

McCusker
ALZHEIMER'S
RESEARCH
Foundation

Year in Review
2015



THE FOUNDATION

In our shared fight for memories, the Foundation remains on course with our vision, mission, objective and values as our continuing inspiration.

Our Vision

A world in which Alzheimer's disease no longer exists.

Our Mission

To support research that makes Alzheimer's disease treatable and preventable.

Our Objective

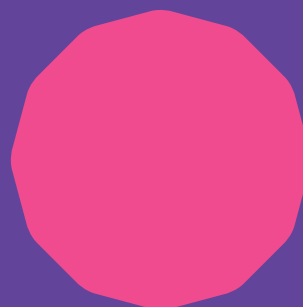
The McCusker Alzheimer's Research Foundation becomes a self-sustaining Foundation that raises funds to support Alzheimer's disease research.

Our Values

For our stakeholders and customers we will always focus on supporting Alzheimer's disease research; act with integrity; be transparent in everything we do; and celebrate our achievements.

Our key pillars are revenue generation through fundraising, grants and research fee-for service activity; research focused on understanding, preventing, diagnosing and treating Alzheimer's and other neurodegenerative diseases; and community services related to education and awareness.

To ensure our continued operations and sustainability we will always have a clear and shared understanding of our risk appetite and have mechanisms in place to ensure we operate within this; ensure appropriate policies and procedures are in place and complied with; maintain strict financial discipline; and refuse to compromise on quality and competence in anything we do and represent.



FROM THE CHAIRMAN

Thank you for your interest in the Annual Report for the McCusker Alzheimer's Research Foundation for 2015.



As Chairman of the Foundation I am, as always, privileged to be able to provide you with an introduction to the challenges and opportunities we have embraced over the past year.

The important work we undertake in support of a world free of Alzheimer's disease would not be possible without the sustained and generous support of our donors, supporters and Ambassadors. We thank you for being part of our quest to seek prevention and ultimately a cure for Alzheimer's disease, which affects a growing number of our friends and family.

With your support we continue to focus on assisting a quality research team, led by Professor Ralph Martins. We do this by providing funding to the Cooperative Research Centre (CRC) for Mental Health and ECU, and more directly by the provision of facilities, staff and services. We also maintain a strong research fee-for-service arm through our Tommorrow trial and trials conducted in our clinical trials division under the supervision of Dr Roger Clarnette. Since 2011 the Foundation has sponsored trials in its own right and currently oversees eight such activities.

We remain grateful to all those who believe in the cause and who support our endeavours, in particular to our Patron, Malcolm McCusker AC CVO QC, and to Ms Carolyn McCusker and to Mrs Tonya McCusker for their ongoing support of the Foundation. The McCusker family continues the early support received by Sir James McCusker which allowed for significant expansion of Alzheimer's research. The Foundation is also indebted to its Vice Patron, Mrs Terrie Delroy and her family for their long-term support.

The Foundation's partners continue to provide a valuable commitment. Our collaborations with Lions Clubs Australia, Hollywood Private Hospital, Edith Cowan University and the CRC for Mental Health remain fundamental in our dedication to continued excellence in scientific endeavour.

We continue to focus on strong governance and a solid operational infrastructure to support our shared mission. Refining our internal operational requirements continues to be a priority and this has allowed strengthened governance and financial stability. A recent review by Deloitte was a helpful exercise and acknowledged positively the course of reform being undertaken. This was followed by strategic planning sessions to reinforce a focussed future.

With your continued support, the Foundation team, including the board, research team, staff, volunteers and the many collaborators who work tirelessly because they believe in the cause, will meet the challenges to come with optimism. Not only are we on this journey together, we shall also take great pride in the successes to follow.

Enzo Sirna AM
Chairman

OUR WORK

Professor Ralph Martins and our dedicated Alzheimer's disease research team continue their work to discover an early diagnosis and develop interventions and treatments. The past year has seen considerable growth in the Foundation's research which focused on preventing or delaying the onset of the disease.

The discovery of a reliable and readily accessible method to diagnose Alzheimer's disease remains a priority for researchers supported by the Foundation. Currently, the only definitive ways to diagnose Alzheimer's disease during life are through brain imaging or by analysing cerebro spinal fluid (CSF). The limitations to these approaches mean they are precluded from routine clinical use.

Early Diagnosis of Alzheimer's

The **Australian Imaging, Biomarkers and Lifestyle Flagship study of Ageing (AIBL)** is one of the world's largest and most comprehensive longitudinal studies. By focusing on early detection and lifestyle interventions AIBL aims to develop early diagnostic preclinical tests for Alzheimer's disease (AD) and understand the contribution of health and lifestyle on the disease.

The study has now completed its sixth year of analyses with the 90 month time point expected to be completed in 2016. The long term nature of AIBL means information gained from the collaborative studies' extensive psychological, cognitive and lifestyle assessments, blood analysis and brain imaging is considered one of the highest impact collections of data world-wide.

It is hoped that going forward the comprehensive data from this study will also accelerate the design of clinical trials and speed the understanding of lifestyle interventions to inhibit progression to the disease.

Another project will discover if imaging the eye can diagnose pre-clinical AD. Several discoveries have been made to date. Thinner retinal layers (retinal nerve fibre layer and the Ganglion cell complex) have been found to be present in those

diagnosed with AD compared to healthy older adults. However, its association with cognition in healthy older adults is yet to be determined.

Study findings show that the Ganglion cell complex thickness, which is comprised of three retinal layers is associated with executive function in cognitively healthy older adults with subjective memory complaints. Further research will concentrate on whether these individuals are at a higher risk of developing Alzheimer's.

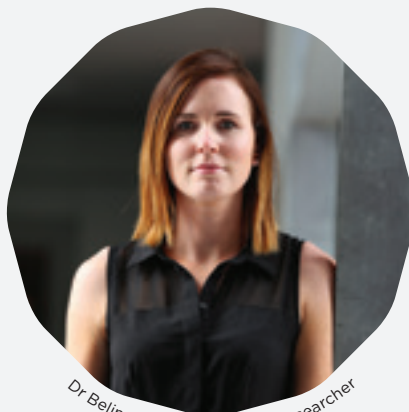
The preliminary findings of this ongoing study have been submitted to the Alzheimer's Association International Conference (AAIC) July 2016 and a manuscript is currently under preparation.

Inherited Alzheimer's

The McCusker Alzheimer's Research Foundation is a partner in the **Dominantly Inherited Alzheimer's Network (DIAN)** observational



Professor Ralph Martins, Director of Research



Dr Belinda Brown, Lifestyle Researcher



Dr Hamid Sohrabi, Neuro Psychologist



Professor Ralph Martins and key team leaders

study. This unique international effort involves 28 sites across eight countries. This study investigates individuals from families who are effected by early onset inherited Alzheimer's disease, a rare form of the disease caused by genetic mutation.

The information gained from participants in this study will allow the testing of potential therapies to prevent, delay, or reverse the development of disease symptoms. The results will be invaluable, not only for those at risk of inherited Alzheimer's but also those affected by the more common older onset disease.

The Foundation is also participating in the DIAN Clinical Trials - a multi-centre study of two potential disease modifying therapies in individuals at risk for and with dominantly inherited Alzheimer's disease. This commenced at the Foundation's Clinical Trials Division in April 2014 with four patients currently randomised to this important trial.

Delaying or Preventing the Disease

The **Testosterone Trial** is a groundbreaking study investigating the effect of Testosterone and DHA (the Omega-3 fatty acid found in fish) in delaying or preventing the onset of Alzheimer's. From the 3,000 volunteers initially interested in participating, 330 participants are now eligible to go to the next stage beginning in mid 2016.

In recognition of his pioneering work on the protective role of testosterone in Alzheimer's disease, Professor Ralph Martins was recently invited to submit a manuscript to the highly prestigious journal, *Nature Review Neurology*.

Recent reports from Stanford and other international teams using large populations continue to confirm a role of testosterone and demonstrate that risk of Alzheimer's disease is doubled when testosterone is lowered by ADT treatment in men with prostate cancer.

Exercise to Protect the Aging Brain

Previous work in the study of exercise and brain health has found that people undertaking higher levels of physical activity have lower levels of brain amyloid (the toxic protein implicated in Alzheimer's disease) and larger volume of a brain region important in short-term memory. Results also showed that individuals undertaking more intense levels of physical activity performed the best on tests of memory and thinking. Further research will investigate the role of intense physical activity in protecting the ageing brain.

Research going forward will evaluate the effect of a six month high-intensity exercise intervention versus low-intensity exercise on measures of brain volume and connectivity, as well as performance on tasks assessing memory and thinking.

Brain Imaging

The Foundation is the grateful recipient of a grant from the Western Australian Government (Office of Research and Innovation) that enables the funding of brain imaging undertaken by Professor Ralph Martins and his team. The purpose of the grant is to help speed up the discovery and refinement of biological markers to detect Alzheimer's disease, with the ultimate goal of developing a blood test for easier diagnosis.

During 2015, 174 specialised brain scans were undertaken through this funding. Of these scans 70 utilised Fluorodeoxyglucose (F18-FDG), while 95 scans utilised a special marker C11 Pittsburgh Compound-B (C11PiB) and nine F18 Flutemetamol. These last two compounds highlight brain amyloid β (the toxic protein behind Alzheimer's disease).

These amyloid imaging techniques and markers are now regarded as the gold standard test for confirming the presence of amyloid β in the brain in living subjects. Where a person has symptoms of Alzheimer's disease, this test confirms the diagnosis. In other cases a positive brain scan indicates a strong risk of Alzheimer's disease and the likely emergence of symptoms in the next 10 to 20 years. The ability to track this amyloid β build up in the brain will enable us to determine the effectiveness of particular Alzheimer's disease treatments and interventions. Some clinical trials are now seeking out amyloid positive participants.



A blood test is far simpler to perform, and is cheaper, quicker and less invasive than a diagnostic brain scan. It is therefore highly desirable to have such a blood test for Alzheimer's disease and the Foundation is pleased to be able to help support this work.

Grants for Alzheimer's Research

In a highly competitive funding landscape, during 2015 a number of members of Professor Martins' research team were awarded grants from the Federal Government and others to conduct cutting edge research.

Dr Belinda Brown and Dr Prashant Bharadwaj were both awarded the highly competitive NHMRC-ARC Dementia Research Development Fellowship. Associate Professor Giuseppe Verdile, based at Curtin University, was awarded a prestigious NHMRC grant to study the interactions of Alzheimer's disease and diabetes. Associate Professor Simon Laws, Edith Cowan University, has received funding from the CRC for Mental Health to collaborate with Pfizer to identify genetic factors in the AIBL cohort that contribute to the risk of Alzheimer's and its rate of progression.

Clinical Trials Division

The past year has been busy and productive for the Foundation's small Clinical Trials Division led by A/Professor Roger Clarnette. The team based at the Hollywood Specialist centre took part in ten clinical trials, most involving people already being treated for memory problems or Alzheimer's disease. These trials are intensive with detailed questionnaires, a series of blood and brain imaging assessments and regular clinic visits. They require a strong commitment from participants and their families, and the Foundation is very grateful for this contribution from those involved.

The Division was very pleased at the end of 2015 when it successfully attracted an arm of the Biogen trial to our site. This monoclonal antibody trial had received considerable attention at the 2015 AAIC (Alzheimer's Association International Conference) when preliminary findings were outlined. These results marked the first time an investigational drug for Alzheimer's had demonstrated a statistically significant reduction on amyloid plaque as well as a statistically significant slowing of clinical impairment in patients with prodromal or mild disease. The Foundation is delighted to be playing a role in further studies seeking to replicate this result in larger populations.

This trial is part of an emerging trend that focusses on people with evidence on PET scan of amyloid accumulation and who have early stage memory problems or the first stages of Alzheimer's disease.

Thank You

We are very fortunate to have an extremely talented and dedicated team who we can all be very proud of.

We are indebted for the support of Edith Cowan University and all our donors which is critical to sustaining research efforts towards understanding, early diagnosis and prevention of Alzheimer's.

For further information on these research projects and other research developments, please visit www.alzheimers.com.au.



ALZHEIMER'S KEY FACTS



1,800

Over 1,800 Australians are diagnosed with dementia every week.



353,800

More than 353,800 Australians currently live with dementia and Alzheimer's disease.



1,000,000

Without a significant medical breakthrough this is expected to soar to almost one million by 2050.



2nd

Alzheimer's is the 2nd leading cause of death.



\$83b

The spending on dementia by 2060 is projected to be \$83 billion, and will outstrip that of any other health condition.



1,000,000

It is estimated that over one million Australians directly support people with dementia.



There is no cure for Alzheimer's.

PARTNERSHIPS

Initiatives that allow researchers from diverse streams of science to come together and share their knowledge and expertise to tackle these diseases are a priority for the Foundation. These examples highlight the dedication and commitment researchers have to a better world through scientific endeavour and excellence.

Cooperative Research Centre (CRC) for Mental Health

The Foundation is a partner in the Cooperative Research Centre (CRC) for Mental Health, a partnership of industry, universities, research institutions, and clinical end users.

Established in 2011 with the support of the Federal Government, the CRC for Mental Health researches early detection and treatment of neurodegenerative diseases including Alzheimer's and Parkinson's diseases, and psychoses such as schizophrenia and mood disorders.

In June 2015, the CRC underwent a rigorous independent review conducted on behalf of the Department of Industry and Science. Its comments were highly complimentary, noting the "very high quality" science undertaken by the CRC, and highlighting the "collaborative study to provide longitudinal data for biomarker discovery in Alzheimer's disease".

The McCusker Alzheimer's Research Foundation contributes significant funding to the CRC for Mental Health and is very proud of CRC achievements to date. These include:

- Identifying several novel biomarkers that can reliably predict whether a person has an elevated level of amyloid protein in the brain, a possible predictor for the development of Alzheimer's disease. This is a very promising lead to developing an inexpensive, reliable blood screen for people with pre-symptomatic Alzheimer's disease.
- New methods and clinical reagents to enable high resolution PET and MRI brain scans to identify individuals at early stages of brain pathology in Alzheimer's disease and monitor the effectiveness of new therapeutics.
- Development of unique education programs for its PhD students, designed to augment and complement those offered by their institutions. These programs focus on "industry specific" skills through working with industry partners, end user clinical organisations and not for profits, as well as a variety of workshops and conferences with experts across a range of different fields.


KARVIAH

Significant headway has been made in the KARVIAH study which is located within the Anglican Retirement Villages (ARV) in Sydney.

This study is an excellent example of a unique collaboration that delivers research direct to the aged care industry, applies new technology and procedures, and furthers knowledge in the field.

Volunteers have already undertaken a comprehensive lifestyle assessment including a health review, neuropsychological tests, blood tests, three brain images (MRI, PET FDG & PET Amyloid) and retinal imaging. The enthusiasm and commitment of residents towards the KARVIAH study to date is remarkable, and evidence of the level of exposure and understanding the aged care population has about Alzheimer's disease. The next step in this study will examine the influence of the Indian curry spice curcumin in the prevention of Alzheimer's disease.

The study has shown that up to 30% of participants recruited in this research have beta-amyloid levels in the brain which are consistent with the pre-clinical stages of Alzheimer's disease. This further highlights the importance of finding approaches that will help prevent progression.



Other outcomes to date include a publication within the British Journal of Nutrition, 'Examining the potential clinical value of curcumin in the prevention and diagnosis of Alzheimer's disease'; and submission of two abstracts with preliminary findings to the Alzheimer's Association International Conference in July 2016.

TOMMORROW Study

The McCusker Alzheimer's Research Foundation is one of 59 study centres involved in an exciting international collaboration - the TOMMORROW study. Sites are situated in North America, Europe, Queensland, Victoria and at the McCusker Foundation in Western Australia.

This novel clinical trial is conducted in collaboration with the major Pharmaceutical company Takeda.

The trial has two main goals. It aims to evaluate whether an investigational test can predict the genetic risk for developing mild cognitive impairment (MCI) due to Alzheimer's disease (AD) in the next five years. It will examine two specific genes - APOE and TOMM40. The second goal is to explore whether a drug often used in type two diabetes treatment will delay the first symptoms of Mild Cognitive Impairment due to AD in people who are cognitively normal.

The prediction of risk would allow for those who know they are at risk of developing the disease to better plan for their future (or tomorrow), and make changes to lifestyle etc. TOMM40, one of the genotypes, inspired the name.

The Foundation's Perth site is the second highest recruiting site worldwide with 320 participants randomised to the study.

Edith Cowan University

The Foundation values its strong partnership with ECU. This is centred on Foundation support for Professor Ralph Martins, ECU's Foundation Professor of Ageing and Alzheimer's and the Foundation's Director of Research.

The nature of the partnership is such that the Foundation provides the facilities for the people centred/ clinical component of Professor Martins' work, through its various study centres and labs in Nedlands, where study participants attend for blood, memory and medical assessment. The detailed research work - in specialised fields including genetics, lipidomics and proteomics then occurs in fit for purpose labs at ECU Joondalup. Much of this work is funded through the Foundation's contribution to the CRC for Mental Health, with Professor Martins leading the CRC's Perth neurodegeneration program.

The Foundation is committed to continuing and strengthening this partnership and help fight Alzheimer's disease as effectively and rapidly as possible.

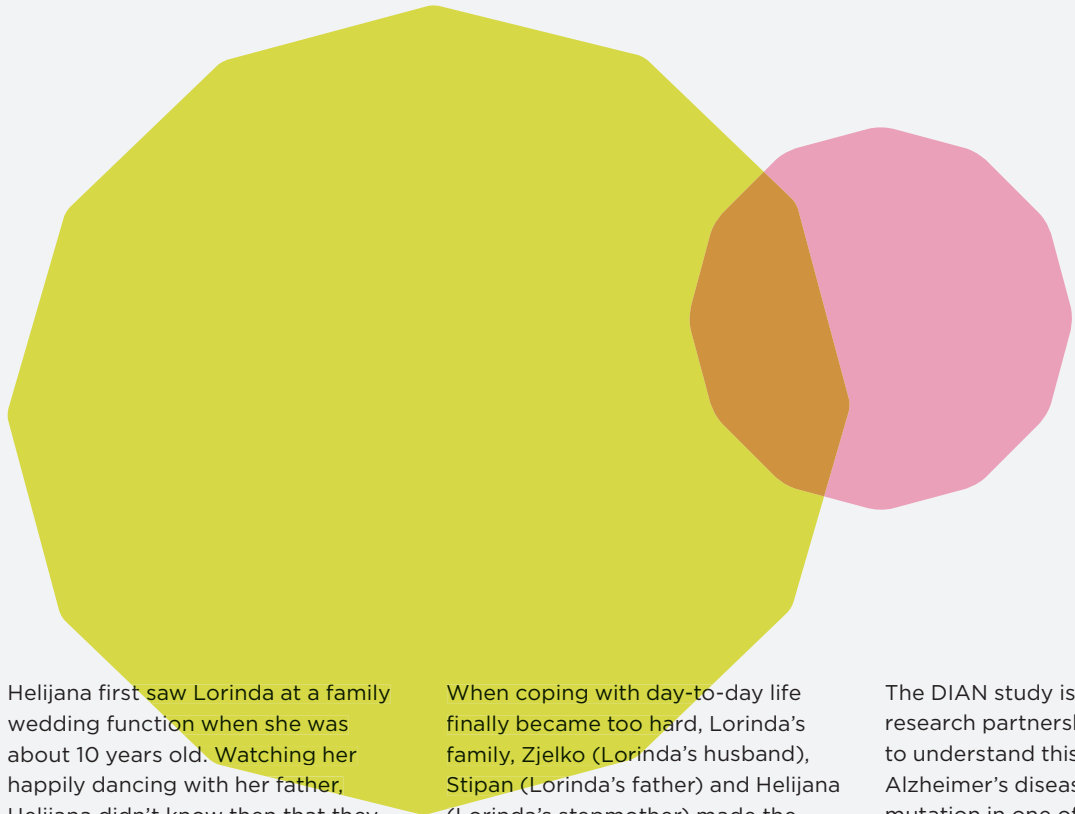
THE PERSONAL IMPACT



Helijana and Lorinda

“We all knew something was wrong with Lorinda, so in fact the diagnosis wasn’t a huge surprise, but still incredibly devastating to us all”

Helijana Pratazina, Lorinda’s stepmother.



Helijana first saw Lorinda at a family wedding function when she was about 10 years old. Watching her happily dancing with her father, Helijana didn't know then that they would become such huge parts of each other's lives.

Lorinda was a beautiful child who grew to be a beautiful woman. Her beauty was not only in her looks but also from within. She was an intelligent strong young woman, a woman of great humour and grace who was deeply respectful of others. She was also a young woman who watched her own mother, and then her aunt, die from early onset Alzheimer's.

In 2002, Lorinda moved to Croatia with her new husband and soon had three children. Her own journey with Alzheimer's began there. Those around her could see that the easiest tasks became too hard, and Lorinda finally realised something was wrong. Fearing she was suffering from the same disease that took her mother, Lorinda finally went to doctors with her concerns. They sent her home saying she was too young.

When coping with day-to-day life finally became too hard, Lorinda's family, Zjelko (Lorinda's husband), Stipan (Lorinda's father) and Helijana (Lorinda's stepmother) made the decision to bring her and her family home. Arriving in Australia in 2010 the focus was first to get a diagnosis, and then to concentrate on care for Lorinda and her young family. Throughout this process, Lorinda understood what was happening. She'd already seen it happen to those she loved.

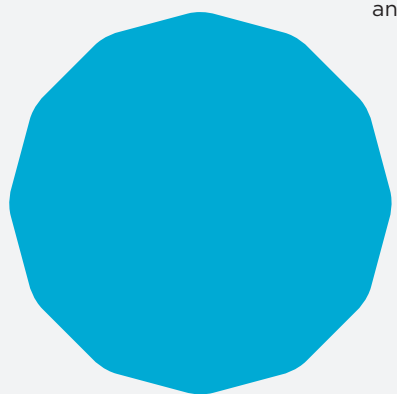
One of Lorinda's greatest concerns was what the future held for her three daughters, the eldest now only just a teenager. They too are at risk of having inherited the disease.

Lorinda was absolutely committed to taking part in Alzheimer's research for answers, as she saw this as the best hope for her children. Her own goal was to do whatever she could to try and prevent this disease, then, now and in the future.

As a result, Lorinda became part of the Dominantly Inherited Alzheimer's Network (DIAN) study. The McCusker Foundation is one of the outstanding research institutions spanning the United States, Australia, Europe, Asia and South America.

The DIAN study is an international research partnership determined to understand this rare form of Alzheimer's disease caused by a mutation in one of three known genes. By understanding this form of Alzheimer's the knowledge gained is providing information for other types of dementia and will lead to better tests that detect Alzheimer's, and provide the next step towards developing dementia treatments.

Lorinda's humour and courage shone through right to the end. Today Lorinda's family continue the fight for memories to give Lorinda, and all those affected by Alzheimer's, the legacy they deserve.



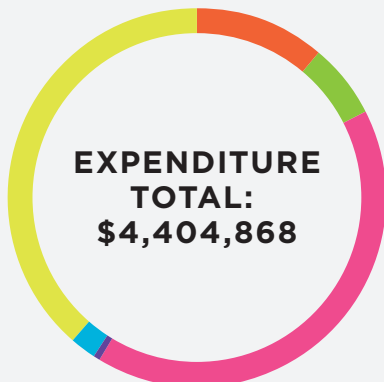
FINANCIAL INFORMATION



- Grants: **\$149,446**
- Donations and Fundraising: **\$662,397**
- Lions Club of Australia: **\$109,935**
- Research Income: **\$4,962,432**
- Other Income: **\$206,380**



- Clinical Trials Income: **70%**
- Funded Research: **30%**



- Facility Expenses: **\$497,423**
- Administration: **\$278,598**
- Employee Costs: **\$1,806,587**
- Insurance: **\$31,837**
- Marketing and Communications: **\$98,574**
- Research Expenses: **\$1,691,849**
(*includes \$857,000 to CRC for Mental Health)



- Administration: **16%**
- Clinical Trials: **61%**
- Research: **23%**

Full copy of accounts available on request.

LOOKING FORWARD

2015 was an exciting year, consolidating past successes to pave a new successful future. There is still much to do and 2016 and beyond are filled with exciting challenges and prospects.

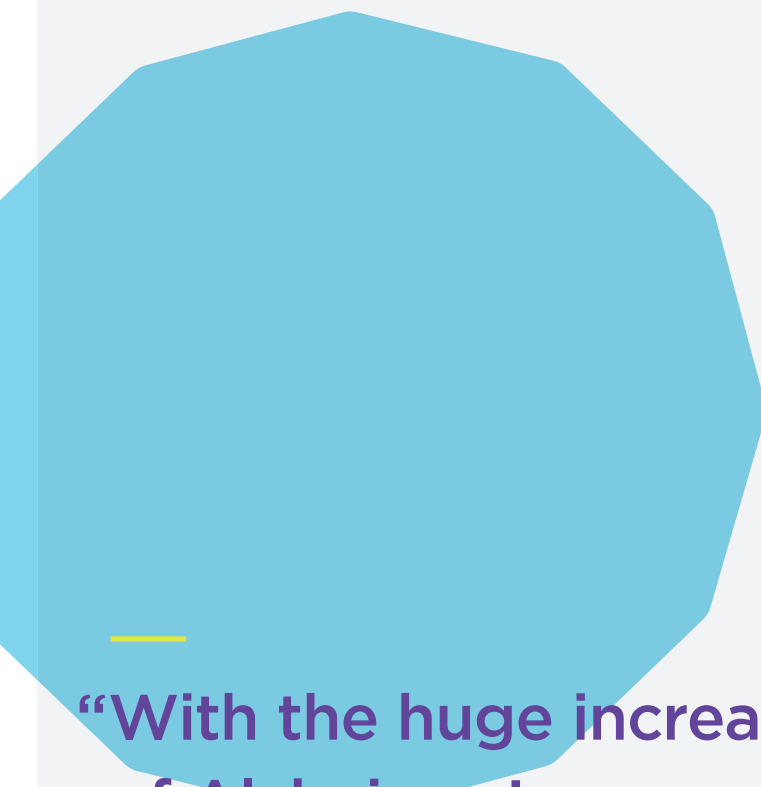
The Ralph and Patricia Sarich Neuroscience Research Institute (NRI)

Due to be completed early 2017, the NRI is an exciting collaboration of the major neuroscience research groups in Western Australia. The centre will be situated at the QEII Medical Centre in Nedlands and provide the state of the art facilities required for the consolidation of the McCusker Alzheimer's Research Foundation team. It will also support sharing of equipment, methods and outcomes among the groups and with other internationally recognised researchers.

With a \$2.4million grant from Lotterywest already committed, as well as a partnership with Lions Clubs who are raising funds Australia-wide for provision of essential laboratory equipment, the NRI will allow the McCusker Foundation the opportunity to lead the future and advance world class Alzheimer's disease research. The facility will be shared with the Western Australian Neuroscience Research Institute, Ear Science Institute Australia, Curtin University and other groups. The Foundation will be strengthening its relationship with Edith Cowan University by hosting Professor Ralph Martins' ECU Joondalup based research group along with team members undertaking the more clinically focussed work, which is currently conducted at the Foundation's Nedlands facilities.



Although the projected cost of providing these new facilities for Alzheimer's disease research is significant, the long-term benefits are substantial. By bringing our group together not only will we be able to better develop our researchers' collaborative efforts, we will ensure the long term saving of operational costs allowing even more funds to be directed towards research projects.



“With the huge increase of Alzheimer’s cases on the horizon, it is critical there be a greater investment in research to allow us to prevent, delay and cure this devastating disease”

Professor Ralph Martins



Barry Cable*

Campaign to Save Memories

To ensure the successful provision of these new world leading facilities, the Foundation is launching a multi-year campaign. Although we all wish for a cure for Alzheimer’s disease to be found soon, we need to ensure sustained support is available until this is a reality. The longevity of partnerships and supporter relationships built in the past and in the future will sustain the long term Alzheimer’s disease research efforts required.

We are honoured to have several individual and corporate supporters already confirming their support for this campaign and Alzheimer’s disease research into the future.

With thanks to the following supporters:

- Barry Cable (Legend of Australian Football and Hall of Fame member)
- AHG
- Seven West Media
- PPR
- West Coast Eagles
- Student Edge

We look forward to working towards a world free of Alzheimer’s with all those on this journey with us.



Strategic Plan Review

2015 saw the review of the Foundation's strategic direction. The result was a three year strategic plan approved in early 2016. The plan will ensure the Foundation builds on its work to date, and expands its research to meet the challenge the growing numbers effected with Alzheimer's will bring. The plan will result in the formation of a dedicated scientific advisory committee and the development of a research road map to help guide the Board and Foundation decision-making and effort.

The vision of the Foundation - a world in which Alzheimer's disease no longer exists - remains at the forefront of the decisions we make. Building on the sound work of 2015 and focussing on the strategies for 2016, along with the increasing interest in the disease and the greater appreciation of the role of research, the Foundation is in a strong position to grow, moving from strength to strength.

“The staggering personal impact of Alzheimer’s disease seen in my clinical trials work drives my team and I to strive even harder to find the answers”

A/Professor Roger Clarnette

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