CURTIN HEALTH INNOVATION RESEARCH INSTITUTE

Curtin University

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Proud supporter of the Australian Synchrotron's Annual User Meeting

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.

Shedding new light on age-associated diseases

Advances in synchrotron science are assisting CHIRI's research team to continue to deliver cutting-edge research for the diagnosis, prevention and treatment of age-associated diseases. The unique properties of synchrotron light afford our researchers more accurate, clear specific and timely results than they could obtain using conventional laboratory equipment.

Dr Mark Hackett.

Studying the role of trace metals within the brain using x-ray fluorescence microscopy at the Australian Synchrotron

Trace amounts of metals are essential for life, and the metals iron (Fe), copper (Cu) and zinc (Zn) are especially important for brain function.

Metal homeostasis represents a double-edged sword for brain health however, as increased concentration of metals in the brain, or the wrong chemical form of a metal (e.g. altered metal oxidation state) can create damaging or neurotoxic conditions.

Understanding how metal levels change during brain disease and the natural ageing process may be critical to drive the development of therapeutic strategies to treat neurodegenerative diseases, such as dementia.

Unfortunately, very few techniques are available to image the different types of metals, and the different chemical form of a metal (e.g. oxidation state), which exist inside a brain cell.

My research group is using synchrotron light to reveal the distribution of Fe, Cu, and Zn within individual brain cells, and to monitor how this changes during natural ageing and brain disease[1,2] – Dr Mark Hackett.

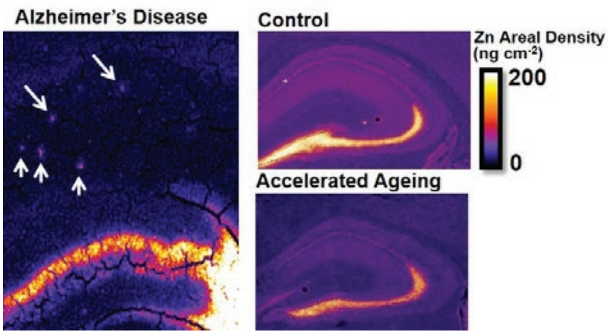

Figure 1: Examples of XFM data collected at the Australian Synchrotron, which has been used to study Zn accumulation in amyloid plaques during Alzheimer's disease (white arrows), and to observe Zn deficiency within the hippocampus in an mouse model of accelerated ageing.

1. N. Fimognari, et. al. Biospectroscopic Imaging Provides Evidence of Hippocampal Zn Deficiency and Decreased Lipid Unsaturation in an Accelerated Aging Mouse Model. (2018) ACS Chem Neuroscience
2. K. L. Summers, et. al. A Multimodal Spectroscopic Imaging Method To Characterize the Metal and Macromolecular Content of Proteinaceous Aggregates ("Amyloid Plaques"). (2017) Biochemistry

Light at the end of the tunnel for some debilitating diseases?

The team: Prof. John Mamo, A/Prof. Ryu Takechi and Dr Virginie Lam.

In collaboration with Dr Mark Hackett, our team uses the Australian synchrotron (AS) to characterise metal ions and biochemical composition (protein aggregates and lipid oxidation products) of brain tissue acquired from genetically modified murine models of Alzheimer's disease, diabetes and accelerated ageing.

The sheer brightness of synchrotron light uniquely allows us to image and characterise brains at a subcellular level at an impressive 1um spatial resolution, without the need to chemically stain the tissue, impossible with confocal microscopy platforms currently available to us.

Through several of the different beamlines available at the AS, we integrate a 'multi-modal' platform to collocate and study lipids and metals in relation to proteinaceous plaques and metabolic disturbances in the brain. Ex vivo imaging at the AS is not only confined to neuroscience and vascular research.

The capability of label-free imaging methodologies allows tissues from a wide array of disease states to be imaged in relation to their biochemical profile in great detail – Dr Virginie Lam

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

1. Vascular and metabolic disorders

Identifying new treatments for age-associated blood vessel disorders including bleeding and clotting disorders, heart disease and stroke. Targeting blood vessel growth and function to treat age-associated cancers, blood-vessel inflammatory disorders with ageing, age-linked energy disorders, liver disorders and age-associated infectious diseases.

2. Immune disorders

Stopping the decline in immune function with ageing, targeting the immune system to treat adult cancers and immune function for treatment of infection and muscle repair.

3. Neurological disorders

Exploring novel and new approaches to the prevention and treatment of Alzheimer's disease and other dementias, as well as the prevention and treatment of neurodegenerative diseases such as multiple sclerosis and epilepsy.

4. Cancer

Researching novel interventions for age-associated cancers such as breast, pancreas and prostate cancer and melanoma,with a focus on how the immune system influences cancer risk and progression and trialing novel interventions.

How synchrotron measures up for liver researchers

My lab investigates how iron is involved in the accumulation of fat in the liver. We also have collaborations looking at the role of iron and copper in mesothelioma.

We use the Infrared beamline (IRM) to investigate the concentration and distribution of fat and other organic molecules in the liver and the X-ray fluorescence (XFM) beamilne to measure metals. We also use particle-induced X-ray emission (PIXE) at ANSTO (Lucas Heights) to measure iron.

The Australian Synchrotron allows us to image fats and metals at sub-cellular resolution with a sensitivity and speed that are unobtainable by other methods.

Approximately one-third of patients with fatty liver disease also have elevated liver iron. We aim to understand how iron is involved in the regulation of fat in the liver with a view to developing more targeted preventative and therapeutic approaches to treat these patients – Dr Ross Graham

PhD student Clinton Kidman, Dr Ross Graham and Dr Mark Hackett at the XFM beamline.

chiri.curtin.edu.au

chiri@curtin.edu.au