

A 20-year snapshot of Australian medical research discover and success

[Children's Cancer Institute Australia \(CCIA\)](#)

World-first clinical trial increases the survival rate for most common childhood cancer

A decade-long international clinical trial undertaken in March 2013 doubled the survival rate from 35 per cent to 70 per cent for high-risk acute lymphoblastic leukaemia (ALL). The pioneering clinical trial was initiated at the Sydney Children's Hospital Randwick and The Children's Hospital at Westmead and was conducted across Australia, New Zealand and the Netherlands. Children with ALL at the highest risk of relapse were identified early in their treatment plan using a novel test developed by scientists at Children's Cancer Institute Australia (CCIA). This test detects Minimal Residual Disease (MRD) in the bone marrow of children with ALL, who would otherwise appear to be responding well to treatment. The trial represented a major step toward personalised cancer care and was one of the first studies to show that, by identifying high risk patients early in the treatment plan, consequent changes in treatment can improve the chance of cure. Media release here:

<http://www.ccia.org.au/index.cfm?pageCall=content&ContentTypeID=25150&startRow=7&menuItemID=54584>

CCIA works round the clock, collaborating worldwide, to beat neuroblastoma

In 2012, CCIA launched a clinical trial around neuroblastoma, the most common solid tumour of young children, based entirely on their own research. Another of CCIA's clinical trials (co-funded by the Cancer Institute NSW and a National Cancer Institute USA consortium) will commence shortly across USA and Australia, and the Institute is developing a novel anti-cancer drug for clinical trial with a US-based industry partner.

[Lions Eye Institute](#)

- World first development of a retinal vein bypass treatment for retinal vein blockage.
- Completion of Phase II clinical trial of new treatment for Age-related Macular Degeneration.
- Development of the world's first dissolvable glaucoma tube for microsurgery to control glaucoma.
- Design of a robotics ultra-microsurgical system which will allow surgical treatments to be performed currently limited
 - by the tremor of a surgeon's hand.
- Development of an animal model to study diabetic retinopathy.
- Research and development of AlphaCor™, the world's first soft artificial cornea.
- Cutting edge immunological research leading to the development of novel strategies and treatments to control viral diseases including those that affect vision.

[Victor Chang Cardiac Research Institute](#)

Donor heart preservation

A world-first technique was developed by Australian scientists at the Victor Chang Cardiac Research Institute and St. Vincent's Hospital, doubling the time a donor heart can exist outside the recipient. Publishing in the prestigious *American Journal of Transplantation*, the scientists reported that they had successfully trialled a new combination of drugs in animal models, extending the time a donor heart can spend in transit from 4-5 hours, up to 14. The work has potentially huge benefits for human transplant patients, especially in a country the size of Australia given the significant time it could take to transport a heart from a donor, to the recipient.

Impact of nature *and* nurture on congenital birth defects

Scientists from the Victor Chang Cardiac Research Institute demonstrated for the first time how both nature and nurture can increase the severity and likelihood of developing birth defects, which affect a third of all babies born in Australia. Publishing in *Cell*, their findings showed how a period of low oxygen during pregnancy, combined with a genetic risk factor of having only one functioning copy of a gene, dramatically increases the chance of a baby being born with congenital scoliosis, a malformation of the spine. Their findings could help women minimise, or even avoid the risk of having a baby born with a congenital birth defect.

World first gene research

In a world first, scientists from the Victor Chang Cardiac Research Institute used gene-based therapy to reverse an inherited heart disorder, despite some members of the family being told they had only months to live. The research team identified and treated a rare gene variant in members of a family affected by arrhythmia and dilated cardiomyopathy, two conditions which increase the risk of stroke and heart failure. Affected family members received a medicine shown in laboratory tests to target the gene mutation. Many of these patients returned to full health within six months.

[Brien Holden Vision Institute](#)

Brien Holden Vision Institute researchers designed and conducted research that led to the development of silicone hydrogel polymer, released by CIBA VISION as the Focus® Night & Day™ contact lens in 1999. This new class material accounts for more than 50% of the soft contact lens market in the US.

[Murdoch Children's Research Institute](#)

USING BOTOX TO HELP CHILDREN WALK Researchers here and overseas worked on the link between botulinum toxin, a well-known muscle relaxant, and reducing spasticity in the limbs of children with cerebral palsy. The finding has given children with cerebral palsy the chance to lead a more active lifestyle, helping them walk and play. The ongoing work of researchers on gait analysis and botulinum toxin has resulted in a paradigm shift in treatment of children with cerebral palsy worldwide.

LEADING THE WAY IN ALLERGY RESEARCH

We found that babies given egg after 12 months of age were up to five times more likely to develop egg allergy as they grew older than infants introduced to egg at four to six months of age. This contradicted Australian and international guidelines that previously recommended that infants with a family history of allergy delay introducing allergenic foods until two or three years of age. Egg allergy is the most common food allergy in infants and toddlers.

PIONEERING NEW TECHNOLOGY

We were co-leaders in an international study that found 'next generation' DNA sequencing could accurately diagnose a rare genetic disease more quickly and cost effectively than current techniques. Because current testing can only screen one gene at a time, many children need to undergo painful muscle and liver biopsies to identify which genes should be tested, a process that can then take anywhere from a few months to several years. Next-generation sequencing can test many genes at the same time through a simple blood test. The finding will lead to more accurate diagnosis and will improve pre-natal diagnosis and prevention of rare disease mutations.

[Neuroscience Research Australia \(NeuRA\)](#)

NEURA (Neuroscience research Australia) IN BRIEF

As a direct result of 7 years of research by NeuRA, **new child restraint laws were introduced** in NSW and other states. **The new legislation** requires all children up to the age of seven years to use an appropriate child restraint or booster seat when travelling in cars.

The Rat Brain in Stereotaxic Coordinates by NeuRA's Profs George Paxinos and Charles Watson has been cited over 50,000 times, **making it the most cited book in neuroscience**. They were the first to construct an accurate atlas for experimental animals in the world. Over the past 40 years, they have worked on atlases of the mouse, monkey, human and bird brain used.

NeuRA researchers made a **major breakthrough in research into Parkinson's disease** through the discovery that certain cells in the cortex are missing in people with PD. The discovery explained why treating PD with a particular medication was only effective for ~5 years leading to therapeutic changes in treatment.

NeuRA researchers **discovered a new form of dementia** often confused with Alzheimer's disease: Dementia with Lewy Bodies.

NeuRA's Falls Clinic developed a "**Falls Screening Kit**" which is used by aged care specialists worldwide in identifying people at risk of falls.

NeuRA researchers advanced the development of a new technique to allow a **quadriplegic patient to deliver an effective cough, treating a key complication** of spinal cord injury which often leads to death.

Researchers at NeuRA are the first to demonstrate that patients with frontotemporal dementia (FTD) lose the emotional content/colour of their memories. The research team **discovered that a region of the brain, called the orbitofrontal cortex, plays a key role in linking emotion and memories. This breakthrough will improve how clinicians diagnose different types of dementia.**

Centenary Institute

Researchers discovered the:

- Genetic basis and prevention of sudden death syndrome in young people
- The identification of markers for human regulatory T cells
- The role of TNF and lymphotoxin in the control of Tuberculosis and immuno-pathology in auto-immune brain disease
- The basis of tolerance in liver transplantation
- Discovery of the genetic basis of amino acid transport defects in Hartnup's disease

The George Institute for Global Health

Landmark study showing that blood pressure lowering reduces the risk of cardiovascular disease in people with diabetes. We showed blood pressure lowering reduced the risk of cardiovascular death by 18% in people with type 2 diabetes, and found that intensive blood glucose control protects patients against serious kidney complications

Landmark studies for the treatment of critically ill patients with fluids, providing evidence for safer treatment options. We have shown that the choice of resuscitation fluids significantly affects the recovery of critically patients such as those with brain injury.

Hunter Medical Research Institute

ASTHMA

A Hunter Medical Research Institute asthma management program has the potential to halve asthma attacks in pregnant women, the most common chronic medical disorder they experience.

Researcher Professor Peter Gibson developed an algorithm that adjusts inhaled therapies to better match airway inflammation. Results of a randomised controlled trial found that the asthma exacerbation rate of pregnant women can halve if airway inflammation is closely monitored using a marker known as Fraction of Exhaled Nitric Oxide (FeNO).

A follow-up study found that by halving asthma attacks in pregnant mums it also yielded a 90 per cent postnatal reduction in bronchiolitis and croup episodes among their children.

Of the babies born to mothers who were managed according to FeNO, only 1.5 per cent had recurrent bronchiolitis in the first year of life compared to 16 per cent for mothers managed according to symptoms.

Figures for croup showed an almost tenfold difference in incidence rate, with 1.5 per cent compared to 11 per cent. Combined for both diseases, it was just 3 per cent for the FeNO group versus 26 per cent for the symptoms group.

STROKE

A new clot-busting drug therapy has achieved significant treatment benefits for acute stroke victims in a ground-breaking three-year study by the HMRI Stroke Research Group.

Findings published in the prestigious New England Journal of Medicine showed two-thirds of patients treated with the drug Tenecteplase demonstrated major neurological improvement within 24 hours and 72 per cent experienced excellent or good recovery three months after their stroke.

Of those administered the standard drug Alteplase (tPA) during the trial from 2008-2011, only 36 per cent showed improvement at 24 hours and 44 per cent experienced good or excellent recovery after 90 days.

The trial is now being expanded to 20 acute stroke centres nationally and 50 world-wide.

[QIMR Berghofer Medical Research Institute](#)

QIMR Berghofer scientists were important contributors to the development of the active ingredient in a solar keratoses (sun spot) gel now available on the US and Australian market.

QIMR Berghofer Medical Research Institute's scientists developed a cartoon DVD for school children in the Hunan province of China, which was responsible for halving parasitic worm infection rates amongst students, by educating them about proper hygiene practices.

[Burnet Institute](#)

After six years of development in the laboratory, the Burnet Institute's innovative point-of-care (POC) CD4 test was [officially launched](#) at the AIDS 2012 Conference in Washington.

VISITECT® CD4, developed by Institute Deputy Director Associate Professor David Anderson, Co-Head of the Centre for Virology Professor Suzanne Crowe AM, and their team, is an affordable point-of-care (POC) test aimed at reaching HIV-positive patients around the world.

Before HIV infected patients are treated with anti-retroviral drugs their CD4 T-cells must be below 350 cells per microlitre (according to current WHO treatment guidelines).

The conventional way to measure CD4 T-cell levels is through sending blood samples to be tested via flow cytometry (FACS), which is an instrument that requires large capital investments to purchase and then train scientific staff to maintain and operate. As such, the majority of laboratories and clinics in the countries most affected by HIV and AIDS are unable to monitor CD T-cells, particularly in remote and rural settings.

Associate Professor Anderson and his team have developed a novel rapid point of care for the measurement of CD T-cell levels in a similar format to a pregnancy test and only requires a finger pick of blood. The test does not require highly trained personnel to operate and can be performed in remote settings by health out-reach workers giving a simple treat or no treat result.

The test works by measuring the amount of cell associated CD4 using a sandwich capture assay where the sample line is checked against the test line to give a treat or no- treat result. The test is currently due to start field trials in the US and Africa.

[Menzies Research Institute Tasmania](#)

Menzies' research on Sudden Infant Death Syndrome (SIDS) recommended changing to infant sleeping positions, which is attributed to the dramatic decline in SIDS deaths since 1991. This has seen a decrease of SIDS-related mortality of 2.18/1000 live births in 1987 to 0.6 in 1997. This would equate to 7,440 infant lives saved between 1993 and 2008. Access Economics calculated a statistical value of life at approximately \$8m per life, therefore Menzies has contributed \$60 billion to the nation through its work on SIDS alone. (Exceptional Returns. The Value of Investing In Health R&D in Australia II, Prepared for the Australian Society of Medical Research, Prepared by Access Economics, June 2008)

Cardiovascular disease begins at an early age and progresses silently throughout the life span before clinical complications such as heart attack and stroke present. Adverse blood lipid levels (dyslipidaemia) are an important contributor to the disease and have been the target of consensus statements for paediatric screening and treatment issued by the American Academy of Pediatrics, the US National Cholesterol Education Program, and the National Heart, Lung and Blood Institute since 1992; the most recent update being 2011. The basis of these documents is that treatment of lipid disorders beginning in childhood or adolescence may reduce the lifetime risk of cardiovascular disease.

However, there has been substantial debate concerning which children should be screened, at what age, and the level of dyslipidaemia that identifies children who have increased risk for cardiovascular disease later in life.

Menzies-led work that used data collected from children in the 1980s who were subsequently followed up as adults that was published in the two highest-ranked cardiovascular disease journals worldwide has contributed to this

debate. We were able to show strengths and limitations of the cut-points and screening strategies for paediatric dyslipidaemia that were then in use by the American Academy of Pediatrics and were able to identify the critical age when screening for child dyslipidaemia might commence. This work contributed to major changes in screening for child dyslipidaemia in the current guidelines released in 2011 by the US National Heart Lung (NHLBI) and Blood Institute Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents and endorsed by the American Academy of Pediatrics. In the current guidelines, the age at which children were to be screened, the screening approach, and the cut-points used to identify youth with paediatric dyslipidaemia were all modified from the previous guidelines.

Peter MacCallum Cancer Centre

Clinical trials for breakthrough melanoma treatment

- In 2008, the Peter MacCallum Cancer Centre's refined pathology techniques, advanced cancer imaging technologies and expertise to evaluate cellular responses resulted in the organisation being selected as the only site outside the United States to host first-in-human clinical trials of the first BRAF gene inhibitor, vemurafenib, to treat patients with advanced melanoma.
- Led by Professor Grant McArthur: Head, Cancer Therapeutics Program and Chair of the Melanoma Service, Peter Mac researchers established a new translational research platform that enabled patients with advanced, inoperable or metastatic BRAF-mutant melanoma (50 per cent of all cases) to be matched to the new drug.
- While melanoma was the primary target for the first BRAF inhibitor, mutations of the BRAF gene are present in around 5–10 per cent of all human cancers, providing tremendous potential to identify other patients who might benefit from 'next generation' BRAF inhibitors.

World-first blood cancer drug enters clinical trials

- Laboratory researchers and clinicians at the Peter MacCallum Cancer Centre drove the development of a new first-in-class compound targeting 'ribosome biogenesis': the process by which cells produce protein-making 'factories', complexes of molecules that make proteins,
- Although essential for the growth and survival of all cells, the research team, led by Associate Professor Ross Hannan, discovered cancer cells are more dependent on ribosome biogenesis than healthy cells.
- Partnering with Peter Mac haematologists and Cylene Pharmaceuticals, the laboratory researchers developed CX-5461, a world-first drug that blocks ribosome biogenesis in cancer cells, selectively killing them and sparing healthy cells; first-in-human clinical trials of CX-5461, led by Associate Professor Simon Harrison, begun at Peter Mac in late 2012 for patients with incurable blood cancers.

Pioneering adoptive immunotherapy in blood cancers

- In 2010, clinicians at the Peter MacCallum Cancer Centre dosed a patient with acute myeloid leukaemia with a new form of adoptive immunotherapy, for the first time, removing T cells from the blood, bioengineering them to more readily detect and attack cancer cells and transfusing them back into the patient.
- The adoptive immunotherapy approach, developed through laboratory research led by associate professors Michael Kershaw and Phil Darcy, is based on targeting the Lewis Y antigen, which the team discovered is highly expressed on the surface of many different types of cancer cells but only minimally expressed on healthy cells.
- In 2012, a phase I clinical trial, led by Peter Mac Haematologist, Professor Miles Prince was completed which confirmed the safety, efficacy and durability of the adoptive immunotherapy approach in people with acute myeloid leukaemia; the research team plan to develop clinical trials in solid tumours within three years.

Menzies School of Health Research

Established Australia's longest and largest study of Aboriginal people. In 1986 the Aboriginal Birth Cohort Study began with 686 babies to identify the risk factors contributing to chronic disease such as diabetes, heart and renal diseases at different life stages. Its currently in its fourth wave of data collection.

Introduced continuous quality improvement systems to 208 primary healthcare centres across Australia - which resulted in 100% increases in clinic attendances and major improvements in quality of care across maternal and child health, chronic disease and mental health

[Walter and Eliza Hall Institute of Medical Research](#)

Identified the hormones (CSFs), that control white blood cell development, helping more than 10 million cancer patients recover from chemotherapy, and revolutionising stem cell transplants.

Improved understanding of how the malaria parasite invades blood cells, which has led to the development of four vaccines currently in clinical trials.

[The Florey Institute of Neuroscience and Mental Health](#)

The Florey has pioneered research into gene discovery in epilepsy and the work is actively changing clinical practice.

[Baker IDI Heart and Diabetes Institute](#)

Revolutionising treatment for people with resistant high blood pressure A world-first breakthrough in the treatment of high blood pressure has resulted in a paradigm shift in the management of this condition. Research by Professors Murray Esler and Markus Schlaich from Baker IDI Heart and Diabetes Institute led to the development of a catheter-based clinical treatment for severe and resistant high blood pressure. The procedure involves the insertion of a catheter through the femoral artery and uses radio frequency to 'silence' sympathetic nerves in the artery that deliver blood supply to the kidneys. Following a pivotal paper in *The Lancet* in 2010 describing the successes achieved with this new treatment, the procedure has been approved for use in Europe and Australia, and is offered in more than 10 hospitals nationally. It is estimated that 30-40 per cent of the population suffer from high blood pressure and of that group, 15 per cent are resistant to traditional therapies.

New insight into the role of good cholesterol in diabetes could shape prevention and treatment strategies

Researchers in the Metabolic and Vascular Physiology laboratory at Baker IDI Heart and Diabetes Institute, headed by Professor Bronwyn Kingwell, demonstrated that HDL cholesterol (good cholesterol) has an important role in glucose and fat metabolism. This pioneering work represents a significant shift from HDL being a bystander to an active player in glucose intolerance of the metabolic syndrome, and is critical to the rising epidemic of diabetes and its dramatic impact on cardiovascular disease. The researchers are now looking at whether prolonged HDL elevation produces a sustained benefit on blood glucose control, which may translate to a new therapeutic approach to the prevention and treatment of type 2 diabetes.