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In 2019, FightMND will commit another $9M into MND research projects across Australia. Research proposals were assessed by both national and international MND experts and an expert panel of MND clinicians and researchers to identify and support projects with the most promising potential to fast track a more effective therapy or cure. This year the successful research projects include.

- 3 Clinical Trials
- 1 Drug Development Project
- 7 IMPACT Projects
- 3 Research Fellowships
- Sporadic ALS Australian - Systems Genomics Consortium (SALSA-SGC)

OUR IMPACT

A snapshot of how the money has been invested to fight MND since 2014:

$37.6 million
Committed to research initiatives

$13.44 million
Ten new clinical trials

$9.73 million
Ten drug development research grants

$4.5 million
World-first drug screening project

$2.8 million
Other research grants and initiatives

$2.14 million
Sporadic ALS Australian - Systems Genomics Consortium (SALSA-SGC)

$2 million
Precision medicine program

$1.74 million
IMPACT research grants

$1.3 million
Research Fellowships and Scholarships

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Clinical Trials

Clinical Trials test promising new therapeutics or re-purposed medications in MND patients.

PHASE III CLINICAL TRIAL - THE LIGHTHOUSE TRIAL 2 (TRIUMEQ)

Prof Julian Gold, The Albion Centre, Prince of Wales Hospital, Sydney & **Prof Leonard van den Berg**, University Medical Centre, Utrecht, Netherlands

Background

Activation of an ancient virus that is hidden in the genome may lead to the death of motor neurons and be responsible for the onset and progression of ALS. This type of virus, called a HERV (human endogenous retrovirus), is in the same class of viruses as human immunodeficiency virus or HIV. A specific HERV, known as HERV-K, is the likely culprit in ALS. A combination antiviral drug used to successfully manage HIV, Triumeq, is highly effective against HERV-K, and importantly, can cross into the nervous system. In the recent Lighthouse clinical trial supported by FightMND, Triumeq was shown to be safe and well tolerated in MND patients.

The Project

The study will be a Phase III clinical trial investigating the safety and efficacy of Triumeq, and its ability to block HERV-K and slow disease progression in a large number of MND/ALS patients. The large multi-national trial will be conducted on 363 patients in 17 centres across Australia, Europe and the UK. It aims to enrol 75 Australian patients at 5-6 sites across Australia. Outcomes from this trial will identify if Triumeq is an effective treatment for MND.

PHASE II CLINICAL TRIAL - NANOCRYSTALLINE GOLD (CNM-AU8)

Prof Steve Vucic, Westmead Hospital, Sydney & **Prof Matthew Kiernan**, Brain and Mind Centre, Sydney

Background

Researchers have identified a new molecule, Nanocrystalline-Gold (CNM-Au8), that is able to target and reduce a number of cell stress responses that occur in motor neurons in MND. They have shown that CNM-Au8 protects motor neurons from oxidative stress, toxicity and hyperactivity, and that it lengthened the lifespan of MND models in the laboratory. CNM-Au8 was safe and well tolerated in people a Phase I clinical trial.

The Project

This study will be a Phase II clinical trial testing the safety of CNM-Au8 for treating MND and aims to demonstrate if CNM-Au8 slows progression of MND/ALS in patients. The trial will be run across two clinical sites in Sydney with 42 MND patients to be enrolled. A promising trial outcome would inform the design of a larger Phase III trial in the next 2-3 years.

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PHASE I CLINICAL TRIAL - RE-PURPOSED MEDICATION TRIMETAZIDINE

Dr Shyuan Ngo, University of QLD

Background

About half of all patients with MND experience an increase in their energy consumption (termed hypermetabolic). Researchers have shown that hypermetabolism accelerates the spreading of MND throughout the body, increases the risk of death and accelerates the rate of disease progression in people with MND.

Researchers aim to reduce hypermetabolism in patients with MND and counter its detrimental consequences. Trimetazidine, a partial fatty acid oxidation inhibitor, is already used to reduce hypermetabolism in patients with chronic heart failure and is a licensed treatment for angina. Trimetazidine has a favourable safety profile and, more importantly, reduces the expression of oxidative stress markers that are also increased in patients with MND.

The Project

This Phase I clinical trial tests the ability of Trimetazidine to normalise metabolism and determine if it can be safely administered to MND patients. This study will be conducted across 3 sites in the Netherlands, UK and the Royal Brisbane and Women's Hospital in Australia. Positive outcomes from this study would lead to a Phase II study where the effect of Trimetazidine on the slowing of MND progression would be investigated.

Drug Development Projects

Drug Development Projects advance promising new drug candidates from the laboratory towards the clinic.

RESCUING MOTOR NEURONS USING A NOVEL DRUG THAT BLOCKS HDAC6

A/Prof Anna King, University of Tasmania

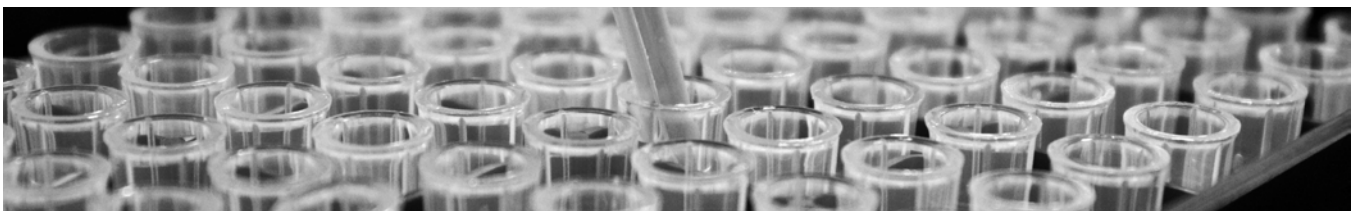
Background

Motor neurons are nerve cells that create signals to communicate with and regulate the activity of muscles. The enzyme HDAC6 is involved in maintaining the structure of motor neurons but in MND, HDAC6 becomes damaging to motor neurons leading to their death and failure to communicate with muscles.

Researchers hypothesise that blocking these damaging effects of HDAC6 will slow the progression of MND.

The Project

This research team will test if the drug ACY738, which blocks HDAC6, is able to protect motor neurons and their processes and can rescue communication between motor neurons and muscles. They will test ACY738 in 3 laboratory models of MND. In addition, they will also screen another 150 compounds for their ability to block HDAC6, to identify the best drug candidate to advance to clinical trial.



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IMPACT Projects

IMProving and **AC**celera**T**ing (IMPACT) Projects are focused on overcoming key hurdles that are preventing promising drugs in the laboratory from being effective in the clinic.

DISEASE SUSCEPTIBILITY, PRECISION MEDICINE AND MND

Prof Julie Atkin, Macquarie University

Priority area: Disease variability in MND

This project investigates diversity in MND, aiming to categorise patients based on their distinct symptoms and presentation of unique biochemical markers. The purpose is to establish a platform that enables optimal and tailored treatments for MND patients, specific to the unique disease features of each individual.

NEW BIOMARKERS FOR MND

Dr Fleur Garton, University of Queensland

Priority area: MND Biomarkers

This project aims to develop a rapid, sensitive and economical way to diagnose MND. By genetically assessing blood samples from individual MND patients, markers that accurately predict and track the progression of MND will be identified. This will advance the design of therapies that effectively treat MND.

ESTABLISHING A NEW MODEL OF MND

Dr Mouna Haidar, Florey Institute of Neuroscience and Mental Health

Priority area: MND Disease Models

This project will create the first mouse model that replicates features of the most common form of MND, by causing regions of the brain that control movement to become overactive. This model will be used to test the effectiveness of potential treatments that may slow the progression or cure MND.

ENHANCING DRUG DELIVERY IN MND - DRUG DELIVERY

A/Prof Joseph Nicolazzo, Monash University

Priority area: Drug Delivery

This project examines the function of the barrier that normally prevents the transfer of substances from the blood to the brain. The aim is to improve the ability of potential drugs to access the brain and treat MND more effectively.

ASSESSING CHANGES IN BREATHING AND MUSCLE STRENGTH IN MND

Dr Frederik Steyn, University of Queensland

Priority area: MND Biomarkers

This project will develop and validate a new way to diagnose MND by detecting abnormal breathing and weakening breathing muscles using on-the-spot blood tests.

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PRE-CLINICAL STEPS TOWARDS A STEM CELL TRIAL FOR MND

A/Prof Lachlan Thompson, Florey Institute of Neuroscience and Mental Health

Priority area: Regenerative medicine

This project will provide a thorough understanding of the effectiveness and benefits of stem cell therapy in a model of MND and advance the pathway to a well rationalised stem cell clinical trial for MND patients.

TREATING OVERACTIVE IMMUNE DEFENCE SYSTEMS IN THE BRAIN

A/Prof Anthony White, QMIR Berghofer Medical Research Institute

Priority area: MND Disease Models

This project will develop a way to test the effectiveness of potential drugs designed to prevent the harmful effects of an overactive immune system in the brain, using immune defence cells obtained from MND patient blood samples.

Mid-career Research Fellowships

Dr Shyuan Ngo, University of Queensland

This fellowship is in support of an established MND researcher to lead projects that investigate how deficiencies in the use of the body's energy stores contributes to the onset and progression of MND.

Dr Fazel Shabanpoor, The Florey Institute of Neuroscience and Mental Health

This fellowship will support an established MND researcher to lead projects that develop new potential treatments for MND that prevent the production of toxic substances in motor neurons and improve the ability of a motor neuron to clear the toxic substances it produces.

Early-career Research Fellowships

Dr Rebecca San Gil, University of Queensland

This fellowship will support an up-coming MND researcher to develop a new way to prevent the formation of toxic substances in, or their removal from, motor neurons to prevent them from dying.

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Other Research Initiatives

SPORADIC ALS AUSTRALIAN - SYSTEMS GENOMICS CONSORTIUM (SALSA-SGC)

Professor Naomi Wray, University of QLD

In 2015, Prof Naomi Wray was awarded the Ice Bucket Challenge Grant from MND Australia to establish and support the Sporadic ALS Australia - Systems Genomics Consortium (SALSA-SGC) for 3 years. SALSA-SGC brought together seven major MND clinics across Australia to collect clinical data (symptoms, rate of disease progression) and biological samples from MND patients, creating a research bank that integrates clinical, lifestyle and biological information.

The aims of the SALSA-SGC project are to:

- Establish consistent collection of longitudinal clinical information from people with MND, and create a resource for current and future research that guides the generation of new effective patient-specific preventive therapies.
- Increase the understanding of genetic and non-genetic factors that contribute to MND, and guide the generation of new effective patient-specific preventive therapies.

This funding from FightMND provides continued support of the SALSA-SGC Program for the next 3 years. By investing in SALSA-SGC, FightMND will support researchers in the program and research nurses at 8 MND clinics across Australia, giving MND patients at each of these sites the opportunity to be involved in important research that advances the development of effective treatments for MND.