CURTIN HEALTH INNOVATION RESEARCH INSTITUTE

Curtin University

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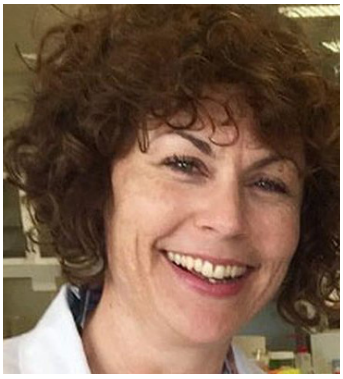
Proud supporter of the Symposium of Western Australian Neuroscience

Based at Western Australia's Curtin University, the Curtin Health Innovation Research Institute (CHIRI) is dedicated solely to developing new ways to prevent, diagnose and treat diseases that commonly occur with older age.

Advances in neuroscience are assisting the CHIRI team to continue to deliver cutting-edge research for the diagnosis, prevention and treatment of age-associated diseases. Here's an insight into some of the key research projects.

CHIRI's research focuses on four key areas, covering major disorders and diseases that impact on the quality of adult life:

1. **Vascular and metabolic disorders**
2. **Immune disorders**
3. **Neurological disorders**
4. **Cancer**



Prof. Lindy Fitzgerald.

Understanding and preventing loss of function following neurotrauma

Our team, which includes CHIRI researchers Terry McGonigle, Jacinta Thorne, Ola Gozt, Lily Toomey and CHIRI collaborator A/Prof. Ryu Takechi, along with several other collaborators, uses innovative analytical techniques to understand changes to key biochemical, cellular and structural components of nerves following injury.

As part of this work, I am currently assessing treatment strategies including nanotechnologies and combinatorial pharmacotherapeutics.

Driven to translate my research findings to the clinic, I recently collaborated in a clinical trial assessing biomarkers and Magnetic Resonance Imaging for prediction of post-concussion syndrome. Meanwhile,my clinical work is extending into a national traumatic brain injury research initiative which I Chair.

We hope our research will help to define the unifying mechanisms of oxidative damage to oligodendrocyte DNA in neurotrauma, neurodegenerative and demyelinating diseasewhich would allow for the development of broadly applicable therapeutic strategies.

Another of our aims is to identify predictors of outcome following traumatic brain injury of all degrees of severity from concussion through to severe injuries and assess promising interventions to improve lives following traumatic brain injury.

If we can predict outcome following traumatic brain injury, particularly the milder injuries like concussion, we can direct patients to appropriate clinical care more swiftly and reduce the risk of them have ongoing symptoms.

– Professor Lindy Fitzgerald (CHIRI/Perron Institute for Neurological and Translational Sciences)

Understanding amyloid beta generation and the links between Alzheimer's disease and Type 2 diabetes

Research Program Leader
A/Prof. Giuseppe Verdile

Our team focuses on selectively targeting the enzyme responsible for amyloid-ß (Aß) production and investigates underlying mechanisms linking Type 2 diabetes and Alzheimer's disease (AD).

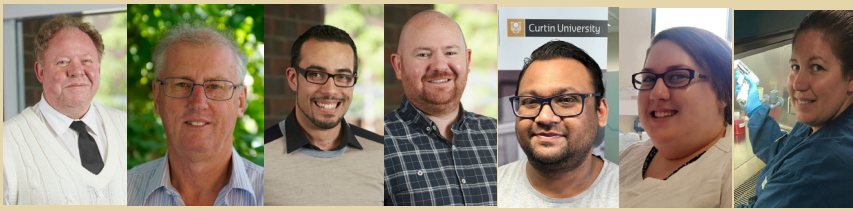
We are addressing a major hurdle to developing drugs that lower Aß production, by selectively targeting the enzyme, gamma secretase.
We have developed an integrated research program, involving local, national and international researchers combining their collective experience in innovative cell and animal models (zebrafish), protein structure and modelling. Our approach uses these experimental tools to identify and refine critical regions within the enzyme to inform future small molecule drug development.

Diabetes is a major risk factor for the development of AD and they share many features, including brain atrophy and impaired brain insulin signaling, potentially underlying the neurodegenerative process. We and others have shown that diabetes and insulin resistance is associated with changes in cognition and AD biomarkers.

Through investigating the roles of amyloid and tau, two proteins involved in the development of AD, we have found from studies on novel animal models of AD and diabetes that the amyloid may also be affecting the development of diabetes, through its deposition in the pancreas and in promoting insulin resistance. We are now exploring how amyloid and the potential role for tau in promoting diabetes may inform novel therapeutic approaches for AD and diabetes. We are also evaluating insulin and novel insulin mimetics in mice models to restore brain insulin signalling, particularly in the presence of a diabetic phenotype.

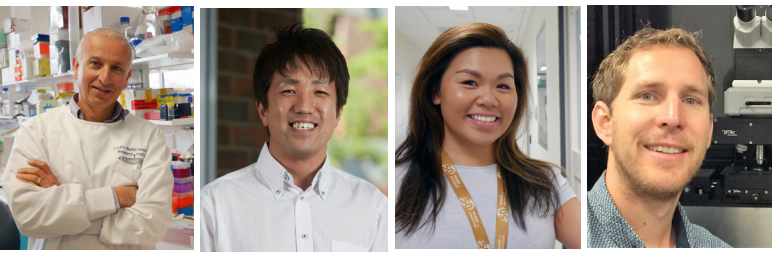
Major collaborations include: Prof. Ralph Martins and his team (SNRI, ECU, Macquarie University), Prof. Paul Fraser (University of Toronto), A/Prof. Simon Laws and his team (SNRI, ECU), A/Prof. Michael Lardelli (University of Adelaide).

– **A/Prof. Giuseppe Verdile(CHIRI)**



The research team: Prof. Philip Newsholme, A/Prof. David Groth, Dr Mark Agostino, Dr Kevin Keane, Dr Imran Khan and PhD students Melissa Eccles and Joanne Rowles.

Investigating the cerebrovascular and peripheral origin of neurodegenerative disorders



The research team: Prof. John Mamo, A/Prof. Ryu Takechi, Dr Virginie Lam & Dr Mark Hackett.

Our team is investigating the aetiology of various neurodegenerative disorders including Alzheimer's disease through the aspect of cerebrovascular and peripheral origin, as opposed to other mainstream research which focuses predominantly on central nervous system origin.

Emerging evidence consistently suggests that the dysfunction of the cerebrovascular blood-brain barrier may be central to the aetiology of neurodegenerative disorders.

Our team, led by CHIRI Director Prof. John Mamo, myself, Dr Virginie Lam and Dr Mark Hackett, pioneered research demonstrating that in wild-type mouse models, diets enriched in saturated fats and cholesterol compromise the integrity of the blood-brain barrier, resulting in peri-vascular neuroinflammation and cognitive decline.

Furthermore, we found that nutraceutical supplements with vascular protective anti-inflammatory properties, as well as certain anti-inflammatory pharmacological agents, are able to protect the integrity of the blood-brain barrier from various 'insults' and maintain healthy CNS function and cognitive performance.

Such considerations are highly applicable and important to age-related neurodegenerative disorders including Alzheimer's disease and multiple sclerosis, and offrer potentially promising therapeutic opportunities.

Our team also has key collaborations with: Prof. Lindy Fitzgerald (CHIRI/Perron Institute for Neurological and Translational Sciences) to explore potential mechanisms for multiple sclerosis; Prof. Rob Trengove (Murdoch) to analyse vitamin D homeostasis in the brain; Prof. Peter Meikle and Dr Corey Giles (Baker Institute) to perform LC-MS lipidomic analyses in the brain; and, Zelda Therapeutics Ltd to investigate potential therapeutic effects of medical cannabis on diabetes-associated dementia.

– Prof. Ryu Takechi (CHIRI)