National Foundation for Medical Research and Innovation

NFMRI

2020

ANNUAL REPORT

About Us

Founded in 1977, the National Foundation for Medical Research and Innovation (NFMRI) is a not-for-profit organisation that is entirely independent. It is not affiliated with any university, hospital, government or state body. The Foundation provides financial and in-kind, skill-based support to advance research projects whilst conserving and building its capital base.

The Foundation is classified as a health promotion charity and is endorsed as a Tax Concession Charity (TCC) with Deductible Gift Recipient Item 1(DGR 1) status.

Our Mission

"To advance innovations in medical research related to the nature, prevention, diagnosis, treatment and incidence of disease and other health problems that have a significant impact on the health of humans"

Our Vision

NFMRI believes more than funding alone is needed to advance discoveries and innovations. Our culture is one where we look to make a social investment in medical research. By partnering with researchers to provide support and knowledge, and facilitating connections with industry, we aim to maximise the social returns from our grants. The Foundation is looking to become a partner of choice with both researchers and funders of research, and a national ambassador for medical research and innovation.

Our vision is to be recognised as the leading Foundation, efficiently and effectively supporting biomedical research, advancing innovations and creating impact.

Our Approach

NFMRI takes a uniquely proactive approach by partnering with grant recipients to provide support along the innovation pathway. It is a prerequisite that we only fund research of the highest quality. When reviewing applications and research projects, NFMRI looks for more than good science. We also assess the ability and willingness of the researcher and the institution to collaborate and to plan and manage research along the innovation pathway. Most importantly, we analyse the potential commercial and social success of the innovation.

NFMRI also considers the need for and size of any potential impact, the potential for the research and innovation to make a significant difference and whether the opportunity may become attractive to a potential next-step partner who can make a product or service accessible to the community. To do this, we harness skill sets from a variety of scientific, clinical, business development, commercial, industry and financial sources.

The Foundation is looking to increase its impact by partnering with other trusts and foundations, Private and Public Ancillary Funds (PAFs and PuAFs) and corporate donors. NFMRI does not proactively solicit donations, but we are always grateful for the donations and bequests that we do receive.

Message from our Chairman

This has been an unprecedented year for the Foundation and for many others in the community. Despite the ups and downs of 2020, due to existing systems in place, there has been little impact or change with the Foundation's operations. This year we have been able to reinforce our commitment to our existing projects, providing flexibility and reassurance, while also supporting an increasing number of innovative projects across a number of diseases and conditions throughout Australia. Together with our partners, we continue to focus on achieving the vision and goals of our benefactors – both past and present.

With a focus on research translation, good giving and strong governance, NFMRI's contributions and work continue to scale. Over recent years, we have carried on building a successful track record by generating a large number of success stories and supporting projects which have since successfully secured their next-step partners. This contributes to our ability to establish funding partnerships with other leading donors, charities and organisations aligned with our Foundation's mission and strategy. By applying our networks, skills and expertise together with funding, we are more effective in our giving and we are better placed to achieve impact together with our partners.

This partnership approach is proving to be highly successful, with a number of existing robust partnerships in place. In particular, I wish to thank The Mason Foundation, The NSW Community Foundation, the Nicholas & Phyllis Pinter Trust and the Vernon Sinclair Fund (all managed by Equity Trustees). They have been a pleasure to work with and are true collaborators in all aspects of our partnership. We also thank the NSW Department of Primary Industries for their continued support towards infectious diseases research, which will be winding down in 2021. We were also pleased to partner with the Cure4CF Foundation and run a second cystic fibrosis grant round during 2020.

It's pleasing to report that since the Foundation's establishment in 1977, over $19.8 million in grants have been committed to support innovative research projects, covering various diseases and conditions throughout the country. Thanks to our partnerships, we have increased our grant commitments in 2020 and hope to continue growing this further over time. This funding and our work have been made possible thanks to our generous benefactors, supporters and partners, including individuals and organisations, who generously contribute their time and expertise. We specifically thank IP Australia, who continue to support our projects by providing complimentary patent analytics reports to some of our funded researchers.

Despite turbulent times in the financial markets, our corpus continued to fare well throughout 2020 thanks to guidance from Pendal Group and in particular, Mr. Scott Glover, in consultation with our Board. We also wish to thank Mr. Mark Boyle and Mr. Eddie Bertan for their continued professional work with this year's annual audit of our Foundation.

I would especially like to acknowledge our team's efforts and achievements over the past year. Dr. Noel Chambers, Mrs. Nancy Ranner and Ms. Di Moore work exceptionally well together as a team and continue to raise the bar for the Foundation year after year.

Likewise, I wish to thank my colleagues and fellow Directors for the dedication and passion they have brought to the organisation. Their leadership, vision and guidance have been and continue to be instrumental to the work and successes of our Foundation. During the year, we welcomed Emeritus Professor Douglas Joshua AO and Ms. Alison Gartner to our Board, who each bring a unique and important skill set to our Board. Our Board greatly appreciates the continued support and advice from our expert Research Advisory Committee (RAC). This year we farewelled Prof. Wendy Cooper, and wish her well with an exciting publishing venture. In April 2021, we welcomed Prof. Lisa Horvath to our RAC, who brings an enormous amount of clinical expertise.

Furthermore, we are grateful to have received pro-bono legal advice from Ms. Alison Choy Flannigan at Hall & Wilcox throughout the course of the year, as well as complimentary venue access and administrative support from McGrathNicol, despite having moved to conduct most our meetings virtually during the 2020 calendar year. We are hopeful of being able to resume meetings in person during 2021.

We are very much looking forward to our 5th medical research innovation conference, 'Research with Purpose 2021', which will take place on the 23rd-25th November 2021 at the Anchorage Hotel & Spa in Port Stephens, NSW. We look forward to sharing with you our impressive line-up of speakers in due course and welcoming you in person at our event.

We greatly appreciate and value our stakeholders' support and are confident both our donors and partners will be pleased with the high-quality research projects their gifts and assistance have enabled. I hope you enjoy reading about our collaborative progress throughout the 2020 calendar year and I look forward to continuing to share with you some of our achievements throughout the course of 2021 and beyond.

Dr. Rob Sauer
Chairman

Message from our CEO

If there has ever been a year that has demonstrated the importance and value of research, translation, quality systems, and other components required to provide community benefits, it was 2020.

The challenges in developing new technologies became more obvious for many with the research and development of new COVID vaccines. Innovations require more than good research but an understanding of translational pathways including manufacturing, storage, distribution and health economics challenges. The need for the whole ecosystem (scientific, business, academia and politics) to work together, collaborating towards solutions that can help address the health challenges for many diseases with new innovations, will hopefully benefit from lessons learned and an increased awareness of both scientific and non-scientific components required for success.

NFMRI has built specialist capability to identify and support potential innovations that may deliver community benefits including new medicines, vaccines, diagnostics, devices, tools and biologicals. Our strategic support fills an important gap in the funding ecosystem, removing barriers and enabling access to external research capabilities and capacity to answer important questions and attract next-step partners.

Throughout the course of the year we continued to help deliver impact to the community by providing targeted, innovation-specific support. During turbulent times in the academic community, we felt it was of utmost importance that we work with each researcher we support to provide flexibility and reassurance. We notified all researchers early in 2020, following the announcement of the pandemic, and tailored individual solutions on a case-by-case basis where time extensions and project modifications were required. We are pleased to report that, so far, we are unaware of any case where the career of a researcher we support is at risk. We are also pleased to report that the majority of projects have since resumed.

Our partnerships continue to forge ahead and together we are supporting a growing list of successful case studies. Sometimes the speed at which the research advances and attracts next-step partners even surprises us. In as little as 6 months of receiving funding, one project successfully partnered with a large international pharmaceutical company and another formed a successful spin-off company - from a $50,000 grant - and recently announced a $30 million deal to fund manufacturing in Queensland. Another project was successful at attracting over $6 million in further funding to their labs. In another example, two separate researchers we support with complimentary innovations are collaborating and both advancing with access to clinical data.

Importantly, the successes NFMRI's support has helped generate, span across various technologies (vaccines, devices, therapeutics, tools, drugs etc.) and diseases and conditions. This demonstrates that our systems and targeted, strategic support are scalable and reproducible, assisting the translation of research. The breadth and depth of our strategy puts us in a unique position where we are partnering with like-minded foundations, donors and other organisations across a broad range of diseases, conditions and innovations to help create impact.

As our funding partnership model grows, so does our ability to support even more high-quality projects. Together with the NSW Department of Primary Industries, we supported Dr. Adam Taylor at Griffith University and A/Prof Joanne Macdonald at the University of Sunshine Coast. Thanks to generous support from the NSW Community Foundation, the Nicholas and Phyllis Pinter Trust and the Vernon Sinclair Fund (all managed by Equity Trustees), we are supporting Dr. James Blackburn's cancer diagnostic research at the Garvan Institute for Medical Research. Via our partnership with The Mason

Foundation (managed by Equity Trustees), we have been able to support a growing number of innovative projects targeting Alzheimer's disease. Researchers supported in 2020 include A/Prof Peter van Wijngaarden (CERA), Dr. Lesley Cheng (La Trobe University), A/Prof Anthony White (QIMR Berghofer) and Dr. Sanjaya Kuruppu (Monash University), Prof Ralph Martins AO (ECU), Dr Lyndsey Collins-Praino/Dr Andrew Care (University of Adelaide), Prof Stuart Dashper (The University of Melbourne) and Professor Michael Parker (St Vincent's Institute of Medical Research). Together with the Cure 4 Cystic Fibrosis Foundation, we supported a number of cystic fibrosis research projects including A/Prof Sarah Vreugde (University of Adelaide), Prof Marc Pellegrini (WEHI) and Dr Leszek Lisowski (Children's Medical Research Institute). I hope you enjoy reading more about these in the project section of this report.

Working with both funding partners and researchers is important as we continue to move research beyond traditional academic measures. Recognising this and maximising opportunities arising from the fact that organisations were largely working from home and developing videoconferencing capabilities, NFMRI led the establishment of a Health and Medical Research Philanthropic Group, which includes over 30 funders from across Australia. Similarly, NFMRI developed a researcher network group to help connect and build relationships across institutions and disciplines. I wish to thank Dr. Phil Kearney, A/Prof Bernard Flynn, Prof. Mark Kendall and Dr. Paul Kelly, who generously gave their time and shared their expertise whilst delivering a targeted masterclass to the researchers we support.

I would especially like to thank our Research Advisory Committee (RAC), who contribute an enormous amount of time reviewing expressions of interest, applications, reports and acquittals throughout the course of the year. The composition of our RAC is unique and includes clinicians, academics, translation and commercial science experts. Each member has a different background and set of skills that helps provide a multi-lens approach in our reviews and support. I also wish to thank our mentors and supporters, whose pro-bono support in IP, research translation, marketing, commercialisation, media and access to networks helps to ensure researchers and their innovations have the maximum ability of achieving the desired outcomes.

Our fifth conference is taking place later this year at The Anchorage Hotel & Spa in Port Stephens NSW on the 23rd – 25th November 2021. At 'Research with Purpose 2021', we will collectively discuss challenges faced by the research community and explore possible solutions. We hope you will be able to join us, learn from our exciting line-up of speakers and participate in the conversation.

Being disease agnostic and impact-driven makes NFMRI an ideal partner of choice. We are actively looking to assist and partner with reputable charities, organisations, PAFs and individuals with a desire to improve health outcomes of the community through biomedical innovations. The nature of our Foundation means we are able to work within the boundaries established by our partners, be they jurisdiction, technology or disease-focused. Every single dollar put on the table by our partners is directed towards the strategically-focussed medical research projects.

Whether you are an organisation or individual interested in a partnership, or if you simply want to learn more about our Foundation, what we do differently and explore how we may be able to help you, I look forward to hearing from you.

Dr Noel Chambers,
Chief Executive Officer

Our Legacy

The Foundation was established in 1977 on the initiative of the late Dr Frank Ritchie who had a number of patients wishing to donate to medical research and for the capital to be preserved. Fundraising activities were conducted under the auspices of the initial Chairman of the Board of the Foundation, Sir Peter Abeles, and Lady Sonia McMahon.

A patient of Dr Frank Ritchie bequeathed a substantial sum, the Stern Estate, to be divided equally between Sydney Hospital and the Foundation. The Foundation was to maintain the capital and use income to fund and facilitate ongoing medical research in perpetuity. Over the years, by way of further bequests and donations, the Foundation has built up significant capital reserves to provide income to facilitate continuing important medical research. The funds of the Foundation and the management of those funds have always been totally independent of the hospital, as has been its management structure. Following an extensive review of the sector, the Foundation updated its mission and changed its name from the Sydney Foundation for Medical Research to the National Foundation for Medical Research and Innovation in 2014.

Emeritus Trustee

We would like to thank Mr Peter Bowen for his continued support and assistance to the Foundation as an Emeritus Trustee.

Past Directors and Major Benefactors

Our Foundation owes its legacy to the following Directors who have served as part of its Board and to those who contributed to the Foundation so generously. Without their vision, foresight and commitment to the Foundation, it would not be where it is today.

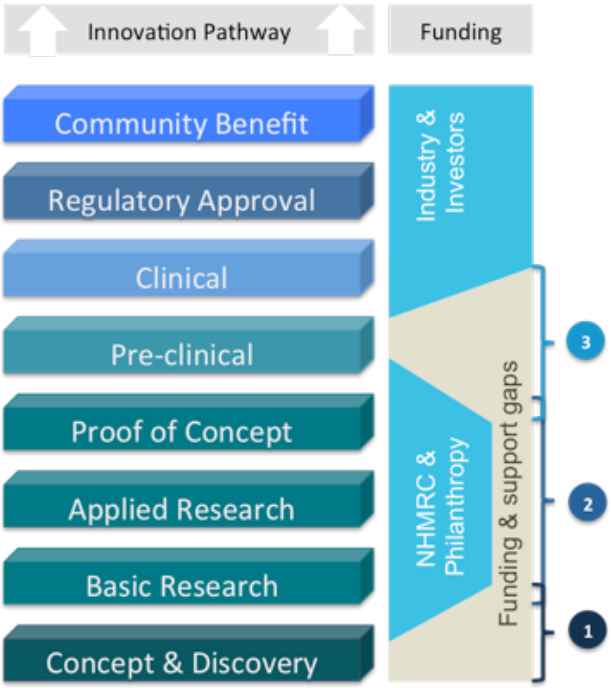
1979-1982	Sir Peter Abeles (Founding Chairman)
1979-1983	Mr ED Cameron
1979-1983	Mr JP Ducker AO
1979-1983	Mr MJ Inglis
1979-1982	Lady Sonia McMahon
1979-1990	Mr TE May (Former Chairman)
1977-1982	Dr FL Ritchie C.B.E.
1977-1995	Mr BF Rose
1979-1982	Dr HH Spiegel
1979-1982	Sir Ian Turbott C.M.G, C.V.O
1982-2007	Dr J Raftos AM
1984-1990	Sir Gordon Jackson
1984-1991	Mr TL Lewis
1984-1987	Mr JW MacBean
1984-1985	Sir William W Pettingell
1987-2003	Mrs SE Ball
1987-1999	Mr RH Minter (Chairman)
1987-2017	Dr V Cowlishaw Shortell
1995-2011	Mr PM Bowen
2000-2003	Prof AJ Young AO
2002-2017	Dr J Graham OAM
2002-2018	A/Prof R Garrick AM
2006-2017	Ms J Schwager AO
2010-2019	Mr K Drewery
2014-2019	Dr A Bates

The Stern Estate
Josephine White and Hiltbrunner Fund
Estate Late Celia Margaret Paine
Estate Late Daqmar Wilhemine Halas
Estate Late Blanche Elizabeth Turner
Estate Late Mary Althouse
The Mason Foundation (managed by Equity Trustees)
NSW Community Foundation – Nicholas and Phyllis Pinter Trust (managed by Equity Trustees)
The Vernon Sinclair Fund (managed by Equity Trustees)
Cynthia & Patricia Gaden Fund
Tempe Mann Fund
Estate Late Bill & Shirley Westbrook
Estate Late Gloria Ida Prejeant
Estate Late Beatrice Gordon Joske
Estate Late James Hoadley
NSW Community Foundation
NSW Department of Primary Industries
Cure 4 Cystic Fibrosis Foundation

Our Strategy

Historically, funding of medical research in Australia has been determined by outputs – research papers and citations validated by scientific peer review. Whilst these factors are important, the advancement of innovation, the formation of collaborations and the ability to deliver impact are the outcomes NFMRI's funding delivers.

To maximise impact, NFMRI focuses on advancing innovation. By looking outwards and supporting the gaps along the innovation pathway and applying resources, networks and knowledge, NFMRI helps philanthropy make a difference. NFMRI supports medical research in three key gap areas we call social investment portfolios.



3 Bridging the 'valley of death'. Supporting research required to facilitate collaborator uptake and investment

Often referred to as the 'valley of death', this is the area where strategic research studies are required to attract potential investors and industry collaborators.

Traditional funding mechanisms do not support or motivate researchers to contract research activities necessary to answer some research questions necessary to form these collaborations.
These research questions are often not attractive to publications as they are "less newsworthy" and not research undertaken by the chief investigator and their team.

By supporting small incremental studies, NFMRI can manage risk and make innovations more attractive to potential commercial partners and investors.

2 Support for strategic collaborative research activities focussed on advancing research and validating directions.

Providing access to the additional research skills not obtainable through currently available funding mechanisms.

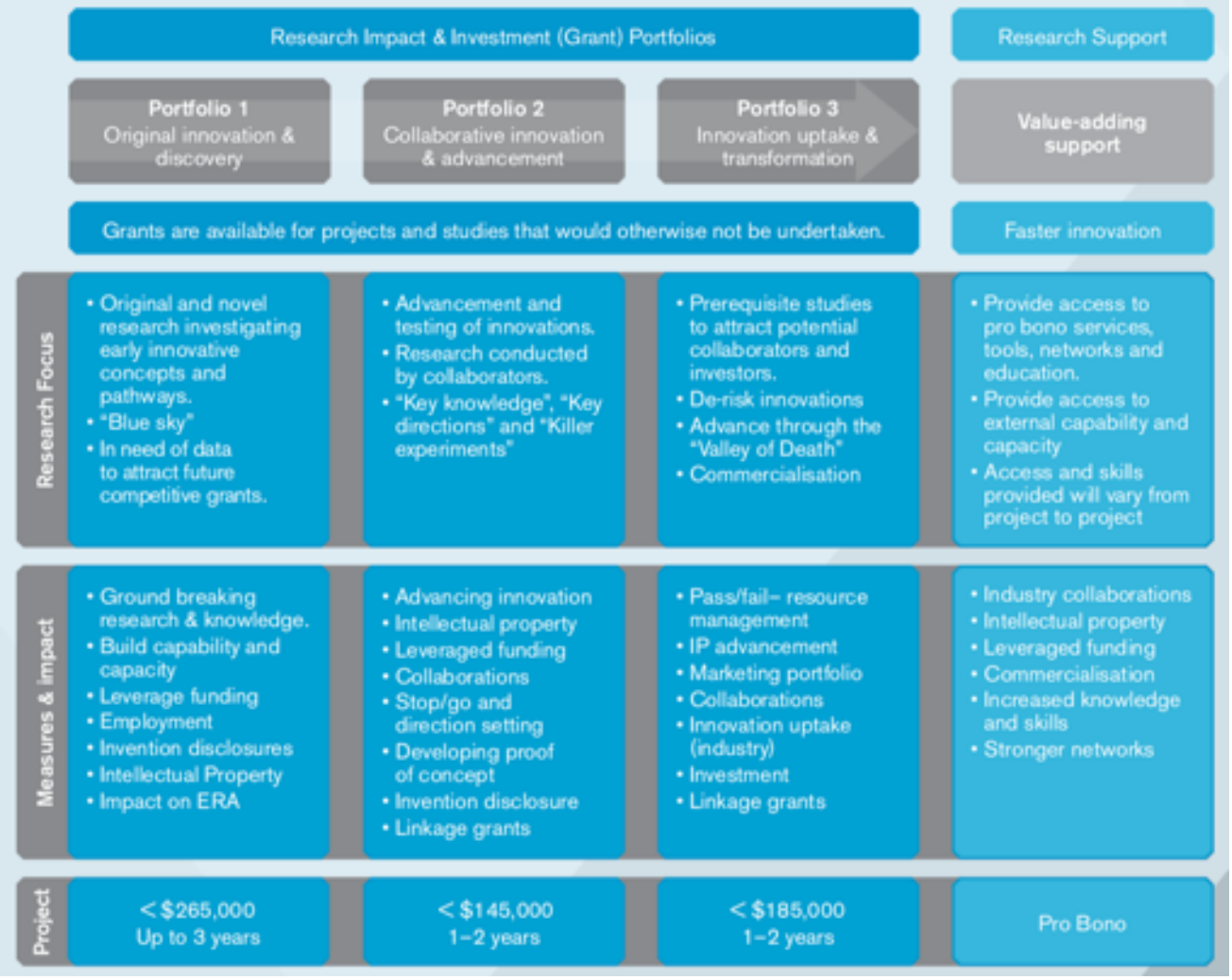
Support for strategic collaborative research activities focussed on advancing innovations and validating directions is needed. NFMRI is uniquely positioned to add value to the advancement of research and innovations in preparation for potential collaborations.

By partnering with researchers, NFMRI supports collaborative research activities undertaken by other research groups that expedite the advancement of the innovation and are important for attracting potential industry partners and investors.

1 **Original Australian innovation and discovery. Frontier research not competitive for NHMRC grants.**

Supporting the validation of new concepts, discoveries and intellectual property creates the foundation for innovations and community benefits of tomorrow. Young researchers, early discoveries and new paradigms need support to become competitive and stand on their own two feet.

Portfolio Summary



Grant amounts and durations are a guide only.

Our Supporters

We wish to acknowledge and thank the following organisations and individuals who have supported the Foundation during 2020. Their assistance has greatly contributed to the Foundation's growth and success:

McGrathNicol

Over many years, McGrathNicol has generously provided support to the Foundation. NFMRI is very grateful to McGrathNicol for kindly providing administrative support and use of office facilities.

BT Financial Group

BT Financial Group has been supporting the Foundation for a number of years, providing strategic guidance to the organisation and management of our investment portfolio.

Equity Trustees

A partnership with Equity Trustees was formed thanks to generous funding from The Mason Foundation to help support mutually aligned research into Alzheimer's Disease. Additional funding from The NSW Community Foundation, the NSW Community Foundation – Nicholas and Phyllis Pinter Trust and the Vernon Sinclair Fund has been provided to support cancer research. This funding has helped support the following grants in 2020: Dr James Blackburn, Dr Joanna Woodcock, Prof Ralph Martins AO, A/Prof Peter van Wijngaarden, Dr Lesley Cheng, Dr Sanjaya Kuruppu, Dr Lyndsey Collins-Praino (Dr Andrew Care), Prof Stuart Dashper and A/Prof Anthony White.

NSW Department of Primary Industries

In 2020, grant funding was provided to both A/Prof Joanne Macdonald and Dr Adam Taylor to support their infectious disease research project via our partnership with the NSW Department of Primary Industries.

Cure 4 Cystic Fibrosis Foundation (Cure4CF)

A partnership was formed with Cure4CF to support research into potential therapies or a cure for cystic fibrosis. Through partnership support, A/Prof Sarah Vreugde and Prof Marc Pellegrini were supported in 2020 and Dr Leszek Lisowski's grant was approved in 2020.

Hall & Wilcox

Hall & Wilcox kindly continues to provide pro bono legal and secretarial advice to the Foundation and has supported many of our past events.

IP Australia

IP Australia kindly provided pro bono patent analytics research to a number of our research projects.

KPMG

KPMG has kindly hosted NFMRI events over the years.

Nexia Sydney Pty. Ltd.

We wish to thank Nexia Sydney Pty. Ltd for being our auditors since 2016.

Special acknowledgements

We also wish to thank the following organisations who promoted and assisted our Foundation and grantees during 2020: AAMRI, Channel 7 (Helen Wellings), AusBiotech, Life Sciences Queensland, Bio Melbourne Network and Biotech Daily. We also wish to thank Gray Design for IT support.

Our Governance

The National Foundation for Medical Research and Innovation (ABN: 85 001 422 895) is endorsed as a Tax Concession Charity and Deductible Gift Recipient (Item 1). The Foundation is also recognised as a Health Promotion Charity and has fundraising licences in relevant Australian states.

The Directors of the Foundation and management are committed to achieving and demonstrating the highest standards of corporate governance. The Directors of the Foundation continually seek to adopt best practice policies and procedures.

In accordance with the Foundation's strong focus on sound governance, the Board has adopted a Governance Charter that supplements its Constitution and details the policies, processes and expectations for the Directors, Research Advisory Committee (RAC), staff and contractors of the Foundation. It outlines a code of conduct, which all members are required to agree to, as well as conflicts of interest disclosures and management procedures.

The annual review of the Foundation's governance frameworks considers best practice guides, including those published by the Australian Securities Exchange and Standards Australia.

The Foundation has continuous improvement processes and adopts a governance review schedule, which includes the review of its skills-based Board, RAC and Staff.

Our Board's Responsibilities

One of the primary responsibilities of the Board is to be the custodian of the purpose of the Foundation as set out in the mission statement within the Foundation's Constitution.

Our Mission

"To advance innovations in medical research related to the nature, prevention, diagnosis, treatment and incidence of disease and other health problems that have a significant impact on the health of humans"

Specific responsibilities include:

- Continually develop and drive the vision of the Foundation;
- Identify any critical gaps in medical research funding in the community;
- Achieve a greater profile within the research community;
- Grant funding to applicants whose research supports the mission of the Foundation;
- Provide guidance to the Research Advisory Committee in respect of the type of research project that the Foundation may fund;
- Increase the Foundation's ability to give via partnerships, bequests and any other suitable avenues; and
- Grow and monitor the financial capital base of the Foundation.

Our Management's Responsibilities

The Board has formally delegated day-to-day management of the company's operations and the implementation of the Foundation's strategy and policy initiatives to the Chief Executive Officer and senior executives.

Our partnerships

NFMRI seeks to engage with like-minded stakeholders that enable the Foundation to fulfil its mission. The Foundation values its stakeholders and believes that in order for its partnerships to be successful, both parties have to be involved and have mutual expectations.

Our processes facilitate discussions to align expectations, establish a governance framework and develop a partnership that benefits both parties to achieve the desired results. To maximise success, our focus is on identifying and working with groups that have aligned interests, where each party stands to mutually benefit from the partnership.

Over recent years, we have had the pleasure of partnering with the following organisations:

NSW Department of Primary Industries: This partnership commenced with a 50:50 joint funding pilot program. Success in the pilot lead to a $400,000 commitment for a grant round managed by NFMRI. Our processes and approach are very transparent and information is shared between both organisations in relation to the funded grant. Each party provided relevant value-adding assistance and mentoring to the applicant. Via this partnership, we have supported Prof Stephen Haswell (Deakin University), A/Prof Eric Gowans (University of Adelaide), A/Prof Joanne Macdonald (University of Sunshine Coast) and Dr Adam Taylor (Griffith University).

Equity Trustees (The Mason Foundation, NSW Community Foundation, NSW Community Foundation – Nicholas and Phyllis Pinter Trust and the Vernon Sinclair Fund): Following an internal strategy review, Equity Trustees' board selected NFMRI as a partner with funding to be managed and distributed by NFMRI. This includes an annual contribution of $600,000 towards Alzheimer's disease research and funding from other partners to support cancer research. NFMRI was seen as a partner of choice due to its strategy and focus on outcomes, independence, ability to value-add to research projects and its ability to support innovation successes that will lead to tangible community outcomes. Together we have supported a large number of projects featured in this report.

Cure4CF Foundation: NFMRI was selected by the Cure4CF Foundation board and team to assist the Foundation with its giving. We assist by running a specific cystic fibrosis grant round to source the most innovative projects across the country. Each year, there is a minimum of $250,000 available for distribution. Together we have supported Prof. Marc Pellegrini and A/Prof Sarah Vreugde and in 2020 we announced a new grant for Dr. Leszek Lisowski.

NATIONAL FOUNDATION FOR MEDICAL RESEARCH AND INNOVATION

Partnering for success

NFMRI partners with funders of medical research to create impact

A focus on creating impact

NFMRI partners with other funders, applying its strategy, systems, networks and expertise to achieve common goals.

Founded in 1977 and with DGR1 status, the National Foundation for Medical Research and Innovation (NFMRI) has an established partnering program assisting other funders of medical research achieve better outcomes.

Supporting medical research that is important in the translation of discoveries leading to new innovations including medicines, vaccines, diagnostics, devices, biologics and tools, NFMRI has built specific expertise, capability and capacity that has enabled success.

Through our partnering program, NFMRI is collaborating with other funders to achieve our missions.

Contact us to learn more and enquire about how we can work together.

Professor Janet Davies
"NFMRI can foster a culture that enhances commercial uptake of our biomedical innovations, mentor academic inventors and facilitate connections between academia, philanthropy and commercial sectors"

A.Prof Bernard Flynn
"NFMRI provides critical assistance to researchers in bridging the 'valley of death' that separates basic science from viable therapies"

1 GOVERNANCE
Strong governance forms the foundation of what we do, our culture and our partnerships.

2 STRATEGY
Our strategy focuses on targeted support that addresses gaps to enable translation.

3 SYSTEMS
NFMRI has built bespoke scaleable systems and capability specific to our strategy.

4 TRACK RECORD
Proven track record of success with breadth & depth across diseases and innovations

nfmri.org.au

enquiries@nfmri.org.au

Advancing medical discoveries and innovations

It is more than funding that is needed to advance discoveries and innovations.

NFMRI takes a uniquely proactive approach by partnering with our grant recipients to provide support along the innovation pathway.

It is a prerequisite that we only fund research of the highest quality. When reviewing applications and research projects, NFMRI looks for more than good science. We also assess the ability and willingness of the researcher and the institution to collaborate, plan and manage research along the innovation pathway.

NFMRI also considers the need and size of any potential impact, the potential for the research and innovation to make a significant difference and whether the opportunity may become attractive to a potential partner who can make a product accessible to the community.

To do this we harness skill sets from a variety of scientific, business development, commercial, industry and financial sources.

Identification, selection and support

Working with our researchers and their institutions, the NFMRI utilises the skills of our staff, Research Advisory Committee, Board and our networks to assist with communication strategies, understanding industry's expectations and the establishment of networks and collaborations.

nfmri.org.au

JODI KENNEDY, EQUITY TRUSTEES

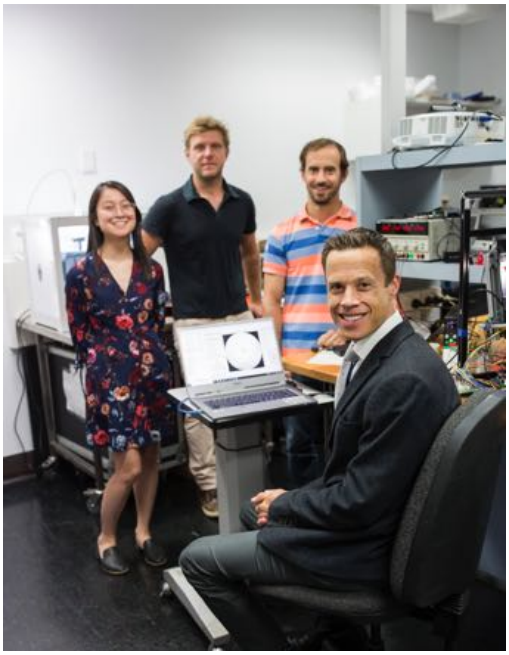
NFMRI is a standout partner due to its strong governance and transparency, but also because of the Foundation's focus on translation of research outcomes across medical innovations including medicines, diagnostics, vaccines and devices. The focus on delivering community benefits from medical research and helping de-risk innovations so they are more attractive to the next-stage partner is an important factor in our decision making. This unique support is critical in helping researchers bridge the 'valley of death' that prevents many research outcomes from ever reaching the community.

Also factored into this decision was NFMRI's unique capability and capacity for holding grant rounds nationally, utilising its developed online programs and software. In addition, the individuals that make up their review committee are unique in that they are from diverse areas including academia, translation, commercial and clinical backgrounds.

Project updates

A/Prof Peter van Wijngaarden, Centre for Eye Research Australia
"Translating an eye imaging biomarker for Alzheimer's disease to the clinic"
$250,000 from 2019-2021
Indication: Alzheimer's disease
Type: Device

A/Prof van Wijngaarden's research group has recently developed a novel imaging method that allows them to non-invasively detect the accumulation of amyloid beta in the retina. Their research has utilised a state-of-the-art, costly research camera that images the retina sequentially with 90 different wavelengths (colours) of light. They have identified a way to develop a low-cost retinal camera with similar capabilities as the costly research camera, opening up the potential to deploy this technology in a wide range of clinical settings to screen for Alzheimer's disease. NFMRI funding is enabling retinal camera development and clinical studies to validate the technology against their state-of-the-art research camera.


L-R: Darvy Dang, Dr Xavier Hadoux, Maxime Jannaud and A/Prof Peter van Wijngaarden

Since the commencement of this project in 2019, it has progressed tremendously well and garnered support from prominent, global funders. Most recently, support was received from the BioMedTech Horizons MRFF scheme for further development of their hyperspectral camera and a joint NHMRC-European Union grant was also awarded.

Some of the key highlights from this project's progress include:

- Project has leveraged over $4.6 million in additional funding as a result of the grant
- Formation of spin-off company already underway
- Results have already been published in a peer-reviewed scientific paper
- New IP identified and provisional applications being prepared
- Has garnered support from the likes of Bill & Melinda Gates and Jeff Bezos via the Alzheimer's Drug Discovery Foundation
- Significant media interest from a number of networks/sources
- Awarded NHMRC-EU Joint Programme for Neurodegenerative Diseases (JPND) research grant
- Received support from BioMedTech Horizons MRFF scheme to develop the prototype retinal camera into a manufacturable medical device

Speaking of the support provided by the NFMRI, A/Prof van Wijngaarden said, *"this funding has enabled us to develop and test several prototypes of our retinal camera. This has been instrumental in our ability to secure additional grant funding and accelerated our progress towards the clinic. In addition, Noel Chambers and his team have provided us with invaluable mentorship and access to some of the leading experts in medical research translation who have generously shared their expertise with us. This know-how has been tremendously helpful to us."*

A/Prof Joanne Macdonald, University of Sunshine Coast
"A rapid, sensitive, and portable molecular genetic test for diagnosis of Malaria in blood"
$140,550, 2019-2021
Indication: Infectious diseases, malaria
Type: diagnostic

In a project previously funded by the Bill and Melinda Gates Foundation, A/Prof Macdonald and her team developed rapid testing technology for the detection of Malaria in mosquitoes. Support was provided by NFMRI to validate the rapid and sensitive Malaria test for detecting subclinical infection levels at a collaborating institute by testing it on human samples containing low levels of infection. NFMRI funding is also being used to determine the optimal manufacturing reagents to achieve the best possible sensitivity, specificity and reliability of testing kits to provide further confidence for potential investors that the test can be reliability manufactured.

Whilst this project is still underway, the following progress has been made:

- Formed collaborative agreement between the University of Sunshine Coast and QIMR Berghofer to work collaboratively alongside existing clinical trials to access patient samples and clinical data
- The standard rapid test has been optimised for improved analytical sensitivity of detection in blood
- The rapid test can detect parasite in blood and detect parasite in human samples including subclinical levels of detection
- Technology has been expanded to also detect Plasmodium vivax DNA, which is notoriously difficult to detect due to lower levels of parasites that circulate during infection

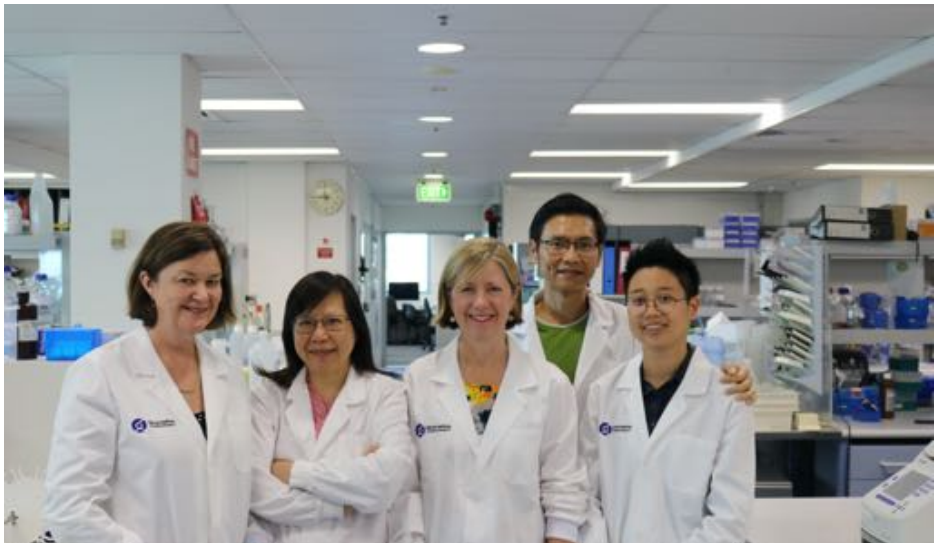
A/Prof Anthony White, QIMR Berghofer Institute of Medical Research
"A personalised medicine approach for screening neuroinflammatory drug efficacy in Alzheimer's disease"
$100,000, 2019 – 2020
Indication: Alzheimer's disease
Type: diagnostic

A/Prof White's team developed a unique approach to screening drugs that target the brain's resident immune cells (microglia) on a person-by-person basis. They are able to generate microglia from a person's blood cells (monocytes) in 2 weeks at a cost of ~$50/person. These cells can be screened for the ability of different drugs to enhance their protective functions, allowing them to determine which drugs will likely benefit each patient. With access to large Alzheimer's disease cohorts, they are in a unique position to establish a screening platform for patient-specific drug efficacy, allowing physicians to prescribe a drug treatment regime tailored to an individual's own microglia. Patient microglia responses can then be monitored over time. NFMRI funding supported research to screen patient specific potential drugs.

A/Prof Anthony White's project commenced in April 2019 and was completed by 31 December 2020. Some of the key highlights from this project's progress include:

- Project is progressing very well and all aims are being achieved
- Industry partnership with Takeda Corporation
- Leveraged $230,000 of funding from private and public sources
- Partnering with Dr Lesley Cheng from La Trobe University

A/Prof Clare Stirzaker, Garvan Institute of Medical Research
"Liquid biopsy monitoring for triple negative breast cancer: a novel epigenetic test"
$141,834 during 2019
Indication: Breast cancer
Type: diagnostic


L-R: Prof Susan Clark, Jenny Song, A/Prof Clare Stirzaker, Dr Phuc Loi Luu, Dilys Lam

A/Prof. Stirzaker and her team have performed the first genome-wide profiling study on DNA methylation (epigenetics) in Triple Negative Breast Cancer (TNBC). Funding from NFMRI was used to develop this TNBC-specific blood-based biomarker test, by providing access to the sensitive methylation assay that has been developed in the laboratory of Prof. Trau and Dr. Korbie at the University of Queensland. This assay is particularly important as it allows, for the first time, up to 50 methylation signatures to be tested on the same clinical sample in one test. In addition, the test employs next-generation sequencing which allows unprecedented sensitivity to be achieved, critical to accurately detecting tumour methylation in a blood sample when circulating tumour DNA may comprise only 1% of the total circulating free DNA.

This project was supported in partnership with the generous support from the NSW Community Foundation, the NSW Community Foundation – Nicholas and Phyllis Pinter Trust (both managed by Equity Trustees) and NFMRI.

Progress to date:

- Methylation test has been optimized, performed on an initial cohort of 100 patient blood samples and progressing into testing up to 500 patient samples.
- They have now shown that they can accurately and sensitively classify normal and tumour circulating DNA
- Established clinical collaborations at The Kinghorn Centre and Chris O'Brien Lifehouse to access clinical cohorts and to help take the test into a clinical pathology lab
- Leveraged over $600,000 from the National Breast Cancer Foundation
- Promoted to Associate Professor
- Led to two publications and a manuscript is currently underway
- Now working on evaluating the epigenetic biomarker test to see if breast cancer relapse can be detected in a simple blood test

A/Prof Stirzaker said, *"The funding we received from NFMRI has been absolutely key in moving this work forward to the point now where we have strong preliminary data that enables us to now embark on prospective clinical testing."*

Prof Michael Good AO, Griffith University
"Producing and testing a GMP grade peptide conjugate vaccine to prevent infection with group A streptococcus"
$251,000 over three years (2015-2017)
Indication: group A streptococcus
Type: vaccine

Prof Good's project focused on producing at clinical grade, a novel GMP grade peptide conjugate vaccine against group A streptococcus, the causative agent of tonsillitis, deep tissue sepsis, pyoderma and rheumatic heart disease, for a Phase1 trial.

Key outcomes/outputs:

- Vaccine manufacture at AusPep in Melbourne, with external funding to complete vaccine manufacture and toxicology
- Exclusive licensing and co-development agreement with Olymvax Biopharmaceuticals (Chgengdu, China) to co-develop the vaccine product for the China market
- Received investment and clinical expertise from the Li Ka Shing Institute (Edmonton, Canada) to support a Phase 1 dose-ranging clinical trial in Canada
- Funding received from The Heart Foundation to undertake a challenge trial in Australia
- Total funding leveraged includes over $7m of funding from government and private sources, including:
    - Received $500k grant from Li Ka Shing Foundation
    - Led to a collaboration with GSK ($222,500)
    - Received $911,915 NHMRC Senior Principal Research Fellowship (2015-2020) along with a number of project grants
    - Received $2,790,000 grant from The National Heart Foundation of Australia
    - Received Health Canada approval on April 27th 2021 to begin a Phase 1 dose-ranging clinical trial on 45 healthy individuals. The trial is scheduled to begin in Q2 2021.

Professor Good said, "NFMRI funding has been critical to the vaccine programme and has enabled the team to cross the 'valley of death' so that we can now assess vaccine safety, immunogenicity and efficacy in Phase I/II clinical trials.

Prof Janet Davies, Queensland University of Technology
"Point of care diagnosis for hayfever and asthma; development and validation of rapid subtropical specific IgE tests"
$99,953 from 2018-2020
Indication: Asthma and allergy
Type: diagnostic

This project focuses on using allergen molecules of subtropical grass pollen for more specific tests and treatments to assist people allergic to grasses in subtropical regions. After identifying and characterizing all the key allergens of two major subtropical grass pollens and making headway in subtropical grass pollens research, NFMRI supported Professor Davies to partner with Abionic SA. The Swiss company has developed an instrument that quickly measures levels of sensitivity to allergens in doctors' rooms, and pre-commercial funding was provided to investigate whether recombinant versions of their pollen allergens are effective as a more specific and rapid point of care diagnostic test for grass pollen allergy in warmer regions of the world.

Since receiving funding from NFMRI, some of the key highlights arising from this grant include:

- Leveraging nearly $217,000 of funding from external sources, including Abionic Switzerland
- Attracted co-sponsorship from potential industry partner, Abionic Switzerland to test the utility of allergens of subtropical Bahia and Bermuda grass pollen to function as an active ingredient in a nanotechnology point of care diagnostic platform.
- Recombinant allergens have been optimized and verified by Abionic
- The newly designed, expressed and purified allergen components have been successfully assessed for quality by mass spectrometry by the Australian Proteomic Analysis Facility (APAF).
- Chief investigator promoted to Professor

A/Prof. Nicholas Opie, The University of Melbourne, Synchron Inc.
"Safety validation of the Stentrode™: a biomedical device for paralysis that convers thoughts into computer commands"
$390,000 from 2017-2018

This project received funding in 2017-2018 from NFMRI to support safety validation of the Stentrode™, which was developed by A/Prof. Nicholas Opie and his team. The Stentrode™ is an endovascular brain-machine interface that can record neural signals from within a blood vessel. This technology is designed to restore instrumental activities of daily living in people with paralysis by sensing brain activity and translating these signals into discrete electrical commands which enable direct

brain control of computers and assistive technology.

In 2019, A/Prof. Opie and his team have successfully implanted the Stentrode™ into four participants with from severe paralysis due to motor neuron disease, enabling them to control a computer with their mind. They can use the system independently and at home to communicate using emails, text and messaging applications and complete daily tasks such as online banking and shopping.

The Stentrode™ has also recently been granted Breakthrough Device designation by the U.S. Food and Drug Administration (FDA), a status reserved for innovative solutions addressing irreversibly debilitating conditions.

This research has been running in parallel with the neurovascular bioelectronics medicine company, Synchron, Inc., he co-founded and directs with neurointerventionalist A/Prof Thomas Oxley. Synchron is developing bloodstream-enabled solutions for previously-untreatable nervous system conditions. The development of this technology platform was enabled by seed funding from the U.S. Defense Advanced Research Projects Agency (DARPA) and the U.S. Department of Defense (DoD), among other competitive Australian grants. Synchron raised over $10M in their Series A fundraise, and is poised to close a large Series B round to expand their clinics to sites in NSW and QLD, and conduct an early feasibility study in the USA.

Headquartered in Silicon Valley, California with presence in Brooklyn, New York and R&D facilities in Melbourne, Australia, they have realised clinical utility of the world's first endovascular neural interface. Through private funding and the award of competitive grants including an NHMRC Fellowship (Opie), the University of Melbourne and Synchron will continue translation of their technology to restore independence and communication to people with paralysis, while also conducting ground-breaking Australian research enhancing the capabilities of the Stentrode system to treat other neurological conditions such as epilepsy, depression and Parkinson's disease.

Other key highlights arising from this grant include:

- Synchron receiving nearly $1 million in funding from the Medical Research Future Fund
- $1.5 million NHMRC grant received by the University of Melbourne to expand the clinical study of the Stentrode™

Professor Mark Kendall, Australian National University
Dr John Dixon Hughes OAM Medallist, $50,000 in 2018-2019

Professor Kendall received a $50,000 award, in the form of a research grant, after being awarded the Dr John Dixon Hughes OAM Medal in 2017. This funding was applied towards the development and evaluation of a Microwearable™ sensor for hydration monitoring. Since then, an Australian spin-off company WearOptimo was formed, developing unique, functional diagnostic wearables for a range of consumer and medical applications.

WearOptimo's life saving Microwearable™ sensor technology is heading into production with a $30 million deal, which includes funding an advanced technology facility in Brisbane, Queensland.

In March 2021, WearOptimo signed a $30 million project to set up an advanced manufacturing facility in Queensland. The funding is from the Queensland Government through the Essential Goods and Supply Chain Program (EGSCP), WearOptimo and the Australian National University (ANU) to build a globally competitive high-tech manufacturing facility to produce up to 26 million Microwearable™ sensors each year. This project is also supported by the Australian National Fabrication Facility

(ANFF) and other partners. The facility will be one-of-a-kind in Australia and will be key in creating hundreds of high-value jobs throughout this decade.

Founded in 2018, WearOptimo is based in Brisbane and became the Australian National University's first innovation company. In 2020, WearOptimo signed a deal with Aspen Medical to be an exclusive distributor/reseller of the hydration Microwearable™ sensors within Australia and globally. The commercial partnership will target the mining, resource, and energy sectors where hydration monitoring of workers is of paramount importance.

Other WearOptimo milestones include:

- Awarded two grants from the Australian Government (>$1.8 million) under the MTP Connect Biomedical Technology Horizons Grants program;
- First Microwearable™ sensor patents filed;
- Prototype integrated commercial Microwearable™ sensor; and
- Established a world-leading interdisciplinary team from the world's leading universities, including the Australian National University, University of Oxford, University of Cambridge and Stanford University.

The Microwearable™

By directly detecting biomarkers and body parameters in the skin, WearOptimo's Microwearables™ instantly enable diagnosis and monitoring of a range of disorders in a simple, wearable format with immediate information available to patients, carers and clinicians.

The Microwearable™ devices offer a unique platform for the interrogation of the human body. They are minimally invasive, pain-free and monitor clinically relevant data; and cloud-based services and analytics provide real-time feedback to the patient and clinicians for rapid decision making. Aggregated data analytics provide new insights to human health.

New grants approved in 2020

From grant rounds held in 2020, a total of six new grants were approved (a total of $1,031,990) and announced in 2020:

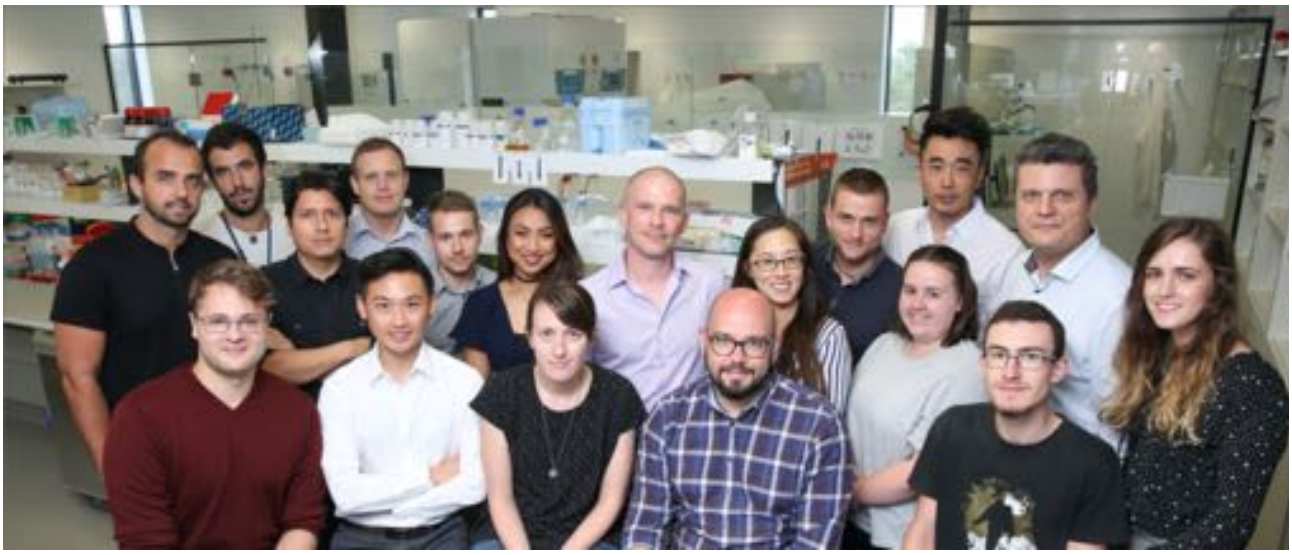
Dr. Leszek Lisowski	**Children's Medical Research Institute**	**$140,000 (2021-2022)**

An all-in-one gene therapy treatment for cystic fibrosis

Dr Lisowski's project aims to develop new gene therapy tools for the treatment of cystic fibrosis (CF). Together with his team, they aim to develop tools that carry the promise of achieving therapeutic efficacy following a single systemic administration of an adeno-associated viral (AAV) vector. Specifically, the project will enable development of two key tools:

(1) novel, human lung-tropic AAV vectors for safe and efficient targeting of the basal cells, which give rise to human airway epithelium (HAE). To increase safety and efficacy, the AAV vectors will be specifically de-targeted from the human liver, which is the primary target of most AAVs following systemic delivery.

(2) AAV-based gene editing strategy to correct CF causing mutations in the fibrosis transmembrane conductance regulator (CFTR) gene in the basal cells.



Dr Leszek Lisowski's team, Children's Medical Research Institute

The combination of these two novel technologies will form the basis of a powerful gene therapy approach to cure cystic fibrosis. The project will also lead to the development of a novel dual liver-lung preclinical model that will enable preclinical studies not only in the area of gene therapy, but also will be an invaluable tool to other researchers studying the disease and/or developing novel therapeutic options for CF. Funding provided by the Cure 4 Cystic Fibrosis Foundation and NFMRI will support the preclinical validation of the gene therapy approach to cure CF.

Prof. Michael Parker	**St Vincent's Institute of Medical Research**	**$192,374 (2021-2022)**

A new approach to tackle neurodegenerative diseases

Currently, the leading strategy to remove toxic proteins (namely Abeta and tau) associated with two types of brain deposits found in Alzheimer's disease, is to treat people with antibodies that recognise these toxic proteins; this is called 'immunotherapy'. To date, all Abeta immunotherapy

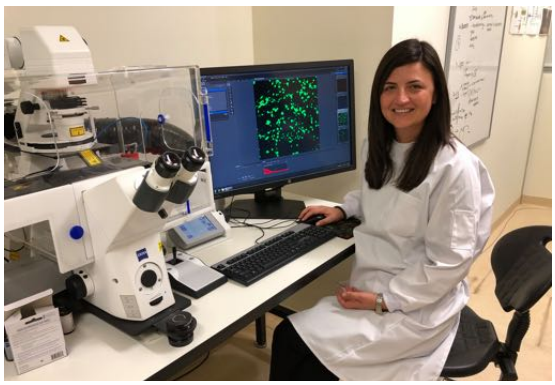
Professor Michael Parker

trials have had serious efficacy and/or safety concerns, in part because the body's immune response to the therapy has resulted in inflammation in the brain. Professor Parker and his team have developed a new type of drug that has the advantage that it does not promote inflammation in the brain and can more effectively cross the 'blood-brain barrier', a barrier which protects the brain from infection but can also block the transport of drugs.

They have tested the drug in brain cells in the lab and found that their novel drug technology successfully increases the removal of toxic Abeta material without promoting increased inflammation. Funding provided by The Mason Foundation (managed by Equity Trustees) and NFMRI will enable Professor Parker to complete important pre-clinical trials in animals to take this therapy a step closer to the clinic. This technology holds great promise for future development and has drawn preliminary interest from industry partners.

Dr Branka Grubor-Bauk The University of Adelaide $220,000 (2021-2022)
Novel T cell-based DNA vaccine against Zika virus infection

Dr Grubor-Bauk has developed an innovative, patented and thermally stable Zika virus DNA vaccine that encodes Zika virus non-structural protein 1, NS1. Extensive evaluation of this vaccine in mouse models of Zika infection has shown that it induces strong immunity and confers complete protection against systemic Zika infection. Funding from NFMRI will progress the development a novel Zika virus vaccine by completing pre-clinical evaluation of this Zika virus DNA vaccine enabling Phase I Human Clinical Trials, and generating data for regulatory filing.



Dr Branka Grubor-Bauk

A/Prof Bernard Flynn Monash University $135,700 (2021)
Gastrointestinal-directed S1P1-receptor modulators in the treatment of inflammatory bowel disease

Inflammatory bowel disease (Crohn's and ulcerative colitis) affects 85,000 Australians and millions of people world-wide and there is currently no cure for this disease. Most current therapeutics are only partially effective, providing temporary relief to a subset of patients. There is significant interest in the development of orally bioavailable agents, with more significant and sustained efficacy and which treat a broader IBD patient group. While a number of small molecule immunomodulators are in use or development, the therapeutic utility of these is compromised by their systemic immunosuppressive effects (opportunistic infection and increased cancer risk through reduced immunosurveillance) and off-target effects. Consequently, there is considerable interest in the development of GI-directed agents that can exert a GI-specific immunomodulatory effect. Recently, small molecule sphingosine-1-phoshate-1 (S1P1)-receptor modulators (eg ozanimod and etrasimod) have emerged as a new class of orally bioavailable immunosuppressive agent showing great promise in IBD clinical trials (Phase II/III). However, these agents suffer from dose-limiting adverse effects on non-GI organs. Funding from NFMRI will support a proof-of-concept to a new class of orally administered, GI-directed S1P1-receptor modulators as more effective treatments of IBD with negligible systemic exposure and improved efficacy and safety profiles.

Prof Stephen Fox **The University of Melbourne** **$144,000 (2021)**

DNA nano biosensor for cancer diagnostics

Precision oncology, which matches a cancer patients' gene test to a specific drug, has transformed the treatment of cancer patients and led to substantial improvements in survival with fewer hospital admissions from therapies with less toxicity, as drugs are only given to patients that respond. Current molecular testing to identify changes in cancer DNA for the above clinical uses is expensive, as specialist pathologists and scientists who rely on complex equipment are needed, which often affects patient outcome. It is also slow due to a combination of time for tissue transport to the central test lab and then time taken to perform the assay. The aim of this research is to validate an inexpensive, (<$100 compared with $1000's using current technologies), rapid and sensitive method to detect genetic mutations that can be used on blood from patients with any tumour type. The identification of such changes will enable screening, diagnosis, prognosis, selection of patients for particular therapies and monitoring of response to treatment. The basis of the assay is an innovative biosensor that detects the presence of abnormal cancer DNA on binding through a change in electrical current. The novel biosensor method Professor Fox and his team are developing will enable a reduction in the time-critical analyses by days to ensure timely reporting that will help realise the improved outcomes of precision oncology.

Professor Stephen Fox

Funding provided by NFMRI will support the further development of the biosensor as well as experiments to delineate the performance characteristics and capabilities of the biosensor to identify different types of mutant DNA.

Prof Roger Pocock **Monash University** **$199,916 (2021)**

In vivo removal of alpha-synuclein aggregates in a Parkinson's disease model

Prof. Roger Pocock

The accumulation of aggregate-prone neurotoxic proteins is associated with the death of brain cells in Parkinson's disease (PD) and Huntington's disease (HD). These toxic proteins can be removed by a process called autophagy (auto = self, phagy = eat) which is a crucial recycling system within cells. The research group lead by Prof Roger Pocock (Monash University) and co-investigators Dr Patrick Ejlerskov (University of Copenhagen) and Prof David Rubinsztein (University of Cambridge), identified an ancient genetic mechanism that promotes autophagy to reduce neurotoxic aggregate-prone proteins associated with PD and HD. This genetic mechanism was initially identified in a worm model by the Pocock laboratory and subsequently the same mechanism was shown to function in human cells by Dr Ejlerskov when working in the Rubinsztein laboratory. The presence of an identical mechanism controlling the removal of toxic aggregate-prone proteins in distant species (worms and human cells), indicates its importance through evolution. This study was published in the internationally-recognized journal eLife (2019) and the same research group was invited to write a review on this research area in the journal Autophagy (2020). The innovation of this research was the identification of a novel pathway that can be manipulated to remove neurotoxic aggregate-prone proteins that cause neurodegenerative disease. Funding from NFMRI will support the validation of these findings in the brain of a mouse model of neurodegenerative disease.

Grants with funding continued in 2020

Following recommendations of our Research Advisory Committee, the Board approved $1,159,840 in grant payments supporting 18 projects during the 2020 calendar year:

Researcher	Institute	Focus Area	Total 2020	Total funding commitment
Prof Marc Pellegrini*	Walter & Eliza Hall Institute of Medical Research	Cystic fibrosis	$131,250	$175,000
A/Prof Sarah Vreugde*	University of Adelaide	Cystic fibrosis	$63,973	$145,000
A/Prof James Chong	University of Sydney	Cardiovascular	$99,999	$200,000
A/Prof Bernard Flynn	Monash University	Cardiovascular	$110,400	$110,400
Dr Wei Deng	University of New South Wales	Cancer	$76,368	$101,825
Dr James** **Blackburn**	Garvan Institute of Medical Research	Cancer	$72,433	$144,865
A/Prof Nuri Güven	University of Tasmania	DNA disease	$72,152	$144,300
A/Prof Peter van Wijngaarden**	Centre for Eye Research Australia	Alzheimer's disease	$125,000	$250,000
A/Prof Anthony White**	QIMR Berghofer	Alzheimer's disease	$25,000	$100,000
Dr Lesley Cheng**	La Trobe University	Alzheimer's disease	$18,825	$95,500
Dr Sanjaya Kuruppu**	Monash University	Alzheimer's disease	$45,000	$90,000
Dr Adam Taylor***	Griffith University	Chikungunya virus	$16,667	$50,000
A/Prof Joanne* Macdonald**	University of Sunshine Coast	Malaria	$70,275	$140,550
A/Prof Lenka Munoz - Medal	University of Sydney	Cancer	$50,000	$50,000
A/Prof Bernard Flynn - Medal	Monash University	Bowel disease	$50,000	$50,000
Prof Stuart Dashper**	University of Melbourne	Alzheimer's disease	$40,000	$160,000
Dr Lyndsey Collins-Praino/Dr Andrew Care**	University of Adelaide	Alzheimer's disease	$62,498	$249,990
Prof Ralph Martins AO**	Edith Cowan University	Alzheimer's disease	$30,000	$170,000
			$1,159,840	**$2,427,430**

**Supported by Cure4 Cystic Fibrosis Foundation and NFMRI*
***Supported by The Mason Foundation (managed by Equity Trustees) and NFMRI*
****Supported by NFMRI and the NSW Department of Primary Industries*
*****Supported by NFMRI, the NSW Community Foundation and the NSW Community Foundation Nicholas and Phyllis Pinter Trust & Vernon Sinclair Fund (managed by Equity Trustees)*

Projects supported in 2020

Prof Marc Pellegrini **Walter & Eliza Hall Institute** **$175,000 (2019-2020)**

Eradicating life-threatening infections in people with cystic fibrosis

The Burkholderia cepacia group of organisms, or microbes, are causing major morbidity and mortality in people living with cystic fibrosis as they have become resistant to most antibiotics. In Australia alone, evolution of drug resistant infections, particularly in the respiratory system, account for 6,300 deaths per year and more than 120,000 hospitalisations per year. These microorganisms which invade and replicate inside our cells, can be efficiently eliminated by killing the host cell, fundamentally disrupting the microorganisms' life cycle and rendering the pathogen unable to develop resistance to therapy. Professor Pellegrini's team at the Walter and Eliza Hall Institute of Medical Research, have proven that this can be done without causing collateral damage to tissues or organs.

The fundamental breakthrough was identifying a way to specifically kill infected cells and this was achieved by harnessing a mechanism that our bodies naturally use to dispose of unwanted cells called apoptosis, or programmed cell death. Professor Pellegrini's team has shown that infected cells are completely reliant on a protein called "cellular inhibitor of apoptosis proteins" (cIAPs) for their survival, but that these proteins are dispensable in healthy cells. After years of research, Professor Pellegrini's team found a class of drugs called SMAC mimetics, which potently inhibit this protein and cause the death of the infected, but not uninfected cells. This mechanism of killing infected cells offers a platform that could be used to treat many types of infection, but the current focus is on treating infections where there is significant resistance to current antibiotics.

Support provided by the Cure4Cystic Fibrosis Foundation and NFMRI will be used to further studies to support and assist with the design of clinical trials.

A/Prof Sarah Vreugde **The University of Adelaide** **$145,000 (2020 – 2021)**

A novel treatment for Non-Tuberculous Mycobacteria lung infections in cystic fibrosis patients

Associate Professor Sarah Vreugde is targeting Non-Tuberculous Mycobacteria (NTM) lung infections in cystic fibrosis patients, which cause severe infection and lung function decline. NTM lung disease is caused by bacteria that are common in the environment and are rapidly rising in prevalence, particularly in those with cystic fibrosis. NTM are naturally resistant to antibiotics and even disinfectants and so, are challenging to treat. Sarah's technology is unique because it is the only treatment in (pre)clinical development that targets the bacterial iron metabolism, which enables the bacteria to thrive and survive.

Funding provided by the Cure4Cystic Fibrosis Foundation and NFMRI is being used to further develop the proof-of-concept of the technology in a preclinical animal model of CF.

A/Prof James Chong **The University of Sydney** **$200,000 (2020 – 2021)**

Development of novel recombinant human platelet derived growth factor therapy for prevention of ischemic heart failure

This project will develop a novel recombinant human Platelet Derived Growth Factor protein therapy for acute ischemic cardiovascular disease. Cardiovascular disease remains our greatest source of death and disability, accounting for billions of dollars in health care costs. The major single cause for this is "heart attack". Despite significant progress in medical and interventional therapies for heart attack, patients can still lose up to a billion heart muscle cells. This is due to the heart's inability to regenerate (unlike other organs such as the skin and liver) and down-stream health issues including heart failure, heart rhythm abnormalities and recurrent chest pain occur. A/Prof Chong's results show that in both rodents and the more clinically relevant porcine model, human PDGF-AB treatment administered after heart attack decreases scar, increases heart function, decreases heart rhythm abnormalities and increases new blood vessel formation. The overarching aim is to progress this experimental therapy into human patients suffering from heart attack and heart failure.

Funding provided by NFMRI is helping develop the therapy towards first-in-human clinical trials for patients with severe heart dysfunction after heart attack.

A/Prof Bernard Flynn **Monash University** **$100,400 (2020-2021)**

Sphingosine Kinase-1 inhibitors for the treatment of pulmonary hypertension

Pulmonary hypertension is a major unmet medical need. A significant body of evidence from a number of different research groups has implicated a certain class of lipids called sphingolipids as key drivers of pulmonary hypertension progression. In particular, the enzyme known as sphingosine-kinase-1 (SK1), which produces a sphingosine-1-phosphate (S1P), is of particular relevance to pulmonary hypertension. A/Prof Flynn's group has generated inhibitors of SK1 that are both more selective and more "drug-like" (able to be administered orally) than existing agents, representing a safe and effective means of treating pulmonary hypertension.

Funding provided by NFMRI is helping develop the therapy towards proof-of-concept and is helping support optimisation, efficacy and safety studies.

Dr Wei Deng **University of New South Wales** **$101,825 (2020-2021)**

Nanostrategy for X-ray triggered chemotherapy towards rectal cancer treatment

This innovative technology stems from Dr Deng's research that photodynamic therapy (PDT) agents can be triggered by low dose X-ray radiation. The stimulated PDT agents produce active species which destabilise liposome structure and trigger the drug release from the liposomes. Inspired by this discovery, her team creatively combined two existing clinical techniques used in cancer treatment – radiation and chemotherapy through a nanoparticle drug delivery system.

The innovative aspect of this technology is the radiation-triggered instant drug release from the liposomes at the tumour site. Using very low radiation doses, the drug is released and becomes significantly more toxic to cancer cells than current administration. What's more, as cytotoxic drugs can only be released within the radiotherapy field (confined to the tumour site), any toxicity to other healthy tissues is largely reduced.

In this manner, this technology has demonstrated impressive anticancer efficacy in a mouse model by one-dose injection and single irradiation. This innovation will be applicable to treat deep tumours due to high penetration depth of radiation. Funding provided by NFMRI is supporting safety and efficacy studies.

Dr James Blackburn **Garvan Institute of Medical Research** **$144,865 (2020-2021)**

Improving sarcoma cancer diagnostics through implementation of a novel fusion gene test

This innovation consists of the development of a clinical test for fusion genes in sarcomas and other solid cancers – the Solid FuSeq test – that surpasses the performance of molecular diagnostic assays currently employed in standard pathology labs. Using multi-gene sequence enrichment, this broad-spectrum assay screens for all fusion gene events in a single test, while detecting individual fusion genes with high sensitivity. The Solid FuSeq test also facilitates the discovery of new fusion events and therefore potentially novel therapeutic targets. Whilst sarcoma patients would be the first to benefit from this innovative molecular diagnostic, the Solid FuSeq assay is designed as such that all solid tumour cancer patients would benefit from the assay.

Funding provided by NFMRI is supporting clinical validation of the assay in an accredited diagnostic facility.

A/Prof Nuri Güven **University of Tasmania** **$144,300 (2020-2021)**

Pre-clinical assessment of toxicity to select drug development candidates against mitochondrial dysfunction

While more than 90% of cellular energy is produced by mitochondria, dysfunctional mitochondria leads to organ failure, disease and even death. Dysfunctional mitochondria are associated with a vast number of diseases and conditions, ranging from neurodegenerative and metabolic disorders, to inflammatory conditions, cancer and ageing in general. Despite this prevalence in a multitude of diseases, there is still a striking lack of approved drugs that aim to directly restore mitochondrial function. This project will select drug development candidates from a novel class of short-chain quinone compounds developed at the University of Tasmania. These new compounds effectively protect cells against mitochondrial dysfunction. More importantly, two of those compounds effectively protect against disease pathologies in several unrelated rodent models associated with mitochondrial dysfunction.

Preliminary results of their experiments already point towards 2 compounds with very high metabolic stability and very low toxicity, compared to the clinically used reference compound.

Funding provided by NFMRI is supporting in vitro toxicity studies.

A/Prof Peter van Wijngaarden | **Centre for Eye Research Australia** | **$250,000 (2019-2021)**

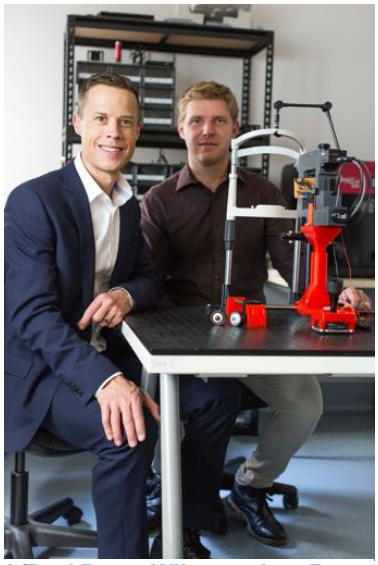
Translating an eye imaging biomarker for Alzheimer's Disease to the clinic

A/Prof van Wijngaarden's research group has recently developed a novel imaging method that allows them to non-invasively detect the accumulation of amyloid beta in the retina.

Their research has utilised a state-of-the-art, costly camera that images the retina sequentially with 90 different wavelengths (colours) of light. They have identified an innovative method of detecting the same signal that could be achieved with a low-cost retinal camera. The team are developing a prototype camera that may eventually be used as a screening test for Alzheimer's disease.

NFMRI funding is enabling retinal camera prototype development and clinical studies to validate the technology against their state-of-the-art research camera.

This project is supported in partnership with the generous funding from The Mason Foundation and NFMRI.



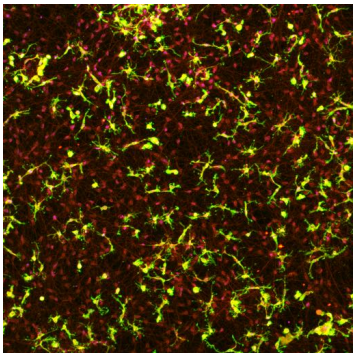
A/Prof P van Wijngaarden, Dr Xavier Hadoux – photo by Anna Carlile

A/Prof Anthony White | **QIMR Berghofer** | **$100,000 (2019-2020)**

A personalised medicine approach for screening neuroinflammatory drug efficacy in Alzheimer's Disease

A/Prof Anthony White

A/Prof White's team has developed a unique approach to screening drugs that target the brain's resident immune cells (microglia) on a person-by-person basis. They are able to generate microglia from a person's blood cells (monocytes) in 2 weeks at a cost of ~$50/person. These cells can be screened for the ability of different drugs to enhance their protective functions, allowing them to determine which drugs will likely benefit each patient.



Microglia stained yellow-green

With access to large Alzheimer's disease cohorts, they are in a unique position to establish a screening platform for patient-specific drug efficacy, allowing physicians to prescribe a drug treatment regime tailored to an individual's own microglia. Patient microglia

responses can then be monitored over time. NFMRI funding is supporting research to screen patient specific potential drugs.

This project is supported in partnership with the generous funding from The Mason Foundation and NFMRI.

Dr Lesley Cheng **La Trobe University** **$75,300 (2019-2021)**

Specificity testing and cross-laboratory validation of a blood test for Alzheimer's Disease

Dr Lesley Cheng

This work is based on the discovery that small vesicles, called exosomes, are released from cells acting as distinct indicators of the health status of the tissues from which they derive. Exosomes thus represent disease biomarkers. The novel hypothesis surrounding Dr Cheng's research is that exosomes secreted from brain tissue migrate across the blood brain barrier into the blood where brain biomarkers are readily detected. This is equivalent to a 'liquid biopsy' of the brain reflecting neurological status.

In preliminary studies she has already identified a panel of 16 serum exosomal miRNAs that are altered in AD compared to heathy patients. NFMRI funding is helping validate the specificity of these potential AD biomarkers using several different clinical biobanks. Therapeutic strategies aimed at limiting neurodegeneration and improving quality of life in AD require methods to diagnose and monitor the disease in pre-clinical patients. Currently, definitive diagnosis of AD is only possible post-mortem or through PET neuroimaging that requires expensive equipment, highly trained operators and cerebrospinal fluid (CSF) collection. In comparison, blood is a conveniently collected, less-invasive source of biomarkers.

Funding is enabling this critical work to go full term and be translated into a reliable, economically viable, routine pre-clinical AD screen. This project is supported in partnership between The Mason Foundation and NFMRI.

Dr Sanjaya Kuruppu **Monash University** **$90,000 (2019-2020)**

Improving the efficacy of a new venom-derived drug for Alzheimer's Disease

Dr Sanjaya Kuruppu

Dr Kuruppu's preliminary data demonstrates that administration of his team's originally discovered peptide can prevent the formation of amyloid beta plaque. Inability to get peptides across the blood brain barrier is a significant factor that impedes the development of drugs for neurodegenerative diseases.

Previous studies have shown that L-arginine can improve the blood brain barrier permeability of drug leads.

This research grant is helping Dr Kuruppu determine if co-administration with L-arginine will facilitate the uptake of the peptide by the brain, thereby

preventing amyloid beta build-up and associated behavioural changes. The results of this study can add significant value to their original discovery, helping to fast track it towards the clinic.

This project is supported in partnership between The Mason Foundation and NFMRI.

Dr Adam Taylor **Griffith University** **$50,000 (2019-2021)**

Liposome delivery of chikungunya virus vaccine candidate: a solution to vaccine production bottlenecks

Dr Taylor has had several partnering discussions with industry around licensing or co-development of their live-attenuated chikungunya virus (CHIKV) vaccine candidate. This highlighted a single barrier for investment: production limits. The modifications that make the virus safe and effective for use as a vaccine, prevent rapid, large-scale production of the virus. It simply doesn't replicate fast enough.

In response to this feedback, they have developed an alternative vaccine delivery vehicle that removes the need for in vitro scale up, and therefore, removes the production limit.
NFMRI funding is supporting efficacy testing on the new formulation to confirm immune response and storage efficacy.

This project is supported in partnership with the generous funding from the NSW Department of Primary industries and NFMRI.

Dr Adam Taylor

A/Prof Joanne Macdonald **University of Sunshine Coast** **$140,550 (2019-2021)**

A rapid, sensitive and portable molecular genetic test for diagnosis of Malaria in blood

A/Prof Joanne Macdonald

Support is being provided to validate A/Prof Macdonald's rapid and sensitive Malaria test for detecting subclinical infection levels at a collaborating institute by testing it on human samples containing low levels of infection. These samples are uniquely available via a collaborator already performing human clinical trials for treatment of Malaria infections. If it can be demonstrated that the test has higher sensitivity and can detect subclinical parasite levels, then the test will be well positioned to attract funding and investment for development into both the clinical detection market, as well as the market for tests that can assist with community screening for eradication programs.

NFMRI funding is also helping determine the optimal manufacturing reagents to achieve the best possible sensitivity, specificity and reliability of testing kits to provide further confidence for potential investors that our test can be reliably manufactured.
This project is supported in partnership between the NSW Department of Primary Industries and NFMRI.

A/Prof Bernard Flynn **Monash University** **$50,000 (2020)**

2020 Dr John Raftos AM Award

A grant of $50,000 was provided to support the research activities of A/Prof Bernard Flynn.

A/Prof Lenka Munoz **The University of Sydney** **$50,000 (2020)**

2020 Dr John Raftos AM Award

A grant of $50,000 was provided to support the research activities of A/Prof Lenka Munoz.

Prof Stuart Dashper **The University of Melbourne** **$160,000 (2020-2021)**

A polymicrobial aetiology for Alzheimer's disease

A growing number of studies are now linking bacterial infection and/or periodontitis with sporadic Alzheimer's disease (AD). Two recent studies have provided strong evidence for a potential causal link between the pathogenic oral bacterium Porphyromonas gingivalis and AD. There are also reports of oral bacterial proteolytic enzymes and genomic DNA, particularly those of P. gingivalis and Treponema denticola, in the brain tissue of AD sufferers. Professor Dashper's and Dr Catherine Butler's research will seek to demonstrate a causal link between specific oral bacteria and the onset and progression of Alzheimer's disease. If successful, it may open a whole new field of research into the bacterial aetiology of Alzheimer's disease.

L-R: Su Tolson, Deanne Catmull, Prof. Stuart Dashper, Rita Paolini, Prof. Neil O'Brien-Simpson

Funding provided by The Mason Foundation (managed by Equity Trustees) and NFMRI will enable further development of this project.

Dr Lyndsey Collins-Praino / Dr Andrew Care **The University of Adelaide** **$249,990 (2020-2022)**

"Cage vs. Age": Development of an innovative nanotechnology to halt the spread of abnormal Tau protein in Alzheimer's disease

Dementia is a significant global problem affecting 50 million people worldwide, with a staggering 10 million new cases diagnosed each year (WHO). Alzheimer's disease (AD) is the most common cause of dementia, accounting for 60-70% of all cases. A major contributor to the spread of AD throughout the brain is the transmission of an abnormally-folded protein called tau. Tau is released from diseased brain cells and taken up by healthy cells, triggering misfolding and aggregation of tau within those cells. Thus, AD spreads throughout the brain. The aim of the project is to engineer an innovative nanotechnology that can target and disrupt tau pathology. If successful, such a strategy would lead to modification of the brain mechanisms of AD and the potential development of a treatment strategy that would be of significant benefit to the millions of individuals currently suffering from AD.

Funding from The Mason Foundation (managed by Equity Trustees) and NFMRI will allow for further engineering of the nanotechnology platform, as well as evaluation of its safety for neurological indications.

Prof Ralph Martins AO **Edith Cowan University** **$170,000 (2020-2022)**

In-depth neurofilament analysis as potential biomarkers for Alzheimer's disease

L-R: Dr. Eugene Hone, Prof. Ralph Martins AO, Steve Pedrini

Prof Martins and his team's research, is based on an in-depth analysis of neurofilament light chain (NFL) in plasma and cerebrospinal fluid (CSF) in Alzheimer's disease (AD) patients and healthy controls to determine whether AD affected individuals possess altered neurofilament light chain (NFL) and/or different binding partners. NFL levels in plasma and CSF have repeatedly been reported to be increased in AD patients, strongly supporting a link with the disease state. However, higher levels were also reported for other neurological diseases, making NFL levels a generic marker for neurodegeneration, rather than a specific marker for AD. A specific NFL protein signature found in plasma or CSF that closely associated with AD will allow more accurate and quicker detection of the disease, leading to early medical treatments known to be more effective.

This project is supported thanks to funding from The Mason Foundation (managed by Equity Trustees) and NFMRI.

Our people

A dedicated Board, Research Advisory Committee (RAC) and management team lead our Foundation.

Directors

Directors, qualifications and special responsibilities		Experience
Dr Rob Sauer **Chairman**	2017-	• Chairman, Echoview Holdings Pty. Ltd. • Director, Biopharm Australia Pty Ltd. • Admitted as solicitor of the Supreme Court of New South Wales in 1974 • Admitted as Certified Practicing Accountant in 1980 Formerly: • A Founding Director and shareholder of ResMed • Partner, DibbsBarker (1978-2008) • Inaugural Chairman, R&D Tax Concession Committee • Inaugural Chairman, Tassal Ltd (1984-1990)
Mr John Harkness	1984 -	• NFMRI Chairman (2001-2018) • Partner of KPMG for 24 years and National Executive Chairman for five years. • Former Chairman and/or Director of listed or unlisted companies from 2000-2018 including Goodman Group, Sinclair Knight Mertz, Reliance Rail Group, Charter Hall Retail REIT and Crane Group • Fellow of the Institute of Chartered Accountants in Australia and the Australian Institute of Company Directors.
Dr John Dixon Hughes OAM	1977 -	• NFMRI Director (1977 – present) • NFMRI's RAC Chairman (2000-2018) • NFMRI RAC Member since 1977 • Consultant General Surgeon • Fellow, Royal College of Surgeons (Eng) • Fellow, Royal Australasian College of Surgeons • Fellow, Australian Medical Association • Foundation member of the Australian Association of Surgeons, formerly serving as Chairman of the NSW State Committee and President of the Association Formerly;

		• Board Member, Senior Vice President, Chairman Medical Staff Council, Chairman of Surgical Research Committee and Chairman of Ethics Committee at Sydney Hospital. • Chairman of Infection Control Advisory Group NSW Health • Convener (Chairman) Negotiating Committee to negotiate with the NSW Government, on behalf of the medical profession during the "Doctor's Dispute" in 1984. • Medical Services Committee NSW Chairman (1984-1996) & Administrator (1996-2017).
Dr Kevin Hellestrand	2001 -	• Cardiologist and Cardiac Electrophysiologist for 35 years. • Co-author of more than 50 journal articles, reviews and book chapters. • Fellow of the Royal Australasian College of Physicians, American College of Cardiology, Cardiac Society of Australia and New Zealand, Heart Rhythm Society, European Society of Cardiology. • Member of the North Shore Heart Research Foundation
Mr Anthony McGrath *Honorary Secretary and Director*	1997 -	• Founding Partner, McGrathNicol • Board Member, National Rugby League • Non-Executive Director, Servcorp Limited • Member, Institute of Chartered Accountants in Australia • Member, Insolvency Practitioners Association of Australia • Member, Australian National University • Member, 360 Capital Credit Management Pty Ltd.
Ms Alison Choy Flannigan *Company Secretary*	2014-	• Company Secretary since 2014 • Partner, Leader, Health & Community, Hall & Wilcox • Member, NSW Law Society • Member, Australian Institute of Company Directors • Publications officer, Healthcare and Life Sciences Committee, International Bar Association • Member, AusBiotech
Prof A. Ian Smith Chairman, Research Advisory Committee	2017-	• Vice-Provost (Research & Research Infrastructure), Monash University • Director, Bioplatforms Australia (from 2008) • Director, National Imaging Facility (from 2009)

		• Director, Victorian BioImaging Collaboration (from 2010) • Director, Victoria Endowment for Science, Knowledge and Innovation (from 2011) • Director, Neuroscience Victoria (from 2012) • Director, South East Asia Community Observation (from 2010) • Director, Curtin Health Innovation Research Institute (from 2016) • Director, Population Health Research Network (from 2017) • ARC Centre for Advanced Molecular Imaging since February 2017 • Future Low-Energy Electronics Technologies (FLEET) Advisory Committee since November 2018 • Australian Synchrotron Stakeholder Committee since July 2018 • Microscopy Australia since June 2019 • ARC Centre of Excellence Centre for Gravitational Waves, Advisory Committee since July 2019
Prof Elaine Saunders	2018-	• Adjunct Professor, Faculty of Health, Arts & Design, Swinburne University of Technology • Chair, Swinburne University's Innovation Precinct Advisory Board • Managing Director, Bingarra ScaleUp Solutions • Advisory Board, Ear Genie • Deputy Chair, Victorian Pearcy Foundation • Entrepreneur in Residence, Bionics Institute • Chair, Swinburne University's Biodevices Advisory Board • Non-Executive Director, Australian National Fabrication Facility • Deputy Chair, Victorian Committee, Pearcey Foundation • Member, Technical Advisory Committee to Council, Swinburne University • Advisory Board, Hearing Power Formerly: • Executive Chairman, Blamey Saunders hears • Co-founder & CEO, Dynamic Hearing Pty. Ltd. • Non-Executive Director, Alfred Health
Ms Alison Gartner	2020-	• Co-founder, Evidentli Pty. Ltd. • Project Manager, Chimeric Therapeutics Ltd.

		Formerly: • Portfolio Manager, Asia Union Investments Pty. Ltd. • Investment Manager, Bioscience Managers • Alternate Director, Saluda Medical
Emeritus Professor Douglas E. Joshua AO	2020-	• Professor Emeritus, Hematology at The University of Sydney • Consultant Hematologist, Royal Prince Alfred Hospital • Chairman, Blood Clinical and Scientific Advisory Committee • Scientific Advisor and Member, International Myeloma Foundation • Serves on editorial board of numerous journals Formerly: • Head of Clinical and Laboratory Hematology, Sydney Cancer Centre • Head of Sydney Local Health District in Hematology • Alan Ng Professor in Medicine at the University of Sydney • Director, Institute of Hematology, Royal Prince Alfred Hospital

Research Advisory Committee

Chairman **Prof A. Ian Smith**	Vice-Provost (Research & Research Infrastructure), Monash University
Dr John Dixon Hughes OAM	Consultant general surgeon with over 55 years' experience
Prof Elizabeth Harry	Professor of Biology and Director of the ithree institute (infection, immunology and innovation) at the University of Technology, Sydney.
Em. Professor Douglas E. Joshua AO	Emeritus Professor in Haematology at the University of Sydney and Consultant Haematologist at RPHA.
Professor Mark von Itzstein	Director of the Institute for Glycomics at Griffith University
Alison Gartner	Lifesciences and healthcare investment professional

Dr Noel Chambers	CEO with over 25 years' experience in biomedical research, innovation, commercialisation and biotechnology.
Dr Andrew Cottrill	Medical Director, HCF
A/Prof Wendy Cooper (retired January 2021)	Clinical Associate Professor at The University of Sydney
Dr Ashley Bates (retired June 2020)	National Executive, Pharmaceutical and Biotechnology at META, previously Head of R&D Alliances ANZ at GSK
Prof Lisa Horvath (joined April 2021)	Director of Medical Oncology and Director of Research, Chris O'Brien Lifehouse

Management and Administration

Dr Noel Chambers	Chief Executive Officer
Mrs Nancy Ranner	Grants, Communications and Engagement Coordinator
Ms Di Moore	Bookkeeper and Administrator

National Foundation for Medical
Research and Innovation
ABN 85 001 422 895

PO Box 6247
Highton VIC 3216

W: www.nfmri.org.au
E: enquiries@nfmri.org.au
T: 1 300 233 147