QUEEN SQUARE BRAIN BANK

UCL

Brain Matters 2025

The Newsletter From Queen Square Brain Bank For Neurological Disorders

Professor Tom Warner Head of Queen Square Brain Bank welcomes you to Brain Matters:

2024 has been a year of change at the Queen Square Brain Bank: new staff, new equipment and plans to move to new premises.

Robert Courtney retired from his role as senior laboratory technician, and Professor Tammaryn Lashley resigned from the role of Director of Research. Both Tammaryn and Rob had worked for many years at QSBB and we are incredibly grateful for their work, input and energy supporting the brain bank. We wish them well as our paths part.

We are delighted to welcome three new appointments at QSBB, with Grace Danquah and Patrick Coakes joining the laboratory technical staff, and Phoebe Anscombe taking the role of database manager. All three bring different strengths to QSBB and will help us achieve our goal of increasing capacity and reducing the time to process the donated tissue and send tissue for research around the world.

The funding from the MRC of £1M awarded to QSBB commenced this year to expand the cohorts of neurodegenerative conditions that we collect and curate and improve value by linking to associated data such as genetics and in life imaging, as well as developing a bank of skin biopsies and cultured skin cells, invaluable for researchers. This also led to appointing two excellent research staff, a programme manager Mimi Tambi, and research assistant Jaime Anton Arnal.

The brain bank is unique in that it attracts clinical visitors from abroad to spend a period of time studying and working in the laboratory, clinics and research. This year we had visits from excellent clinicians from Brazil, Spain, Egypt and Lithuania.

Thanks to a scheme at UCL we have been able to replace all of our ultra low temperature freezers for frozen tissue with new more energy efficient models. As part of the work at the Institute of Neurology we are also looking at additional ways of reducing our carbon footprint, and how we can do this with our freezers. Based on this we will be changing the freezer temperature from -80 to -70C, which will reduce the energy consumption by 28%, whilst not affecting tissue quality.

We have been replacing other aging equipment and thanks to a generous donation by the Reta Lila Weston Trust, were able to purchase a new automated slide stainer for producing stained tissue sections with consistent quality in each batch. We have also invested in a new tissue processor which allows us to process the donated brains more quickly and efficiently.

Finally, we are building towards a move to newly renovated premises in the current Institute of Neurology which will allow us to expand activity and staffing, most likely in 2026.

We are very grateful for all the donations, bequests and grants that have been given to QSBB in 2024, and the core funding from the Reta Lila Weston Institute. This allows us to remain as one of the world's leading brain banks.

2025

Research

Dr Patrick Cullinane
Investigating alpha-synuclein oligomers and seeding activity in multiple system atrophy.

Multiple system atrophy (MSA) is a rapidly progressive neurodegenerative disease. There are no treatments available to slow down or stop the progression of this devastating disease. There is considerable variability in the symptoms that people with MSA may experience with some developing stiffness and slowness of movement resembling Parkinson's (MSA-P), while others develop unsteadiness and loss of balance as a consequence of damage to a part of the brain called the cerebellum (MSA-C). Problems with the function of the autonomic nervous system occurs in each subtype causing additional symptoms such as light-headedness or fainting, urinary problems and constipation. There is also considerable variation in how quickly the disease progresses.

MSA causes patterns of brain shrinkage that correspond to the subtypes mentioned above. In affected parts of the brain, one can see clumps of abnormal protein within brain cells that are mainly composed of the protein α-synuclein.

Healthy α-synuclein is normally found throughout the brain but for reasons that are not fully understood, it starts to clump together initially forming small clusters of protein called oligomers, which then combine to form larger filaments that cells are unable to clear. When abnormal oligomers and filaments of α-synuclein are exposed to healthy cells, they cause previously normal α-synuclein to start clumping together thus transmitting the disease from cell to cell.

To study this dynamic process, we need to use different laboratory assays including immunohistochemistry, which highlights the largest clumps; proximity ligation assays, which uncover α-synuclein oligomers; and cell-based seeding assays that show abnormal α-synuclein filaments from human brain tissue causing α-synuclein aggregation in cells growing in a dish. By combining these techniques, we can see the different stages of α-synuclein aggregation in different parts of the brain. We hope that this approach will provide insights into why certain people with MSA develop different symptoms and also why the condition is more or less aggressive from one person to the next.

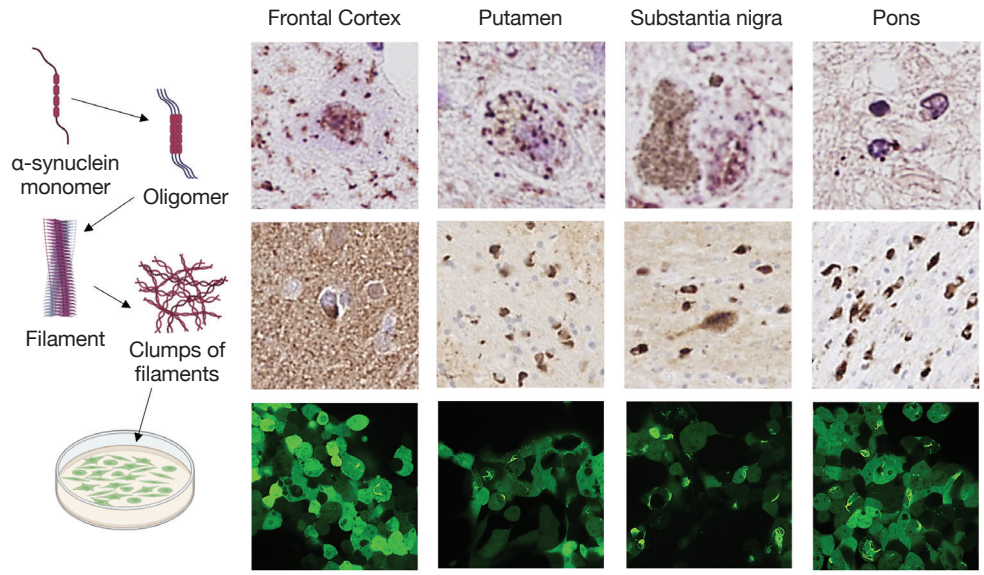


Figure (above): The top row shows α-synuclein oligomers (brown puncta) in different brain regions. The middle row shows larger clumps of α-synuclein filaments within cells (brown spots). Human embryonic kidney cells exposed to filaments from human brain tissue in a dish develop clumps of α-synuclein (bright green spots) as shown in the bottom row.

Dr Zane Jaunmuktane and team

Curating Cells for Cures: Advancing Neurodegenerative Research Through Fibroblast Cell Generation.

Since early 2024, the Queen Square Brain Bank (QSBB) has been building a collection of fibroblasts, taken from skin and the brain's choroid plexus. Found in connective tissue, fibroblasts aid in tissue repair and communication. This collection will be shared globally to study brain diseases like Alzheimer's, Parkinson's, and other dementias and movement disorders.

Fibroblasts can be reprogrammed into induced pluripotent stem cells (iPSCs), which can then become various brain cells like neurons (for memory and movement) and glial cells (which support neurons). This ability enables scientists to study how brain cells function, what happens in disease, and how changes compare to the donor's actual brain tissue.

This collection helps researchers understand how brain diseases begin, progress, and cause symptoms. Combining genetic and environmental factors, fibroblasts offer a flexible tool for studying these conditions. Comparing lab-grown cells with real brain tissue provides insights into disease mechanisms, while testing experimental drugs on these cells accelerates therapy development.

In summary, QSBB's fibroblast collection is a ground-breaking resource for studying brain diseases and finding treatments, offering hope to millions affected by these disorders.

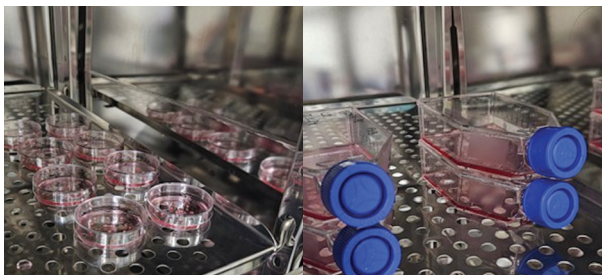
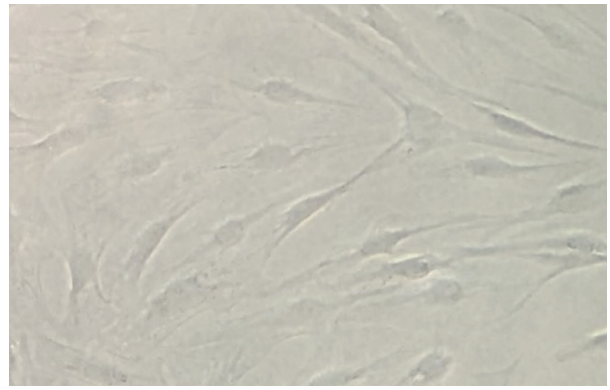


Image (above): petri dishes and flasks containing culture media, where fibroblasts are grown and maintained. These vessels are placed inside an incubator, providing the controlled conditions essential for cell cultivation.

Image (top right): magnified view of fibroblasts revealing their elongated, spindle-shaped forms, and illustrating their growth. These cells can then be used for researching neurodegenerative diseases.



Mapping the Mind: How Spatial Transcriptomics is Uncovering Clues to Movement Disorders.

Recent research has identified distinct molecular patterns in astrocytes – brain support cells – across specific brain regions, based on gene activity studies (transcriptomics). However, how these and other glial cells are affected in neurodegenerative movement disorders like Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy remains unclear. Understanding these patterns could explain why certain brain cells and regions are more vulnerable, shedding light on the varied symptoms of these disorders and potential ways to halt their progression.

Using spatial transcriptomics, we analysed gene activity in astrocytes and microglia (protective glial cells) from post-mortem brain tissue. We focused on the frontal cortex (cognitive and motor functions) and brainstem (vital functions), examining grey and white matter from individuals with and without neurodegenerative diseases to identify disorder-specific patterns.

Our findings reveal significant differences in glial cell gene activity across brain regions in patients with neurodegenerative diseases, varying not only between diseases like Parkinson's and progressive supranuclear palsy but also among subtypes of the same disease.

Some of these gene activity patterns may provide insights into the biological processes driving symptom diversity and disease progression. Further research is needed to understand how these changes affect protein production and their impact on disease mechanisms. Larger studies with diverse patient groups will be crucial for confirming these results and uncovering how specific brain regions and cells are impacted in these disorders.

New Staff Profile – Phoebe Anscombe, Database Manager at QSBB

Q&A

Phoebe Anscombe is the Database Manager at Queen Square Brain Bank, and she joined us in early 2024 from New Zealand.

How did you come to be interested in neuroscience?
I've always been fascinated by the human brain. After leaving school, I completed a Bachelor of Science majoring in neuroscience, and then went on to complete a Bachelor of Biomedical Science (Honours) postgraduate degree, with a research thesis focused on Alzheimer's disease. I'm interested in the ongoing research to elucidate the precise pathological mechanisms underlying neurodegenerative diseases, in order to guide the development of future treatments.

What were you doing previously?
I spent three years working as a research technician in the Neurological Foundation Human Brain Bank at the Centre for Brain Research in Auckland, New Zealand. My primary role there was based in the laboratory, carrying out dissections and processing of the brains that were donated. I loved the experience of learning and working within a brain banking environment.

How did you come to be in the UK?
I moved to the UK from New Zealand midway through 2023, seeking a new experience living on the other side of the world. One of the aspects that most excited me about moving here was the chance to live in such a busy and exciting city as London, as well as the opportunities to travel throughout Europe, experiencing new cultures and places.

What is your role at the QSBB?
I feel very lucky to have been given the opportunity to now be working for the Queen Square Brain Bank. My position of database manager means I am now out of the lab, and instead I work closely with the neuropathologists and brain donation coordinators to maintain an accurate and efficient database system for the brain bank, and I facilitate data requests for researchers.

How does your role contribute to current and future research?
My aim as the database manager is to maintain and uphold the accuracy and integrity of data from the donations that we receive at the QSBB, to ensure that we have a reliable and valuable source of information for researchers to draw from when carrying out their studies. The efficient and systematic organisation of our brain bank database facilitates researchers to maximise the insights that can be derived from these invaluable donations. I hope that this will serve to enable progress in ongoing vital areas of research, such as identifying novel biomarkers for earlier detection of neurodegenerative diseases, and to inform critical research on possible therapeutic targets for future drug development studies.

Contributors and new staff

Left to right: Jaime Anton Arnal, Maggie Burrows, Patrick Coakes, Dr Patrick Cullinane, Grace Danquah, Dr Zane Jaunmuktane, Dr Hemanth Nelvagal, Mimi Tambi.

Donations



Co-ordinators:
Lynn Haddon (above left), Cheryl Pearce (above centre), Natalie Woodman (above right).

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 QSBB Lab Manager **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**

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.

Sponsors

UCL Queen Square Institute of Neurology

Reta Lila Weston Institute of Neurological Studies

Multiple System Atrophy Trust

Aligning Science Across Parkinson's (ASAP)

Medical Research Council

QSBB

Cover image: Immunofluorescence image from the brain of a patient with Parkinson's disease, showing cell nuclei stained in blue, astrocytes glowing vibrant green, and microglia radiating in red. These distinct cell types are carefully dissected using advanced technology tools, to study and identify molecular changes relevant for disease progression.