SAVING LIVES..... SAVING MONEY.....

Australian Case Studies

Dr Moira Clay
President, ASMR, 2003

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Heart attacks, arthritis, cancer, dementia.....

These are just some of the tragic medical conditions that can strike any of us, or our loved ones, at any time. Disease turns our private world upside down and it costs the public tens of billions of dollars per year in hospital and welfare costs.

Australian medical researchers are at the forefront of the world fight against disease and illness. And our success rate is outstanding, if somewhat unheralded. We still have major challenges ahead. One is improving the health and wellbeing of lower socio-economic groups, the indigenous and elderly communities in our society.

This portfolio of case studies showcases some of the world class achievements by Australian medical researchers to improve the quality of life and reduce the burden of disease. Investment in medical research has not only saved and improved countless lives but has also saved significant amounts of money for the Australian community.

The Australian Society for Medical Research urges government, corporate and public investment in Australian medical research, so together we can capture the significant economic benefits of good health and reduce the cost burden of disease.

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The Australian Society for Medical Research

BRINGING HEALTH TO LIFE.

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Professor John Shine – a pioneer's pioneer

Today he's the head of Sydney's world famous Garvan Institute and Chair of the prestigious National Health and Medical Research Council. Thirty years ago he began a research career that has established him as a pioneer's pioneer in medical science and research.

In 1974 Professor John Shine and his PhD supervisor, Lyn Dalgarno, discovered a messaging sequence inside cells. Working in laboratories in Canberra's Australian National University (ANU), the pair's discovery – the Shine-Dalgarno sequence – paved the way for the evolution of the global biotechnology industry.

In layperson's terms, the Shine-Dalgarno sequence explained how cells recognise the information encoded in genes, opening up a world of health treatments that have saved lives and eased sickness for millions.

In pure medical terms, they discovered a key regulatory sequence, the ribosome binding site, which is an essential step in the process of expressing proteins in cells or bacteria. When the ribosome binding site is combined with other DNA discoveries, these technologies enable the efficient expression of human proteins, such as growth hormone and insulin, in simple bacterial cells as well as the production of entirely new biopharmaceuticals.

"Our sequence provided critical instructions to the cell on how to translate a gene sequence into functional proteins. It was a key communication within the cell. In essence we broke the code and learned how to initiate and terminate signals – turning the gene on and turning the gene off," explained Professor Shine.

The discovery was made while Professor Shine was working on his PhD at ANU, with a scholarship from the Federal Government. The research focused on the difference in signaling between insects and mammals. "It was an obscure pursuit, with no way of predicting where it would lead," he said.

The research led to an understanding of how protein synthesis is terminated in all species and it showed how bacteria starts the synthesis of different proteins.

In 1975 John Shine was awarded a CSIRO Postdoctoral Fellowship worth approximately $13,000 a year and he progressed his research by moving to the US and working at the University of California. In 1976 the University of California took over funding his research and he stayed in the US until 1978.

During this time the Australian pioneer became the first to clone a human hormone gene. His revolutionary research centred on tricking the bacterial cell into thinking that the human gene was one of its own, in order to produce insulin and growth hormone.

This scientific breakthrough started the gene technology industry as we know it today. Professor Shine's work on gene cloning at the University of California, coupled with his earlier work on the Shine – Dalgarno sequence, resulted in a streamlined process to produce biopharmaceutical products. The gene cloning discoveries formed the basis of the success of the first biotech company, Genentech. Genetech took the ground-breaking discovery and commercialised it by commencing the development work to manufacture growth hormone and insulin and then conduct clinical trials. Today Genentech is a company employing 5,252 people and has a market capitalisation of $US17 billion.

Professor Shine's research has focused on understanding how the normal machinery of a cell works – how the body's genetic information gets translated into the building blocks of life, the proteins.

"We engaged in 'blue sky' research to find innovative solutions to health problems. In doing so, we also created new industries and major economic benefit," he said.

Recombinant pharmaceutical products incorporating Professor Shine's original research now account for 50% of the top ten selling biopharmaceutical products, worth more than $US3 billion each year.

"I'm very pleased to have been a part of that economic growth and development. But like all researchers, I have been driven by the excitement of fundamental science, the thrill of discovery. I hope Australia will always be a place where such adventurous research is encouraged. Fundamental new knowledge is at the core of social and economic benefit," Professor Shine said.

Professor John Shine AO FAA, Executive Director, Garvan Institute of Medical Research; Chair of the National Health and Medical Research Council; Professor of Medicine, University of New South Wales; Professor of Molecular Biology, University of New South Wales.

Photo supplied courtesy of Australian Biotechnology News.

Snapshot

- Australia's father of biotech industry
- Broke the code for cell messaging
- Focus on fundamental research for breakthrough discoveries

Funding Sources

PhD research and discovery of Shine – Dalgarno sequence:

- Australian Postgraduate Research Scholarship in 1972 –1975 (approxmately $10,000 per annum for 3 years); and,
- Research support from the Australian National University (approximately $7,000 per annum)

Gene cloning research at the University of California in San Fransisco:

- CSIRO Postdoctoral Fellowship 1976 (approximately $14,000); and,
- US National Institutes of Health (approximately $15,000 per annum).

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From under a Queensland microscope to a worldwide cure

Statistics of disease – prevalence/incidence:

- Australia – Cervical cancer is the 8th most prevalent cancer amongst women – about 1000 cases and 200 deaths annually.
- Worldwide – Cervical cancer is the first or second most prevalent cancer in most developing countries – over 500,000 cases and over 200,000 deaths annually.
- Other related cancers also caused by HPV infection and therefore preventable by the vaccine add 30% to these figures.
- The currently proposed vaccine will prevent about 70% of cervical cancer because HPV causes the cancer; however, there are about 20 relevant HPV types and the two that are in the vaccine will prevent about 70% of these infections.

From under the microscope in a Queensland laboratory, two of the most important breakthroughs in women's health have emerged – a preventative vaccine and a treatment vaccine to combat cervical cancer.

Hundreds of thousands of lives can expect to be saved each year from the dual discovery by Australian scientists Dr Jian Zhou and Professor Ian Frazer of the Centre for Immunology and Cancer Research, University of Queensland.

They discovered the means to prevent, as well as treat, genital warts and cervical cancer. Now, working with the University's commercial arm Uniquest and Melbourne based pharmaceutical company CSL, the preventative vaccine has been licensed to global pharma Merck Sharp & Dohme. And the treatment vaccine has passed the test of its first Phase 1 trials in Brisbane hospitals.

Cervical cancer is the second leading cause of cancer amongst women, with over 500,000 women diagnosed with the disease worldwide every year. In Australia, despite a highly successful cervical screening program, cervical cancer claims a significant number of Australian lives.

Professor Frazer's research on cancer immunology was funded by grants from the NHMRC at the time of the original discovery. The preventative vaccine was an unexpected and unpredicted outcome of a sideline of his research. "Often we find that the critical discoveries don't arise from programmed research but by serendipity," Professor Frazer said.

That initial investment in Professor Frazer's research is now expected to generate revenue in excess of $100m per year and save up to $500m per year in direct health care costs. A further element of this super-success story is that the commercial deals have led to a significant expansion of the University's research facility. From a team of 10 in 1991, the laboratory now has 60 highly qualified scientists, including 10 PhDs, working on new medical research programs and commercial projects.

The prestigious New England Journal of Medicine (NEJM) recently reported results of a proof of principal study that demonstrated 100% protection against human papillomavirus (HPV) 16 – one type of HPV commonly associated with cervical cancer. The discovery of the papillomavirus vaccines, their successful initial trials and now, subsequent deployment to combat cervical cancer, forms one of the great success stories in Australian medical research.

Further studies are currently being conducted by Merck Sharp & Dohme to target four common types of HPV—types 16,18, 6 and 11. Worldwide studies to evaluate this multivalent investigational vaccine are under way, including the Australian arm of a multinational Phase III study being conducted at the Royal Women's Hospital in Melbourne.

In an accompanying editorial in the NEJM, Professor Christopher Crum, MD from the Harvard Medical School said, "The study demonstrates that the vaccine not only prevents the disease from developing, but also prevents the causative agent from residing in the genital tract."

It may have taken 18 years from an Australian test tube to worldwide clinical proof but for millions of women all over the world the wait will be worth it.

Professor Ian Frazer (right) pictured with the late Dr Jian Zhou

Snapshot

- 1991 Queensland scientists discover papillomavirus coat protein vaccine
- Australian companies Uniquest and CSL combine to license technology to Merck
- University laboratory expands research efforts
- New England Journal of Medicine endorses trials

Funding Sources

- National Health and Medical Research Council
- Queensland Cancer Fund
- Princess Alexandra Hospital Foundation
- Cancer Research Institute New York
- CSL
- Merck Sharp & Dohme
- US National Institutes of Health

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Clinical trial battles Australia's biggest killer – heart disease

It was one of the biggest clinical trials ever in Australia and it battled our biggest killer – heart disease.

The National Heart Foundation of Australia's seven year LIPID trial involved around 6,000 patients in Australia and 3,000 in New Zealand, with the trial participants being followed for an average of six years. This massive research program into the heart health benefits of a cholesterol lowering drug (pravastatin) was a resounding success.

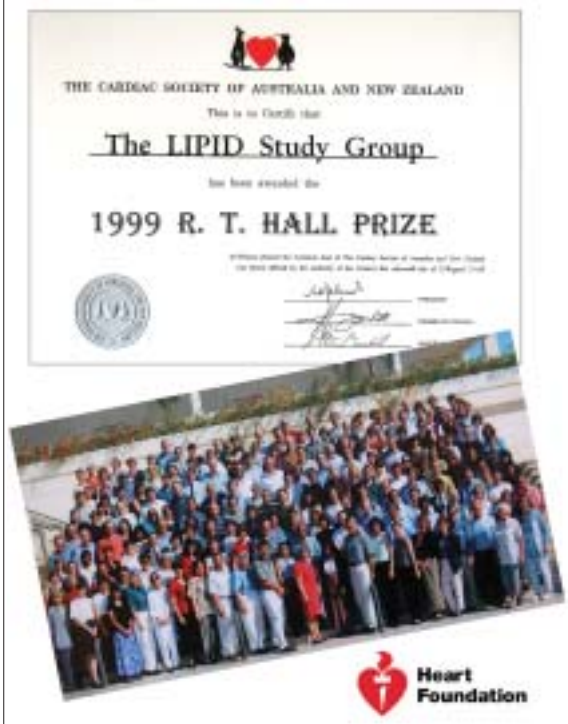
Led initially by the late Professor John Shaw and then from 1994 by Professor Andrew Tonkin, the National Heart Foundation's Director of Health, Medical and Scientific Affairs and a broadly based trans-Tasman medical research team, the primary task of the trial was to determine if pravastatin reduced deaths from heart disease. The answer from the extensive survey showed it did — and more.

"We proved that people with coronary heart disease could reduce their risk of dying from heart attack and stroke by taking a cholesterol lowering agent and benefits occurred even when cholesterol levels were not elevated. Our results showed that a combination of a careful diet and a cholesterol lowering drug significantly increased patients' chances of long term survival," Professor Tonkin said.

More than 53,000 Australians die of heart and blood vessel disease each year. Many thousands more are at high risk because of high cholesterol, smoking, high blood pressure, being overweight and being inactive.

"Heart and blood vessel diseases claim a life in Australia every 10 minutes. One in five of those who die are under the age of 70. Our research which was funded by Bristol-Myers Squibb and coordinated by the NHMRC Clinical Trials Centre at the University of Sydney, proved that treatment with pravastatin saved lives. We also showed that heart attack and stroke could be prevented in patients with previous heart attacks or severe angina and treatment could also reduce the need for heart surgery and angioplasty," Professor Tonkin said.

Not only was there no evidence of difference between patient groups with respect to benefit, but the treatment was very cost effective in comparison with interventions in other areas.



In 1999 the LIPID Study Group (pictured above) was awarded the prestigious R.T. Hall Prize by The Cardiac Society of Australia and New Zealand.

Statistics

- Cardiovascular disease was the leading cause of death among Australians in 1998, accounting for 50,797 deaths (40% of all deaths).
- Coronary heart disease (mainly heart attacks) was the leading single cardiovascular cause of death, accounting for 27,825 deaths (22% of all deaths) in Australia in 1998.
- Stroke was Australia's second greatest single killer after coronary heart disease, claiming 11,982 lives in 1998 (9% of all deaths). It is the leading cause of long-term disability in adults.

Snapshot

The LIPID study showed cholesterol lowering pravastatin:

- Reduced the risk of death from any cause by 22%;
- Reduced the risk of death from coronary heart disease by 24%;
- Reduced the risk of heart attack by 29%;
- Reduced the risk of stroke by 19%; and,
- Reduced the need for heart surgery by 20%.

Funding Source

- The LIPID study was supported by an unrestricted research grant from Bristol-Myers Squibb.

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Aussie pioneers change world view of stomach ulcers

Dr Barry Marshall
Research Professor of Microbiology,
University of WA

Statistics

- Prior to the discovery of H. pylori and its link to peptic ulcer, about 10% of adults were said to have suffered a peptic ulcer episode in their lifetime and about 4% of the adult population were consuming treatment for active ulcer disease.
- Today the most common cause of ulcer is easily cured by the GP on the basis of a simple diagnostic test for H. pylori such as a breath test or a blood test.
- Drugs based on the Perth research now successfully combat the disease and also prevent future peptic ulcer problems for patients.

Twenty years ago they said they were mad. Today their breakthrough research is implemented in clinics all over the world and each year more than four million chronic sufferers worldwide say thank you for their innovations.

In 1983, Perth doctors, Dr Barry Marshall and his colleague, Dr Robin Warren, challenged the medical wisdom of the day when they announced that stomach ulcers were caused by the bacterium helicobacter and not by stress.

Gastroenterologists around the world thought the claim was nonsense, not believing that peptic ulcers could be an infectious disease. But the Perth pair delivered the proof with a series of experiments including self-infection.

More than half the world's population is infected by helicobacter to some degree. Research has now implicated helicobacter in gastrointestinal cancers, such as stomach cancer, a significant killer in Asia.

Today most stomach ulcers are quickly cured with antibiotics. But the presence of helicobacter is an early warning of the possible risk of gastric cancer which remains the world's second most common malignancy.

It is one thing to come up with a cure and quite another to see it put into practice. Dr Marshall, now Research Professor of Microbiology at University of WA, recognised the importance of informing both doctors and the public of the risk and damage of helicobacter. To spread the word, he has developed a suite of tests to diagnose infections and established the Helicobacter pylori Foundation.

In Australia alone, the results of the research have been significant in our public health system. Cases requiring endoscopy of the stomach have decreased by 50%. Chronic treatment for ulcers is no longer needed, saving the system at least $250 million per annum in reduced expenditure on drugs.

"Although we tend to focus on cost savings from such a discovery, remember that the most important benefit is that people who might have had ulcers now live more productive happy lives, a far greater benefit," said Dr Marshall. "Additionally, however, the $200-300 million freed up is now directed towards cure of other diseases.

"Although we may complain about the cost of health care, today the health care we buy really can make an impact on our health. Prior to 1970, treatments were directed at relieving symptoms because we did not know the cause for most diseases.

"Nowadays medical treatment can be proactive because we know the underlying cause of most disorders and can do something about them," Dr Marshall said.

Twenty years on, one major challenge remains for Dr Marshall – to develop a vaccine to eradicate, not just treat, helicobacter.

Snapshot

- In 1983, Dr Barry Marshall and Dr Robin Warren announced stomach ulcers were caused by the bacterium helicobacter and not by stress
- More than half the world's population is infected by helicobacter to some degree
- Today most stomach ulcers are quickly cured with antibiotics
- Endosopies of the stomach have decreased by 50%
- Chronic treatment for ulcers is no longer needed, saving the public health system at least $250 million per annum in reduced expenditure on drugs.

Funding Sources

- NHMRC funded Barry Marshall's salary for three years (1984–1986) to research the cure of ulcers with antibiotics. This was noteworthy as most of the world had not even heard of H. pylori bacterium.
- Supplementary NHMRC grants were awarded in 1985 to allow basic science studies into the H. pylori bacterium.
- Australian pharmaceutical companies, Pfizer and Smith-Kline, financially assisted and supplied free drugs for the early studies.
- Barry Marshall's research was funded for 10 years by US based pharmaceutical company, Procter and Gamble, while he worked at the University of Virginia.
- In 1997 Barry Marshall was awarded a NHMRC Burnett Fellowship to return to Perth and establish the H. pylori research laboratory.

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Don't hush little baby, let's hear you cry...

Australia has traditionally had one of the highest incidences of sudden infant death syndrome (SIDS) or cot death. In the 1970s and 1980s, it emerged that Tasmania, our smallest state, had twice the national average of infant mortality through SIDS. In such a rich, westernised country where human health is so prized, these facts were appalling. SIDS is an especially sad disease because of the innocence of the new-born and the devastating impact on parents and families.

The position was untenable, so epidemiological researchers at the Menzies Centre for Population Health Research in Hobart, led by Professor Terry Dwyer, decided to examine the causes of SIDS. They conducted exhaustive examinations and measurements of more than 3000 babies, born between 1988 and 1990. During that time, the harsh reality of the disease was constantly evident – 23 infants in the study died of SIDS. This information provided the basis of the first major publication by the team in 1991 in the Lancet. By the time the study had finished in 1995, over 10,000 babies had been studied.

Researchers focused their attention on the sleep position of the infant in the cot. Analysis of sleep position and other data showed that prone (lying face down) sleeping position increased the risk of SIDS by 450%.

These findings were strengthened by the results of a concurrent study of 42 SIDS cases in which the prone position showed a 350% increased risk of SIDS.

The outcome of the Tasmanian research resulted in multiple public health campaigns across Australia and the western world, to educate parents about the risks to infants sleeping in the prone position. Subsequent research then proved that sleep position intervention by parents dramatically cut the SIDS death rate from almost 4 deaths per 1,000 live births from 1975 to 1990, to only 1.5 deaths per 1,000 live births in 1991 to 1992. In Australia that translated into a massive 80% reduction, from 507 SIDS deaths in 1990 to 101 SIDS deaths in 2001.

"The research was fundamental and real to so many people. Every parent has had the nightmare fear that SIDS will strike. We were so pleased to be able to uncover the cause and then to be able to see Governments and communities take the lessons and implement them so effectively. We haven't cured SIDS but we certainly have reduced its prevalence and that's a great start," Professor Dwyer said.

The original research project was funded by the Australian Rotary Health Research Fund and the Menzies Centre for Population Health Research. The Centre has since been named a "Tasmanian icon" by the State Premier and core funding has been doubled. Subsequent work is now underway into childhood incidence of asthma, blood pressure and osteoporosis on the same cohort of infants enrolled in the original study.

Professor Terry Dwyer taking vital measurements of a baby participating in the SIDS research project, watched by colleague, Dr Anne-Louise Ponsonby.

Snapshot

- Public awareness campaigns like Red Nose Day have made SIDS a much recognised and understood disease
- The key message is "lie babies on their sides or back, not on their front"
- Since commencement of public health campaigns in Australia there has been a massive 80% reduction in SIDS deaths from 507 deaths in 1990 to 101 deaths 2001

Statistics

Australian Bureau of Statistics total SIDS* rates per 1000 live births for Australia**

*Sudden Infant Deaths under one year
**Chart below is representative of declining trends

Year	Total SIDS cases per annum	Rate per 1000 live births
1988	482	1.96
1993	254	0.98
1998	139	0.56
2001	101	0.41

Funding Sources

- Tasmanian State Government
- Australian Rotary Health Research Fund
- National Health and Medical Research Council of Australia
- US National Institutes of Health
- National Sudden Infant Death Syndrome Council of Australia
- Community Organisations' Support Program of Department of Human Services & Health
- Zonta International
- Wyeth Pharmaceuticals
- Tasmanian Sanatoris After-Care Association

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