NSW BRAIN TISSUE RESOURCE CENTRE btrc

Brain Matters

Issue 37 Using our Brains Donor Program

From the Director

Associate Professor Greg Sutherland

2022 was the first year in a while where things felt back to normal at the BTRC. For the first time in three years the team travelled to Orlando, Florida to attend the *Research Society on Alcohol* conference. This is the prominent event of our major funder, the *National Institute for Alcohol Abuse and Alcoholism*. We were able to re-acquaint ourselves with many of the researchers who use our tissue to understand the basis of addiction and brain tissue damage associated with chronic alcohol use. I also attended the *Australia and New Zealand Addiction Conference* on the Gold Coast, which brings together clinicians and people with lived experience, and is a timely reminder of why we work hard to understand how and why some people become addicted to substances like alcohol, and others do not.

We are also pleased to be working closely with two organisations that promote brain research. *Step Up for Dementia* was started by Professor Yun-Hee Jeon in 2019 to link volunteers and dementia researchers, and last year expanded to include broader age-related studies which might be of particular interest to our UoB donors who would like to take part in research. In March 2022 we celebrated Brain Awareness Week, working closely with the *Brain Foundation* to spruik the importance of brain donation for research.

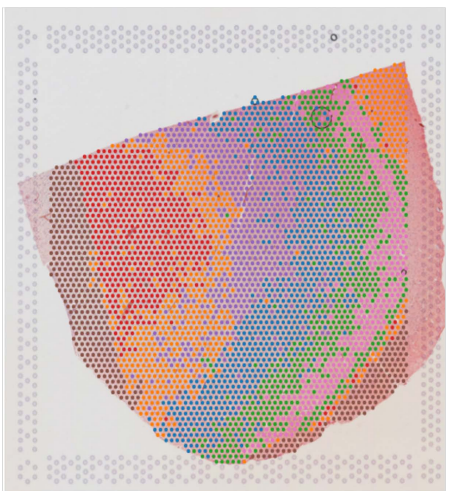


Figure 1. Spatial transcriptomics showing layers of in the human brain. *A Genomics 10X Visium slide shows the distribution of neuronal subtypes across the six layers (different colours) that make up the grey matter in the human cerebrum.*

I also wrote an article for The Conversation describing how brain donation works in Australia which was picked up by radio stations in Adelaide, Perth, and Sydney. We are keen to grow the UoB donor program as it is unique in the world for recruiting donors who have maintained healthy brains throughout their life. For Brain Awareness Week this year we will be working again with the *Brain Foundation* to promote their theme of Healthy Brain Ageing.

The BTRC is always developing new protocols to test the latest techniques in brain tissue research. One technology we expect will change the field is called spatial transcriptomics. Currently, frozen tissue is used for molecular studies and fixed tissue is used for cellular studies. Spatial transcriptomics allows us to combine these methods in the same tissue section which is incredibly exciting (Figure 1). We have been collaborating with A/Prof Marina Gimeno at the School of Veterinary Sciences in using sheep brain tissue to investigate how we can improve our preparation of human tissue to make it more suitable for these new methods. Each year the BTRC runs a retreat which offers a chance for the team to be introspective, look forward, and gain feedback from key stakeholders. This year we were joined by Dr Raymond Schwartz, a neurologist, A/Prof Kirsten Morley from the Edith Collins Centre for Addiction Research, and Dr Natalie Matosin from the University of Wollongong, who explores how stress contributes to mental illness. In 2023 we will be working with Raymond, Kirsten and Natalie to broaden the scope of the BTRC activities.

Lastly, big data is becoming an essential part of medical research and the BTRC. Donor tissues are only as good as what we know about the donor's life and medical history. As modern life presents challenges such as COVID-19, we work hard to keep our questionnaires updated while also responding to new research that may link disrupted sleep, alcohol or low physical activity to poorer brain ageing, so we thank you for continuing to keep us updated through the annual surveys.

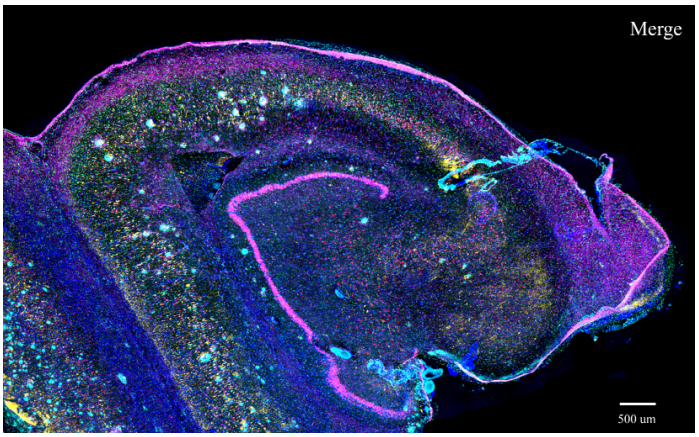
I wish all our UoB donors a prosperous 2023. We couldn't do what we do without your interest and valuable time, so thank you.

Kindest Regards,
Greg

Multiplexing

The BTRC is constantly employing new and novel techniques for brain tissue processing, and we have recently been working on a protocol to improve brain imaging using a technique called multiplexing. Multiplexing is an immunohistochemical (IHC) technique whereby multiple antibodies are used to visualize multiple targets in the same tissue section. IHC makes use of immune complexes within the tissue sample to allow for the staining of various targets, such as cells or tell-tale signs of disease.

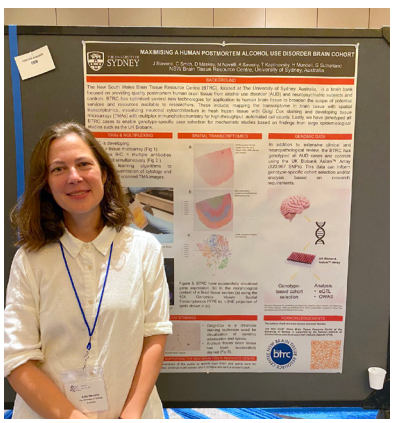
Traditional IHC techniques used at the BTRC generally allow for the visualization of up to three targets at the same time. By applying a multiplexing technique called iterative staining, dozens of targets can be studied in the same piece of tissue. This is particularly advantageous when working with scarce tissue samples. Most importantly, by visualizing multiple markers in the same section at the same time, cell-cell and cell-pathology interactions that may have otherwise been missed can be studied. As technology advances, diseases are increasingly studied on a sub-cellular level. By combining genetic information with spatial information that multiplexing and similar techniques allow, researchers hope to better understand the healthy brain and various disease states.



A merged fluorescent micrograph (fluorescent image captured on a microscope) of the hippocampus of an Alzheimer's Disease case that has been stained for 5 different markers over 3 rounds of staining.

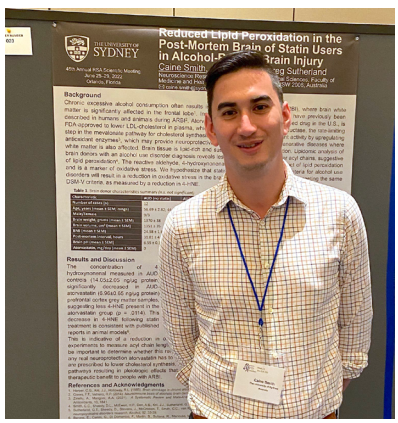
Research Society on Alcohol

In June 2022 BTRC staff attended the *Research Society on Alcohol* conference in Orlando, Florida to speak about the contributions of the BTRC toward research on Alcohol-Related Brain Damage. Julia presented on various tools and techniques for analysing human brain tissue, Greg spoke about genomic data generated from BTRC tissue samples, and Caine presented his work exploring how taking statins may provide some protection against brain damage from chronic alcohol use.



Julia Stevens BTRC Manager

A/Prof Greg Sutherland BTRC Director



Caine Smith BTRC Research Assistant/ PhD Student

Perceptions of brain donation

In September 2022 we wrapped up our Perceptions of Brain Donation survey and are excited to share some preliminary results.

Globally, rates of brain donation for medical research are dwarfed by those of organ donation for transplantation. There are two conflicting explanations for this, neither of which have been explored systematically. The first is that lay people consider the brain "special" or different from other organs, rendering them unwilling to donate. The other explanation points to the lack of public knowledge about brain donation that has been reported by several studies globally, indicating that unawareness is a greater barrier to brain donation than unwillingness. There is a sizeable amount of research (including that published by the BTRC) on why people choose to sign up for brain donation, but there is a gap in the literature regarding why people choose not to donate. We sought to uncover whether brain donation rates in Australia are low due to an aversion to the concept of brain donation, a lack of awareness about it, or other factors. To do so we conducted a survey seeking community perceptions of brain donation.

In order to uncover why most people do *not* register for brain donation, participants that indicated being part of a brain donor program were excluded before analysis, leaving us with 225 survey responses. 84% of participants either definitely wanted to donate their brain (44.9%) or were willing to consider it (39.1%) and 92% of respondents were in support of brain donation in principle. 0.8% opposed it and 7.1% were neutral. The two major reasons that emerged for not being a brain donor were not knowing that it is possible to donate the brain (41.3%) and thinking that brain donation is included when signing up as an organ donor for transplant (37.8%). 4% of people reported feeling uncomfortable with brain donation and 2.2% indicated this was in part due to their belief that the brain is different to other organs.

Our preliminary analysis indicates a need to educate the public not only regarding brain donation for medical research, but also on specific details regarding organ donation for transplantation – which is often referred to simply as "organ donation", leading to ambiguity in public understandings of what it entails. Many misconceptions regarding organ and brain donation emerged in the free text responses to the survey questions and we look forward to sharing further results with you once they are published.

We were encouraged by just how many of the participants expressed strong support for medical research more broadly. This is consistent with 2021 *Research Australia* opinion polling that reported an increasing public desire for government investment in medical research. To read more about this head to *Research Australia*.

Staff Profile

Mario Novelli, Lab Assistant NSW BTRC

What is your background and how long have you worked at the BTRC?

I hold a Bachelor of Science in anatomy and physiology. Previously, I worked at the visual neuroscience laboratory of the *Save Sight Institute* investigating retinal ganglion cell sub-populations in human and non-human primates. I joined the NSW BTRC in the middle of 2021.

What are the most rewarding aspects of working at the BTRC?

The opportunity to work with human brain tissue and knowing that our work and the work of associated research groups around the world may help find treatments for various neurological diseases is deeply rewarding. Additionally, developing new techniques which help better preserve the quality of the stored tissue and increasing the opportunity for downstream applications is satisfying.

What are you working on at the moment?

Recently I've been working closely with my colleagues to update our tissue preservation techniques. We have been trialling several new techniques in sheep brain tissue to determine the best way to process and store new brain donations. Also, we have been developing a multiplexing protocol in which we're able to visualise several cell and disease markers in the same tissue section, in the hopes that we can better understand the interactions of various cells in disease states.

A breakthrough in ageing research, powered by you

We are excited to announce that Using our Brains is an organisation champion for the newly launched *StepUp for Ageing Research*. The name may sound familiar – *StepUp for Ageing Research* builds on the successful *StepUp for Dementia Research* that we have championed since 2019. The service has enlisted close to 1,700 volunteers, 26 universities and institutes, 220 researchers and successfully fed participants into over 50 research projects.

The Honourable Dame Quentin Bryce AD CVO (pictured left, with the founder of *StepUp*, Professor Yun-Hee Jeon) is *StepUp* ambassador and believes that active engagement of older people and their families in research is essential to keep them front and centre in health policy development and service delivery.

"Healthy ageing is about older people becoming and remaining healthy. StepUp for Ageing Research will enable the voices of older people, families and communities to be heard and to be included."

Unfortunately, research is costly and one of the significant costs is recruitment. Numerous research studies in ageing encounter problems because they can't get the required number of participants to sign on, and stay on. *StepUp* aims to solve this problem by compiling a register of research-willing participants that can be matched with appropriate studies as they arise. While public support for health and medical research is higher than ever, economic conditions have made it difficult for Australians to sup-port their chosen research charities financially. Consider donating your time instead by participating in *StepUp for Ageing Research*.

Anyone 18 years and over who resides in Australia can register to be involved online, via phone or post. The service is looking to recruit all adults, including the young, older people, those with dementia or cognitive decline, family, friends and carers. By registering for the service you are not committing to research projects. Once you have registered your details at *StepUp for Ageing Research*, the service checks to see if you match any studies. If so, it will send you detailed information on the study and you then decide if you'd like to take part. To get involved head to stepupforageingresearch.org.au

Connect with us...

For more information

Editor: Ali Sweeney

Using our Brains Donor Program
NSW Brain Tissue Resource Centre
Charles Perkins Centre, D17
Level 6 West
The University of Sydney NSW 2006

p: 02 9351 2410
e: medicine.uob@sydney.edu.au

In Memoriam

The Using our Brains Donor Program would like to acknowledge the generosity shown by our donors and donor families. It is an act of great foresight and kindness to give at a time of loss, so that others may be helped in the future.

To the families of donors that have died this year, the Using our Brains Donor Program would like to extend its sincere sympathy and gratitude. Over the years, friends and families of donors have given memorial donations to the Using our Brains Donor Program in lieu of flowers. If you would like to donate to our research program, please contact us for details.