QUEEN SQUARE BRAIN BANK

UCL

BRAIN MATTERS 2023

The Newsletter From Queen Square Brain Bank
For Neurological Disorders

PROFESSOR TOM WARNER, HEAD OF QUEEN SQUARE BRAIN BANK WELCOMES YOU TO BRAIN MATTERS 2023:

All at the Queen Square Brain Bank (QSBB) were optimistic that 2022 would see a welcome return to service after two years of the COVID pandemic with researchers refocusing on their studies into Parkinson's disease, multiple system atrophy and dementia. We were pleased to be able once again to fulfil brain donations and supply tissue to academic centres around the world.

After a promising start, out of the blue a serious power outage occurred in the building where the Brain Bank is housed. Despite intensive input from University College London Estates Department, it became clear that for a period we could not be guaranteed a reliable electrical supply for the numerous freezers containing the frozen brain collection. Decisive action was taken and arrangements put in place for all samples requiring cryostorage at -80°C to be relocated temporarily to alternative facilities. Whilst crucial remedial work on power systems was being completed QSBB activities were put on hold. Robust measures have since been undertaken to ensure the resilience of the infrastructure and prevent a recurrence of this event.

On a positive note, Consultant Neuropathologist **Dr Zane Jaunmuktane** was rewarded for her research, teaching and hard work at QSBB with a promotion to Associate Professor. The arrival of new Neuropathologist **Dr Karl Frontzek** from Zurich is eagerly anticipated following the protracted bureaucratic process that now awaits professionals coming to work in the UK. Thanks to the hard work of **Dr Rina Bandopadhyay**, Principal Research Fellow, a Silver LEAF Award for Sustainable Laboratories was achieved for rising to the challenge of reducing the use of plastics in a busy diagnostic and research environment.

Sadly for the team, retirement beckoned for **Kate Strand**, Brain Bank Manager after twenty years of service dedicated to the analysis and curation of donated tissue. Kate's continuous commitment and diligence have been invaluable, and she will be greatly missed.

We are hoping for a productive and calmer 2023 concentrating on what we do best, effectively operating one of the largest and globally recognised research and tissue resources. I would like to express my gratitude to our donors and families for their continued support and generosity particularly over this difficult period. We are also indebted to all sponsors and funders without whom we would be unable to further contribute to medical and scientific advances.

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RESEARCH

Joanne Lachica, Research Technician and **Dr Christina Toomey**, Research Fellow are working with **Professor Sonia Gandhi**, Clinician Scientist on an Aligning Science Across Parkinson's (ASAP) initiative, in partnership with The Michael J. Fox Foundation for Parkinson's Research. ASAP promotes collaboration and sharing of resources to improve knowledge of the contributing factors to Parkinson's disease development, leading to new therapies. The team consists of several laboratory groups across University College London, The Francis Crick Institute and Cambridge University:

Parkinson's disease is a multi-faceted movement disorder typically recognised by tremor, slowness and stiffness. Evidence suggests that by the time a person is diagnosed the pathological processes associated with the illness have been set in motion years earlier and that non-motor symptoms, such as fatigue and disrupted sleep, can be identified up to two decades prior to that point. Consequently, there may be opportunities to identify the presence of Parkinson's disease in very early stages and intervene before the onset of clinical signs.

The pathological hallmark as seen under a microscope is the build-up of a protein, alpha-synuclein which forms insoluble deposits in brain cells called Lewy bodies. However, before these clumps of alpha-synuclein reach the Lewy body stage smaller structures named oligomers can be observed. Unlike Lewy bodies which spread in a specific pattern from deep within the brain to outer areas in the latter stages of the condition, the purpose and progression of oligomers is still unclear.

By investigating tissue collections from QSBB and other brain banks and working closely with scientists in Cambridge who use super-resolution imaging (high-level microscopes that allow cellular pathology to be observed in detail), the groups aim to create a map of oligomer distribution in early to mid-stage brain tissue.

This exploratory study will provide a greater understanding of the part oligomers play in Parkinson's disease along with an openly accessible resource to aid future research.

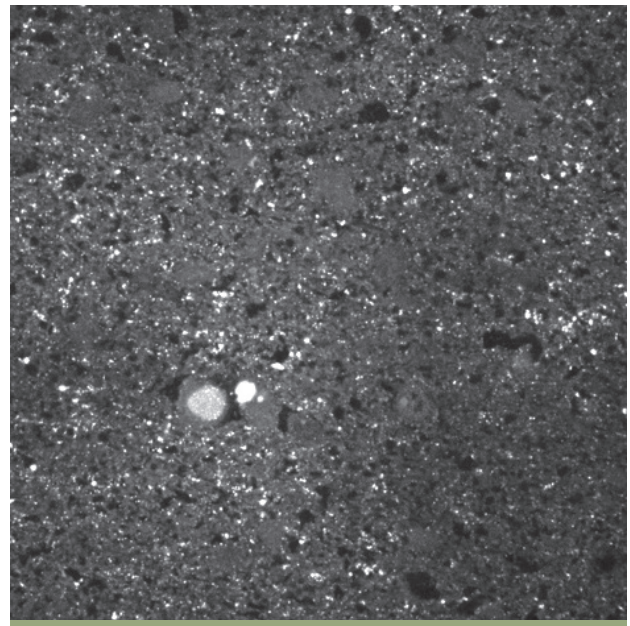
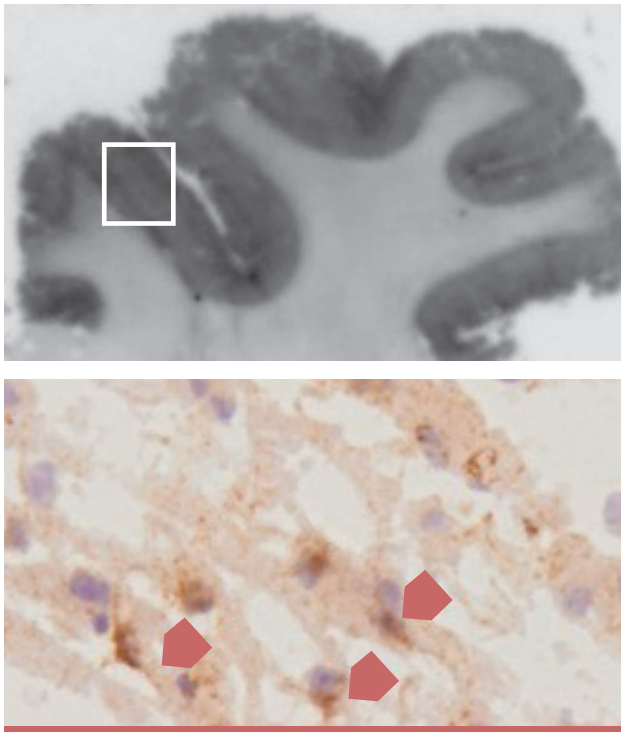


Image above: Microscopic view of oligomers (in white) in Parkinson's disease brain tissue detected by super-resolution imaging.

Dr Barbara Frias, Research Fellow working with **Professor Tammaryn Lashley**, QSBB Director of Research and **Dr Kerstin Sanders**, Lecturer in Radiochemistry and Pharmacology, explains their investigation into a non-invasive method of early detection of dementia:

Frontotemporal dementia is a progressive brain disorder characterised by rapid memory loss and personality changes. It is the most common cause of young onset dementia, often starting between the ages of 45 and 65. Accurately diagnosing the illness remains a challenge and is usually only achieved when the symptoms have fully developed. At present there is no cure and potential treatment options are often hindered by a lack of assessment tools to measure effectiveness in patients. Our aim is to identify a reliable method to aid early detection, provide opportunities to accelerate remedial strategies and monitor progression.

Inflammation is the body's way of fighting harmful or damaging events. Chronic inflammation happens when this response lingers and over time may have a negative impact on tissues and organs. Scientific research has suggested that chronic inflammation could play a role in a range of conditions, including frontotemporal dementia, although it is unclear how inflammatory events correspond to developing disease.



Images above show microscopic views of:
a) Autoradiography technique showing PET radiotracer binding in an area of brain tissue, highlighted in the white box. b) Immunohistochemistry technique showing brain cells involved in neuroinflammation, highlighted with pink arrows.

Positron emission tomography (PET) is an imaging technique that uses radioactive substances known as radiotracers to visualise and measure changes in the body. By using novel PET radiotracers we hope to detect brain areas affected by inflammation before clinical signs become apparent, and to track the progression of the disorder.

To ascertain the usefulness of this method, our group is researching PET in volunteers who are genetically predisposed to frontotemporal dementia and are likely to develop the illness. In parallel, by examining post-mortem tissue through laboratory techniques such as autoradiography and immunohistochemistry, we can check the accuracy of PET in identifying neuroinflammation in the same areas.

Dr Patrick Cullinane, Clinical Research Fellow gives an update on his PhD project looking into a possible link between type 2 diabetes and progressive supranuclear palsy:

Progressive supranuclear palsy (PSP) is a rare neurodegenerative disease recognised by impairments in movement, balance, vision, speech and swallowing. While some of the clinical signs are similar to Parkinson's disease, PSP is a more aggressive illness and is often unresponsive to anti-Parkinson's medications. There is an urgent need to understand the causes and improve treatment options.

One risk factor that may influence the development of the condition is type 2 diabetes mellitus (T2D) where the hormone insulin loses its ability to control blood sugar levels. Researchers world-wide have already established that having T2D increases a person's risk of developing Parkinson's or Alzheimer's disease. Importantly, it may be possible to modify the effects of diabetes on brain cells as certain diabetic therapies have shown some neuroprotective effect in animal models of degeneration.

Studying the tissue and medical records of donors with post-mortem confirmed progressive supranuclear palsy has allowed us to investigate further. Our findings indicate that symptoms tended to progress more rapidly in those who already had T2D. Preliminary examination of brain samples suggests there may be changes in various proteins that are required for normal functioning of insulin. We hope this work can offer new insights into whether type 2 diabetes causes more severe loss of brain cells in PSP.

Repurposing (using a medicine for a disease other than the one it was originally intended) of some anti-diabetic drugs has already shown promising results in Parkinson's disease in several clinical trials. However, further research is required to determine if these may also be beneficial for people with progressive supranuclear palsy.

Q&A

The role of **Natalie Woodman**, QSBB Technician is to receive donated brains as they arrive in the laboratory and prepare them for neuropathological study.

What inspired you to become a Research Technician?
I have loved science since childhood and am curious about what makes the human body tick. My father became ill when I was eleven, and I was keen to understand his illness and how I could help. Pursuing a career combining my twin passions of science and helping people came naturally.

How long did it take to reach this position?
After chemistry, biology and physics A-Levels, I went to university to study pharmacology including work experience in a laboratory. I was fortunate to get a job there as a clinical trial technician, staying for five years before moving to the Multiple Sclerosis Brain Bank at Imperial College London and then to The Cancer Biobank at Guy's Hospital.
My enthusiasm for neurology brought me to the Queen Square Brain Bank.

What are the interesting aspects of your work?
I find it fascinating how pathological features seen in a brain can teach us so much about the probable cause of disease symptoms. I also take pride in ensuring valuable donations are processed to exacting standards, providing research scientists with the highest quality tissue.

Are we nearer to unravelling the mysteries of neurodegeneration?
An extremely hard question to answer because whilst undoubtedly there has been progress, it is a vast and complex issue. There is still much to learn that will make a real difference to patients' lives.

Away from the brain bank, what do you enjoy?
I love music, going to concerts and soaking up the atmosphere, and reading biographies. People's experiences and lives are intriguing.

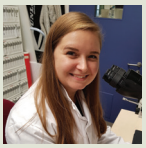
Which medical scientist would be your fantasy dinner guest?
Gertrude B Elion, an American biochemist who changed the way new drugs were developed leading to methods that are still used in current research. She discovered Allopurinol, a treatment for gout, and Azathioprine, an immune system suppressant. In 1988 Elion was awarded the Nobel Prize in Medicine, one of only ten women at that time to achieve this, and one of the few recipients to earn a science Nobel without having a doctorate.

If you were not a Research Technician, what would you be?
Either a make-up artist in film and TV, it is wonderful how they can transform the way a person looks; or a zookeeper caring for a variety of animals and perhaps re-introducing endangered species back to the wild.

CONTRIBUTORS

Top row (from left to right):
Joanne Lachica, Dr Christina Toomey, Professor Sonia Gandhi, Dr Barbara Frias.

Lower row:
Professor Tammaryn Lashley, Dr Patrick Cullinane, Karen Shaw, Brain Bank Nurse and editor of *Brain Matters*.




DONATIONS



Coordinators (above):
Lynn Haddon, Cheryl Pearce, Natalie Woodman.

Brain donation coordinators

QSBB Administrators, **Lynn Haddon** and **Cheryl Pearce** are often the first point of contact for potential donors. Coordinating the brain donor scheme with help from Research Technician **Natalie Woodman**, the team work closely with relatives, hospital staff, funeral directors and couriers to ensure the careful donation and safe receipt of tissue, with the minimum of distress to families.

The importance of controls

We encourage people without a neurological condition, 'controls' to register with our donor scheme. Control tissue is vital for comparison with disease and provides researchers with an understanding of the normal appearance and function of the brain.

If you would like further information please log on to the website: www.ucl.ac.uk/ion/qsbb

Or contact Lynn Haddon **l.haddon@ucl.ac.uk** and Cheryl Pearce **cheryl.pearce@ucl.ac.uk**

Telephone: **020 7837 8370**

QSBB

Brain banking

Brain banking is expensive and we continue to depend almost entirely on charitable benefactions for our survival. The QSBB is primarily funded by donations from the Reta Lila Weston Institute of Neurological Studies. We gratefully acknowledge the generosity of donor families, sponsors and several benefactors.

If you would like to offer a financial donation to help our research, please visit our website: www.ucl.ac.uk/ion/qsbb or contact Lynn Haddon.

Thank you.

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Aligning Science Across Parkinson's (ASAP)

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