

Research milestones 2008



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08 milestones

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Our investment in research



Through the generosity of so many South Australians, Cancer Council SA now spends more than \$3 million each year funding valuable research, which is undertaken by some of Australia's most talented researchers. Each research project undergoes rigorous scrutiny through a detailed application process before funding is awarded.

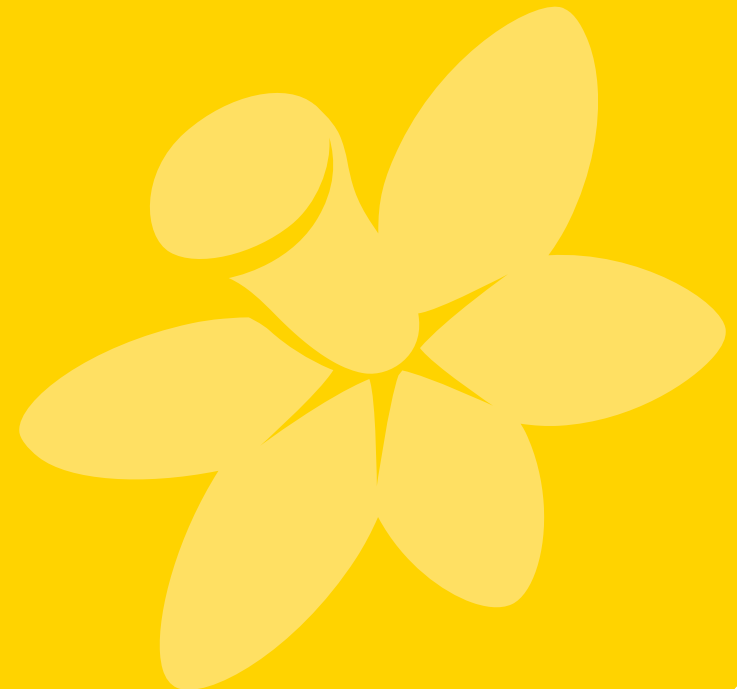
In our 2008 research milestones report, we have highlighted just 12 of the outstanding pieces of work from the past year that have made significant progress towards beating cancer for South Australians.



Project grants

Our annual grants program funds cancer-related laboratory, clinical, epidemiological and behavioral research undertaken by multi-disciplinary researchers in South Australia.

Cancer Council SA project grants are ranked competitively by the National Health and Medical Research Council (NHMRC) and applications in SA priority areas of funding are encouraged. Priority areas of research for funding in 2008 were cancer prevention, early detection, supportive care including palliative care, epidemiology and community education.



Project 1

Project: An integrated approach to the development of advanced nanostructures as cancer diagnostic and therapeutic agents

Researchers: Professor Hans Greisser, Dr Benjamin Thierry, Dr Michael Brown, Professor Peter Majewski, Dr David Taylor; Ian Wark Research Institute, University of South Australia

Funding: \$71,750



Nanotechnology set to improve cancer treatment.

The team of Cancer Council SA funded researchers are developing a method to determine the success of chemotherapy or radiotherapy in cancer patients, through the use of 'nanotechnology'. The research team has successfully developed nanoparticles with the ability to travel to cancer tumours and bond to dead cancer cells.

The human body normally traps nanoparticles in the liver and spleen, preventing them from reaching a tumour. This project has seen the development of an innovative molecular shell for the nanoparticles that stops them being trapped by the body, thus improving targeting to the tumour.

"The nanoparticles have a magnetic core of iron oxide which is visible via MRI scans. If nanoparticles bond to dead tumour cells, we can see the dead cells within a cancer tumour and therefore assess the effects of chemotherapy and radiotherapy on the cancer," said Associate Professor Michael Brown, Hanson Institute at the Royal Adelaide Hospital.

"Traditionally it takes up to nine weeks to determine whether treatments are having an effect but we may be able to determine whether there has been an effect within just a few days," he said.

Patients who are not responding to a treatment could avoid unnecessary and detrimental treatment regimes and be quickly changed to a potentially more effective type of treatment. The nanoparticles can also be used to carry cancer treatment directly to tumours, possibly resulting in better treatment outcomes.

Potentially the most advanced research of its kind, the method has been successful in mice and researchers hope to begin human trials in the near future.

Project grants

Project 2

Project: mRNA targets of MicroRNAs involved in metastasis

Researchers: Dr Gregory Goodall, Department of Medicine, University of Adelaide and Dr Yeesim Khew-Goodall; Institute of Medical and Veterinary Science

Funding: \$77,250



Stopping the spread of breast cancer

A collaboration between Cancer Council researchers, Associate Professor Greg Goodall and Dr Yeesim Khew-Goodall, at Adelaide's Hanson Institute has resulted in a major discovery that could lead to lifesaving treatment for breast cancer.

In what is believed to be a world first, Associate Professor Goodall and Dr Khew-Goodall have found a DNA regulator (MicroRNA) which appears to be an important factor in the spread of breast cancer.

The majority of women survive breast cancer in the first instance, but the cancer sometimes spreads, causing secondary cancers which claim the lives of thousands of Australian women each year. A key to reducing the impact of breast cancer is to stop the spread of the cancer to other parts of the body.

"One school of thought is that MicroRNAs change composition when breast cancer spreads. We have discovered that it is actually the MicroRNAs that may be causing the cancer to change and spread, rather than the other way around," said Associate Professor Goodall.

"Having discovered that this mechanism provides a pathway for cancer cells to spread from the primary site to other parts of the body, we can now work toward blocking the pathway and stopping the cancer from spreading," he said.

Initial trials in cultured cells have shown promising results and the researchers will soon begin trials in mice and if successful, in humans.

Project grants

Project 3

Project: Nutritional and genetic factors associated with genome damage in children

Researchers: Dr Elizabeth Milne, Dr Michael Fenech, Professor Bruce Armstrong, Professor Nicholas de Klerk, Ms Margaret Miller, Commonwealth Scientific and Industrial Research Organisation

SA Funding: \$84,000



Diet and children - the risks revealed

A study by Dr Michael Fenech and his research team investigated the link between children's diet and damage to their DNA and how this contributes to cancer risk. The study, co-funded by Cancer Council SA and Cancer Council WA, is the first of its kind.

Damage to DNA accumulates throughout life and is also associated with risk of cancer and other diseases in adulthood. Evidence that poor diet increases DNA damage in childhood suggests that young children with a poor diet may have an increased risk of cancer and other diseases. It has been estimated that poor diet contributes to approximately one third of preventable cancers.

"If a link is found between poor diet and DNA damage in children it will provide us with valuable health promotion messages for parents, on the importance providing children with healthy diets," said Dr Fenech.

"We recruited 80 children aged between three and nine years from Perth, Western Australia, and collected a blood sample to measure the level of micronutrients in the blood and the extent of DNA damage.

"We also asked the parents to complete a questionnaire on behalf of the child regarding the foods and drinks they typically consumed as well as any regular dietary supplements," he said.

Dr Fenech had previously begun a similar study in adults, but redirected the study to focus on children, as DNA damage from smoking, alcohol or other factors was less likely to confound the study. He plans to apply for more funding to expand this study to children in South Australia.

The study is currently in progress and solid results are expected by July 2009.

Project grants

Project 4

Project: Enhancement of DNA repair as a chemopreventive strategy for colorectal cancer

Researchers: Professor Graeme Young, Dr Ying Hu, Dr Geoffrey Margison, Dr Richard Le Leu; Flinders University

Funding: \$65,000



Dietary strategies to reduce cancer risk

The crucial link between diet and bowel cancer is now a proven fact, thanks to research undertaken by Professor Graeme Young and funded by Cancer Council SA.

Colorectal cancer is one of the leading causes of cancer death in the world and a major health issue in Australia. The majority of cases of colorectal cancer appear to be sporadic but dietary lifestyle is a major contributor.

As diet is one factor influencing cancer risk that can be modified, a promising and cost-effective approach is to take a preventive approach based on dietary or 'chemopreventive' (the use of specific bioactive foods) strategies.

Professor Young, who is Professor of Gastroenterology, Academic Head of GI Services and Director, Flinders Centre for Innovation in Cancer, said that his research explored the impact of dietary choices on bowel cancer especially the capacity of food to regulate damage to cell genes (DNA), as disordered genes are responsible for the development of bowel cancer.

"Our work has convincingly shown that certain dietary factors stimulate inherent cellular processes that repair DNA damage and we can use certain dietary choices to enhance the body's natural defences," said Professor Young.

"We now know that a diet high in saturated fat, red meat (especially if processed), alcohol and refined sugars can increase cancer risk by up to 70 per cent. However increased quantities of fruit, vegetables, nuts, tea, whole grains and dietary fibre actually have the potential to reverse previous damage.

"With continued funding support from Cancer Council SA, we now believe we are closer to formulating a simple diet that could reverse gene damage in the bowel, reduce the adverse effects of bowel cancer and save lives," he said.

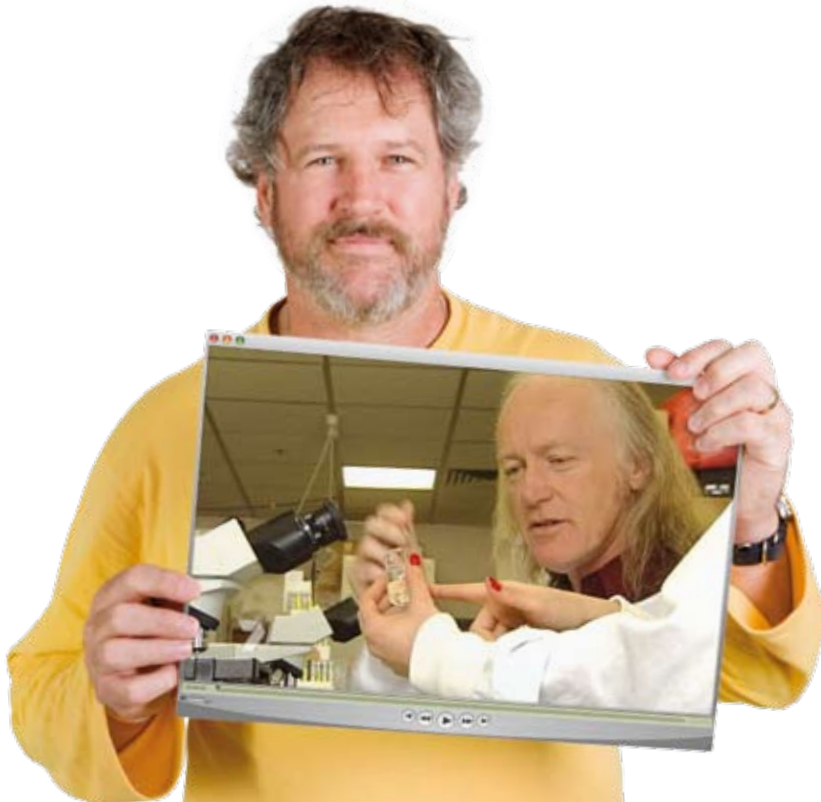
Project grants

Project 5

Project: Novel probiotics and naturally-sourced extracts as treatment strategies for chemotherapy-induced intestinal mucositis

Researchers: A/Professor Gordon Howarth, A/Professor Ross Butler, Dr Adrian Cummins; Children, Youth and Women's Health Service

Funding: \$82,750



New hope from natural therapies

Intestinal mucositis is a serious and potentially life-threatening consequence of chemotherapy administered for the treatment of a wide range of cancers. It is usually characterised by nausea, bloating, cramping and diarrhoea. Mucositis is generally experienced by 40–60 per cent of cancer patients and almost 100 per cent of patients undergoing more aggressive chemotherapy treatment.

Associate Professor Howarth says that at present, there is no satisfactory treatment for mucositis. “The condition limits the amount of chemotherapy a cancer patient can withstand. Eliminating mucositis would mean that patients could be given higher doses of chemotherapy, resulting in better treatment outcomes,” he said.

Research undertaken by Associate Professor Howarth and his team has revealed that natural therapies such as lyprinol (an extract from a New Zealand shellfish), emu oil and grape seed extract have great promise in relieving the symptoms of mucositis. The discoveries have also generated international interest.

“Slowly but surely we are applying more rigorous scientific scrutiny to alternative and complementary therapies. It is an exciting time as we have shown that these treatments, many of which have been handed down over thousands of years, are indeed very useful,” said Associate Professor Howarth.

In December 2008, Associate Professor Howarth won the prestigious Sally Birch Fellowship in Cancer Control for his work in reducing the side effects of chemotherapy. He faced a competitive national field to win the three-year Cancer

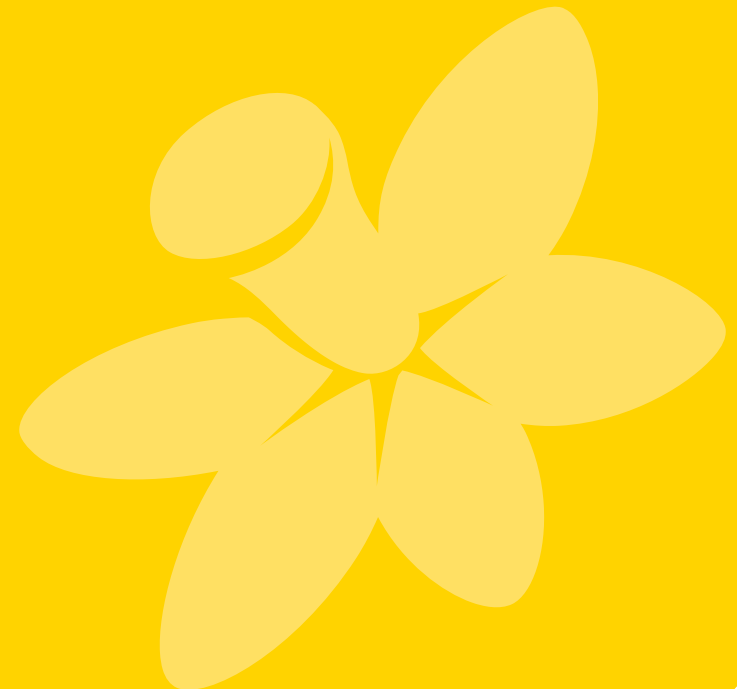
Council Australia Fellowship worth \$100,000 each year, commencing in 2009.

“This significant funding from Cancer Council Australia will help facilitate the development of new treatment strategies for mucositis, including the exciting clinical potential for specific ‘probiotics’ (health-promoting bacteria) to protect the intestine from injury,” he said.

Project grants

Cancer Council SA Research fellowship

Cancer Council SA funded six Cancer Research Fellowships in 2008. One of our current Cancer Council Research Fellows is Dr Anna Brown, based in the Acute Leukaemia Laboratory at the Centre for Cancer Biology at the IMVS. She has several projects investigating genes affected in acute myeloid leukaemia (AML). Dr Brown completes her Fellowship at the end of 2009.



Cancer SA Research fellowship

Study: Conducting research to identify genes and characterise their roles in controlling normal leukaemic myeloid cell growth and differentiation

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Researcher: Dr Anna Brown, Child Health Research Institute
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Funding: \$49,192



The search for leukaemia genes

Acute myeloid leukaemia (AML) is a devastating disease that affects both adults and children. Dr Anna Brown's research aims to find the genes responsible for causing this disease, in order to aid in the development and application of better treatments.

"One of the genes we are working with, the KLF5 gene, makes a molecule that can control the activation of many other genes. This means that activation of this gene needs to be very carefully controlled within the cell," said Dr Brown.

"In many human AML samples, the level of KLF5 is lower than normal. This suggests that it is an important molecule for controlling normal blood cell growth.

"We have also shown we can reverse leukaemic cell growth in blood cells by returning KLF5 levels to normal. In recent data we have been able to 'silence' KLF5 through a process called DNA methylation.

"These results are extremely important as it means that we may now be able to identify patients who will respond better to epigenetic

therapies, through which cells are affected without directly affecting DNA. There are already several new drugs on trials that use epigenetic therapy," she said.

Dr Brown's research into KLF5 is very promising and it is hoped that it will lead to clinicians being able to identify patients who will respond better to epigenetic therapies, some of which are included in several new types of drugs currently in trials.

Research fellowship

Internal research

Cancer Council SA also funds internal research projects, utilising the skills of the Cancer Statistics Unit. This group uses epidemiological principles and available cancer statistics to provide information to underpin cancer control activities. The unit also conducts internal research in specific areas of Cancer Council SA competence to fill key gaps, including epidemiological support and training, exploring opportunities to develop programs of applied research and producing statistical monographs. These are two of the many studies undertaken during 2008.



New study shows big improvement in child cancer survival

A study into child and adolescent cancers by the Cancer Statistics Unit found that while the survival rate for children has significantly improved during the past 25 years, the incidence of cancer in adolescents (aged 15 to 25) was on the rise and the survival rate had only improved marginally.

The 'Monograph of cancer among young South Australians' is the first comprehensive study of its type investigating survival rates.

Cancer Council SA Chief Executive, Associate Professor Brenda Wilson said that the study will assist research institutions in focusing their efforts on cancers where survival rates are lower.

"Work needs to be done in improving the treatments for bone cancer, brain tumours and leukaemia, where survival rates range from 59 per cent to 65 per cent. These are cancers where Cancer Council SA is directing research funds," she said.

The study found that the number of cancers diagnosed had increased by about two per cent per year. "This is largely due to an increase in the adolescent cancers of melanoma and lymphoma," Associate Professor Wilson said. "These are areas where we need to focus our prevention programs and direct research."

On a positive note, improvements in treatment and potentially in diagnosis of cancers in young children had helped lift the survival rate for those under the age of 15 to 77 per cent.

Investigating breast cancer incidence at the Women's and Children's Hospital, Adelaide

The Children, Youth and Women's Health Service (CYWHS) sought the services of Cancer Council SA's lead epidemiologist to investigate a suspected cluster of breast cancers cases occurring among staff working at the Women's and Children's Hospital, Adelaide (WCH). The independence of Cancer Council SA from a hospital management or funding role was an important consideration in selecting a Cancer Council epidemiologist to undertake the investigation.

The study was undertaken with the guidance of a steering committee comprising staff, union representatives and public health researchers, with ethical review from the human research ethics committees of CYWHS and the Department of Health, and in a manner that ensured the privacy of all past and present staff and volunteers at the WCH.

The main approach was to trace all cases of invasive cancer that had occurred among WCH female staff and volunteers between January 2000 and December 2007. Cancer incidences were linked with cancer registration notifications and the numbers of cases at the WCH compared with expected numbers based on cancer rates for the state as a whole.

While the number of breast cancer cases at the WCH was found to be elevated, the number of cancer cases overall did not differ from the population. In addition, some cancers were found to have occurred at lower than expected rates.

A subsequent investigation of the earlier period from 1995 revealed no elevation. The number of breast cancer cases at the WCH was too small to identify any causal factors.

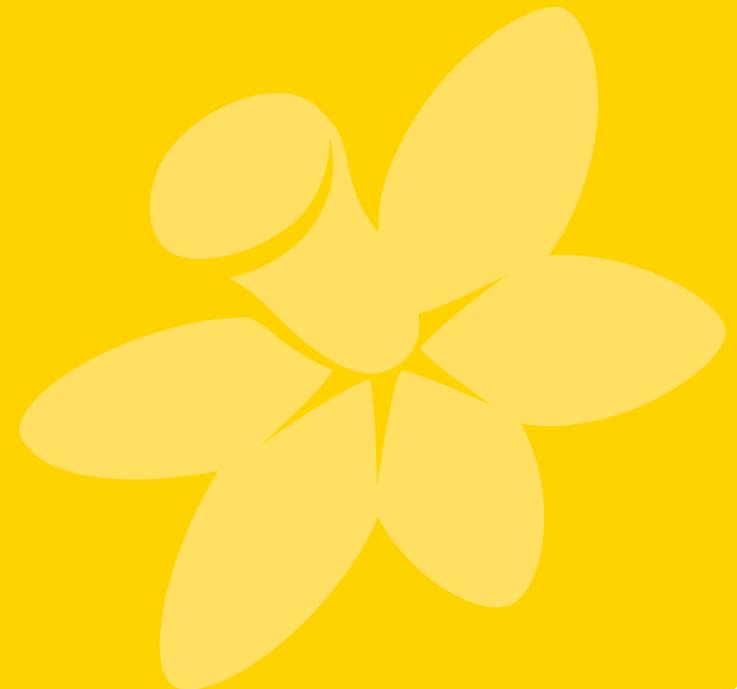
While the possibility of some environmental factor could not be ruled out, other explanations for the elevated number of breast cancers include increased participation in mammographic screening among WCH staff and chance variation. Ongoing monitoring of breast cancer risk at WCH is planned to ensure that the elevation is not sustained.

Peter Nelson Leukaemia Research Fellowship Fund

(administered by Cancer Council SA)

The Peter Nelson Leukaemia Research Fellowship Fund (PNLRFF) was established through the efforts of Marjorie Jackson-Nelson AC, CVO, MBE. In 1975, Marjorie's husband, Peter was struck down with leukaemia and after a very short time it took his life. Marjorie emerged from retirement to raise money for research in a battle to beat the disease. She enlisted the aid of Rotary to establish the fund and has tirelessly worked for it ever since.

The aim of the PNLRFF has been to support researchers early in their career in an accredited research department, enabling them to obtain further independent funding at the conclusion of their Fellowship. Dr Hayley Ramshaw is the current PNLRFF Fellow and commenced in April 2008.



Study: Targetting the leukaemic stem cell

Researcher: Dr Hayley Ramshaw, Human Immunology,
Centre for Cancer Biology

Funding: \$51,867



Novel treatment to eliminate leukaemic stem cells

Leukaemia is a devastating form of blood cancer affecting both young and old. Current therapy is poorly tolerated and the majority of patients ultimately die of relapse. Dr Ramshaw's laboratory has developed a novel non-chemotherapy treatment for leukaemia which specifically aims to target the cells that are more than likely responsible for relapse. The cells are called leukaemia stem cells and have some overlapping features with normal bone marrow stem cells.

"These cells have been shown to divide slowly and are resistant to the current forms of chemotherapy commonly used today. It is vital that new treatments are developed to specifically eliminate these stem cells, in an effort to provide long-term management of the disease, if not a cure," Dr Ramshaw said.

"The antibody we have developed targets the receptor for a growth factor that is important in the development of blood cells. My investigation centres around the role of this growth factor receptor which is expressed at high levels in leukaemia stem cells but not normal stem cells," she said.

Current therapies for patients with acute myeloid leukaemia do not kill the stem cell, meaning patients often relapse with the disease following treatment. Older or weaker patients can also struggle to cope with the side effects from chemotherapy. The antibody being investigated by Dr Ramshaw may provide a non-toxic therapy for leukaemia stem cells.

**Peter Nelson Leukaemia Research
Fellowship Fund**

Chair in Cancer Behavioural Research

Funding: \$151,670



Dr Carlene Wilson is Cancer Council SA's Professor in Cancer Prevention (Behavioural Science) at Flinders University.

The key responsibilities of this role are to establish recognition of the contribution of lifestyle to cancer prevalence, develop a strategic behavioural research agenda, build capacity, provide academic leadership, facilitate the advancement of the cancer prevention research agenda and promote Cancer Council SA. Here are some key highlights of her significant work across 2008.

The cancer prevention research agenda has incorporated both ongoing and new efforts in seven areas. Each one is focused on the identification of the drivers and reinforcers of lifestyle decisions likely to increase or decrease risk of cancer.

The specific topics are:

determining participation in cancer screening and re-screening

communication strategies to increase participation in cancer preventive behaviours

factors that impact on the diet and lifestyle choices that impact on cancer risk

utilising social influence to optimise health promoting behaviour

the role of the family in developing and supporting healthy lifestyle choices

prevention of cancer at the workplace

fast food consumption, time pressure, and their influence on weight and decision-making about lifestyle.

From March 2008 to March 2009, 12 publications appeared or were accepted (11 refereed journals, one book chapter) and three additional publications were submitted. Several of these publications cited work carried out in the cancer prevention research agenda.

During 2008, a Cancer Council SA grant was completed, three grants were awarded (Centre for Intergenerational Health, SHRP, NHMRC) three grants were submitted (all to NHMRC) and one remained ongoing (NMHRC).

Dr Wilson participated in two national committees concerned with dietary behaviour and cancer screening participation, two state committees concerned with either research or clinical practice in cancer prevention (including a sub-committee of the Cancer Clinical Network), and one group involved in designing behavioural research at Cancer Council SA.

During 2008 and into 2009, several projects concerned with behavioural factors in cancer prevention were ongoing or planned, with a number of local, national and international collaborators. There are 14 South Australian collaborators currently involved in ongoing research and five additional potential collaborators have been identified in South Australia. There are also collaborators in Melbourne and Washington.

Dr Wilson also worked with Cancer Council SA on the collection and analysis of South Australian bowel cancer screening data and developing and piloting workplace intervention for dietary improvement.

Chair in Cancer Medicine

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Funding: \$287,000



Professor Dorothy Keefe is Cancer Council SA's Chair in Cancer Medicine, based at The University of Adelaide.

Professor Keefe continued to play an active role in cancer clinical practice, research and teaching throughout 2008. With the development of the Statewide Cancer Clinical Network and its drive to improve standards of care across the whole state, Professor Keefe has played a lead role in the network as well as in integrating network activity with regional activity in the Central Northern Adelaide Health Services (CNAHS).

Her committee roles have included the Steering Committee for the New Royal Adelaide Hospital and the SA Health and Medical Research Institute building. National roles included the Cancer Australia National Strategic Forum and chairing a grant subcommittee for the Cancer Institute NSW.

CNAHS has had several reviews of cancer treatment during the past year and Professor Keefe played a lead role in each review. The Delaney review

into radiotherapy, the Fox review into chemotherapy prescribing and the Commuio Report into safety and quality all required a regional response that was led by Professor Keefe, who is now the Director of Regional Cancer Services.

She also played a key role in developing and supporting The University of Adelaide Cancer Research Institute and the evolving Statewide Cancer Research Collaborative. Research funding and staff in the Mucositis Research Laboratories continue to grow.

The Royal Adelaide Hospital Cancer Centre is expanding and staff members continue to do an admirable job in difficult times. Renovations of the outpatients area are almost complete and work on the third stage of the redevelopment (increasing the number of single side rooms for high acuity

leukaemia and transplant patients) is about to start. The Radiotherapy service at Lyell McEwyn Hospital is ready to see patients and is a demonstration of the Health Care Plan in action. The Darwin service is also making great progress.

Cancer Council SA funding for this position continues to provide the ability for Professor Keefe to play a leading role in cancer care within the state and on a national basis, in an academic, clinical and administrative capacity.

Data managers program

Funding: \$195,780

Repatriation General Hospital \$29,750


Familial Cancer Unit \$55,930

Royal Adelaide Hospital,
Flinders Medical Centre,
Ashford Cancer Centre,
The Queen Elizabeth Hospital,
Lyell McEwen,

Women's and Children's Hospital \$110,100

Cancer Council SA provides funding to a number of hospitals to support participation in national and international clinical trials for which no, or minimal funding is provided by other sources. Clinical trials activity is supported by data managers at these hospitals.





“Learn from yesterday,
live for today, hope
for tomorrow.

The important thing is
not to stop questioning”.

Albert Einstein



**Cancer
Council**
SA

202 Greenhill Road
Eastwood SA 5063
PO Box 929, Unley BC SA 5061

t 08 8291 4111
f 08 8291 4122
tcc@cancersa.org.au
www.cancersa.org.au