ABC) drug transporters, higher levels of DNA repair and reduced ability to undergo apoptosis, providing them with high levels of resistance to cancer therapy.

In this project I intend to study the responsiveness of breast cancer stem-like cells to treatment with the mitochondrially targeted drugs, vitamin E analogues. Also I intend to study how these anti-cancer agents kill breast cancer stem cells and whether there is any resistance to the drugs. These results will help to develop new and more effective breast cancer therapies.





<p>Miss Rachel Carter <i>The Peter MacCallum Cancer Centre</i> Integrin $\beta 3$ as a therapeutic target for breast cancer metastasis to bone <i>Victoria</i></p> <p>Lay description: Current treatments are ineffective when breast tumours have spread to distant sites (metastases). In particular, bone metastasis occurs in 70% of advanced breast cancer patients and causes severe morbidity.</p> <p>Cell surface receptors that promote cell attachment and movement are critical for the spread of tumours. One such receptor, $\beta 3$ integrin, is present on breast tumour, bone and blood cells and has been implicated in the spread of breast tumour cells but its role in bone metastasis is still unclear due to the lack of appropriate animal model.</p> <p>The project aims to 1) clarify the critical cell types expressing $\beta 3$ integrin that are required for metastasis to bone and 2) measure the therapeutic benefit of novel inhibitors targeting $\beta 3$ integrin using a unique mouse model of breast cancer metastasis to bone developed in our laboratory. I propose that multiple cell types expressing $\beta 3$ integrin contribute to bone metastases and that blocking the action of this receptor will prevent tumour spread to bone.</p> <p>Thus, this project could lead to the development of novel therapies for bone metastasis and benefit advanced breast cancer patients for whom the mortality rate remains unacceptably high.</p>	<p><i>Photo pending</i></p>
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Post Doctoral Training Fellowships

Dr Samantha Oakes

(Post Doctoral Fellowship Top Up Funding)

Walter and Eliza Institute of Medical Research

Isolation and characterisation of novel progenitor cells in the mammary epithelium and their role in breast carcinogenesis.

Victoria

Lay description:

Stem and progenitor cells in the breast are the undifferentiated cells from which mature committed cells are derived. They are long-lived, resistant to death and can produce multiple types of mature cells. These properties make them candidates for the origins of breast cancer, as over time they can accumulate genetic mutations that ultimately lead to uncontrolled cell growth. The stem and progenitor cells that make up the cellular hierarchy have not yet been fully defined.

We aim to search for novel cell surface markers that will enable the definition of previously undefined progenitor cells in the mouse mammary gland. Once isolated and purified from normal mouse mammary glands, the developmental potential of these progenitor cells will be characterised. We will then artificially express known cancer promoting genes in these cells, and compare their cancer forming ability to purified populations of mature committed mammary cells, in culture and in the mouse. The data gathered from this project may facilitate the development of targeted therapies to the cells of origin in breast cancer.



Dr Barbara Bennett

Prince of Wales Hospital

Development and validation of a semi-structured clinical interview to allow reliable identification of post-cancer fatigue (PCF)

New South Wales

Lay description:

The diagnosis of a post-cancer fatigue syndrome (PCF) after breast cancer treatment is especially difficult as there is no specific measure or blood test. Such fatigue, which for some women may persist for many months after treatment, presents a unique challenge to survivors of breast cancer and their families. A reliable method of identifying such fatigue and differentiating it from other problems (such as depression) requiring alternative management, is an issue of importance to women treated for breast cancer and their treating medical practitioners.

This series of studies is aimed at the development and optimisation of an interview schedule comprised of carefully structured questions to enable health professionals to make an accurate diagnosis of post cancer fatigue (PCF) after breast cancer treatment. This in turn will help measure how effective interventions (such as graded exercise programs) are in managing the fatigue state. The interview will also be an important tool to measure fatigue states in research studies investigating the causes of cancer-related fatigue.



Dr Richard Redvers

Peter MacCallum Cancer Centre

The role of the extracellular matrix protein POEM in breast cancer metastasis

Victoria

Lay description:

Breast cancer is the most common cancer in Western women. It is the spread of cancer cells to distant organs that is responsible for the majority of deaths in this disease. Investigators have recently discovered a protein termed POEM or nephronectin in developing bones and kidneys. Importantly, the Anderson group has discovered elevated levels of this protein in malignant breast cancer using an animal model that mimics the human disease. This laboratory is the first and only to report an association of POEM with cancer thus far and is ideally placed to further investigate this novel discovery.

The proposed project will confirm the presence of POEM in human breast cancer and determine its functional importance in the spread of this disease. Investigations into its mechanisms of action and interactions with other proteins will be undertaken to better understand POEM function in breast cancer. Efforts will also focus on generating therapeutics in an effort to block the spontaneous spread of this disease.

Further characterisation of this protein in malignant breast cancer may yield important insights to improve therapeutic strategies, resulting in greater quality of life and longevity for cancer patients.





National Collaborative Breast Cancer Research Grants

The below are our exciting new \$5 million Collaborative Awards.

Both are large, national, multi-study long term projects that draw together some of the best minds and institutes in Australian research.

Chief Investigator:

Professor Matt Trau

University of Queensland

Novel strategies for prediction and control of advanced breast cancer via nanoscaled epigenetic-based biosensors

Queensland / multi-national

Lay description:

It is widely accepted that early detection is a major weapon which can be used very effectively against cancer. Our program aims to combine the latest developments in molecular genetics (Epigenetics) with the latest developments in Nanotechnology (nanoscaled biosensors) in order to create and clinically test novel diagnostic technology which can be used to make a major impact in the early detection, prediction and treatment of advanced breast cancer.

In patients who are burdened with advanced breast cancer, cancer cells have spread past the breast and underarm lymph nodes to other areas of the body. Once patients develop advanced breast cancer, their prognosis is poor. Because the technology we aim to create does not currently exist, a high percentage of patients presenting with a primary tumour are given unnecessary or ineffective treatment due to the inability of standard tumour examination procedures to accurately predict outcome. These patients derive no benefit but are exposed to the side effects, complications and discomfort as well as the costs of chemotherapy.

This national program involves a truly unique team of outstanding Australian researchers and includes experts in nanotechnology, surgical oncology, epigenetics, cancer genetics, pathology and bioinformatics. By combining our resources we aim to have a significant impact on the early detection and treatment of breast cancer.



Chief Investigator:

Associate Professor Christine Clarke

Westmead Millennium Institute

Identification of nuclear receptor networks as new targets for breast cancer treatment

New South Wales / multi-national

Lay description:

Breast cancer affects 10000 Australian women annually, and despite gains of past decades, remains an intractable disease. Bold new approaches are required for women for whom available treatments offer little hope, and women who develop treatment resistance.

Targeting the estrogen pathway has been highly successful, and the same approach can be reapplied, as a crucial aspect of estrogen receptor (ER) biology has been overlooked in breast cancer. ER forms part of a conserved family of nuclear receptors (NRs), that are master regulators of every aspect of life, including embryogenesis, reproduction, metabolism and cell death. NR family members are highly related, and have overlapping actions in cells. Many NRs are active in breast cancers. Targeting NRs provides a promising new avenue in breast cancer management.

This project will identify NR networks active in breast cancers, to identify new predictive targets of response to treatment in premenopausal women with ER-PR- breast cancer, or women with metastatic disease. The knowledge will be translated within 5 years, by application of treatments with existing NR drugs in women who have failed endocrine or cytotoxic treatments. Beyond this application, new NR drugs will be developed and tested in currently underserved breast cancer subgroups.



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