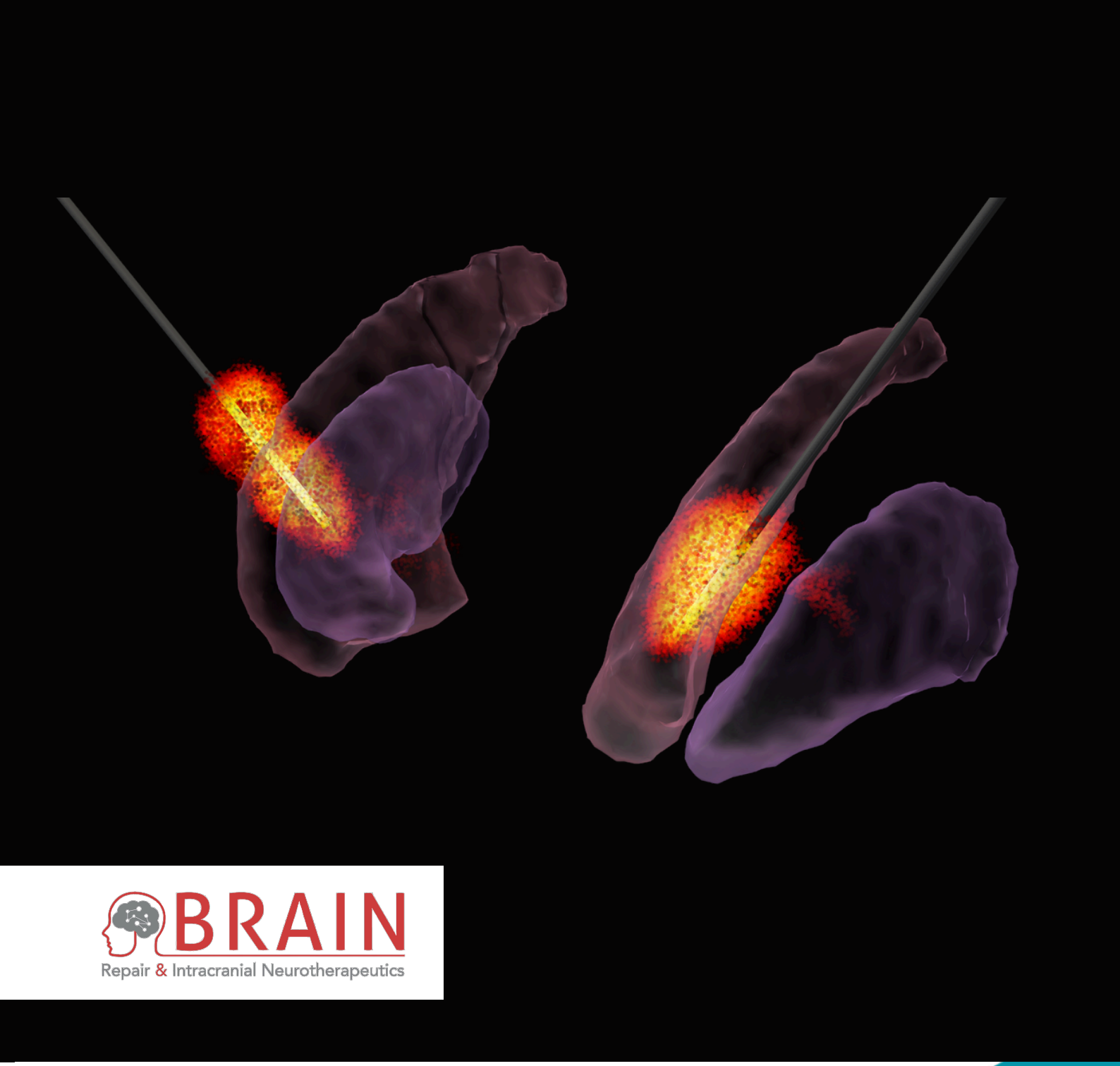


BRAIN
Repair & Intracranial Neurotherapeutics

Ymchwil Iechyd a Gofal Cymru
Health and Care Research Wales

Ariennir gan Lywodraeth Cymru
Funded by Welsh Government

2020-2025
End of award report

BRAIN Unit www.brain.wales

Contents

Cover image: The schematic image demonstrates Advanced Therapy Medicinal Products (AMTP) administration (fiery blobs) into the caudate heads (taupe coloured deep brain structures affected in Huntington's disease) via thin surgical catheters.

Foreword

I'm delighted to present this report, reflecting on the highlights and impact of the research facilitated by the BRAIN Unit during the 2020-2025 period.

Despite beginning this funding period amid unprecedented global challenges, the past five years have marked an exceptional period of growth, innovation, and increasing influence for the BRAIN Unit. We have not merely weathered difficulties—we have thrived through them, emerging as an increasingly recognised centre of excellence in Advanced Neurotherapies.

Our team members have consistently secured prestigious fellowship awards and career advancement opportunities, reflecting both our commitment to talent development and the high calibre of our researchers. We take enormous pride in seeing the success of our trainees and junior researchers and view these transitions as prime opportunities to extend our collaborative network across the advanced therapy research landscape.

We have established robust and productive partnerships with Advanced Therapies Wales and Midlands-Wales Advanced Therapies Treatment Centres (MW-ATTC), enhancing our profile within the UK and beyond.

Their additional funding is both supporting capacity building for delivering Neuro Advanced Therapies Clinical Trials - a cornerstone of our strategic vision, and in determining public involvement and engagement strategies for advanced therapy research and delivery in the UK and beyond.

Our international work addressing the complex challenges of delivering Advanced Therapy Medicinal Products (ATMPs) to the central nervous system has garnered substantial attention from both research and industry communities worldwide. We are positioned to lead significant developments in the development and delivery of advanced therapies for neurodegenerative and other brain-based disease in the UK and beyond in the coming years.

Despite the significant disruptions caused by the global pandemic in 2020, effects that continue to reverberate through the research community even in 2025, the extraordinary dedication and resilience of our teams have positioned the BRAIN Unit, which will now be known as the Advanced Neurotherapies Centre, in a place of strength as we look toward the next five years

We hope you enjoy reading this report.

Professor William Gray
BRAIN Unit Director

The team

Director
Professor William Gray

Deputy Director
Professor Anne Rosser

Work Package Leads
Professor Willliam Gray
Professor Neil Robertson
Professor Owain Howell
Dr Cheney Drew
Peter Roberts

Advanced Neurotherapies Clinical Team*
Dr Jane Davies
Suzannah Peck
Mr Amad Khan

Neuroscience Research Unit*
Professor Khalid Hamandi
Belinda Gunning
Dr Saiful Bari
Dr Aung Saw
Dr Sanchita Bhatia
Dr Karim Kreft
Cynthia Butcher
Alison Johnson
Megan Voisey
Dympna McAleer
Elizabeth Perreira

Research Team
Dr Samantha Loveless*
Dr Anne-Marie McGorrian*
Dr Francesco Bedogni
Dr Chloe Ormonde
Dr Lauren Griffiths
Olivia Squire
Georgia Wilson
Dr Nick Bennion*

Clinical Research Fellows
Mr Dmitri Sastin*
Mr Susruta Manivannan*
Mr Harsh Bhatt*
Mr Ronak Ved*
Mr Richard Moon*

Management, Administration and Communications
Jo Baker
Ashlie Brown
Dr Helen Hughes*
Victoria Saunders*
Catrin Hopkins*
Becs Parker*
Julia Pearce*

These posts receive funding from other sources, including the Medical Research Council, Guarantors of Brain, Brain Research UK, European Huntington's Disease Network, Advanced Therapies Wales, Midlands-Wales ATTC Cardiff University and NHS Research and Development.

Introduction

Funded by Welsh Government via the Health and Care Research Wales infrastructure, the Brain Repair and Intracranial Neurotherapeutics (BRAIN) Unit develops novel therapeutics and treatment delivery systems for neurological conditions.

BRAIN is a multi-disciplinary research unit with strong academic and NHS clinical leadership, operating under the directorship of Professor William Gray along with 24 principal investigators and collaborators. Since 2015, grants led or supported by the BRAIN Unit have secured over £52 million in funding. The BRAIN Unit is primarily based in Cardiff but involves research groups from Swansea University and health boards across South Wales. Our work is informed by individuals who are affected by neurological conditions in Wales and we continue to work with third sector partners to support activities with far reaching membership and input.

Our mission

Our mission is to be a UK national centre of excellence, and on a path towards international leadership for:

1. Delivering advanced therapy medicinal products (ATMPs) to the human brain in early phase clinical trials.

2. Supporting ATMP development for neurological disease.

Our aims

Develop new and refine existing systems for therapeutics delivery into the human brain.

Develop appropriate infrastructure for:

a) Advancing adult and fetal brain tissue resources, supporting translational research and therapy validation across neurological diseases

b) Bio-banking and bio-resource management using linked and deeply phenotyped clinical data

c) Consolidating and extending appropriate clinical trials and expertise, including refinement of appropriate methodologies for evaluating novel complex interventions

Embed cross-cutting excellence in the relation to:

- Public and Patient Involvement and Engagement
- Industry and NHS Engagement and Collaboration

Work packages and cross cutting themes

Cross cutting theme: NHS, Commercial and Industry Engagement

Research programmes

WP1
Intracranial Delivery

WP2
Providing human adult neural tissue to model disease + validate novel therapies

WP3
Welsh Neuroscience Research Tissue Bank **(WNRTB)** + Swansea Neurology Biobank **(SNB)** Delivery

Cross cutting theme: WP4 PPI and Engagement

Glossary

- **In vitro** - (Latin for "in the glass") studies performed with micro-organisms, cells, or biological molecules outside their normal biological context.
- **Stem cell** - Cells of the body (somatic cells) that can divide and become differentiated. When an organism grows, stem cells specialise, and take specific functions. For instance, mature tissues like skin, muscle, blood, bone, liver, nerves, all have different types of cells.
- **Advanced therapy medicinal products (ATMPs)** are medicines for human use that are based on genes, tissues, or cells. They offer ground-breaking new opportunities for the treatment of disease and injury.
- **Neurotherapeutics** - The treatment of disorders that affect the nervous system.
- **Striatum** - The striatum or corpus striatum (also called the neostriatum and the striate nucleus) is a nucleus (a cluster of neurons) in the subcortical basal ganglia of the forebrain. The striatum is a critical component of the motor (movement) and reward (pleasure) systems.
- **Hippocampus** - The hippocampus (Greek for "seahorse") is a major component of the brain of humans and other vertebrates. Humans and other mammals have two hippocampi, one on each side of the brain. The hippocampus is part of the limbic system and plays important roles in the consolidation of information from short-term memory to long-term memory, and in spatial memory that enables navigation.
- **Intracranial** - Within the skull.
- **Cerebrospinal fluid (CSF)** is a clear, colourless body fluid found in the brain and spinal cord.
- **Peripheral blood mononuclear cell (PBMC)** is any peripheral blood cell having a round nucleus. These cells consist of lymphocytes (T cells, B cells, NK cells) and monocytes.
- **Neurogenesis** - The process by which nervous system cells, the neurons, are produced by neural stem cells (NSC).
- **AMPAKine molecules**- A subgroup of AMPA receptor modulators currently being investigated as potential treatments for a range of conditions involving neurological and psychiatric disorders.

Core Metrics

Reporting period: 2023/2024

Health and Care Research Wales infrastructure award to the group

Direct funding awarded

£1.23m

Jobs created through direct funding

CV 14

Grants won during reporting period

Grants won	Led by group	Group collaborating
Number	55	21
Value	£8.98m	£7.3m
Funding to Wales	£8.28m	£6.8m
Funding to group	£6m	£0
Additional jobs created for Wales	30	21
Additional jobs created for group	25	3

102

Number of publications

6

Number of public engagement events

36

Number of public involvement opportunities

Intracranial Delivery

Work package aim: We are on the cusp of a new era of potential disease-modifying therapies for neurodegeneration, with many of the most promising requiring direct delivery into the central nervous system. Despite this, there are no optimised devices or protocols for delivering therapies directly to the human brain.

Our objectives are to:

1. Address this unmet need relating to delivery devices and expertise.
2. Establish Cardiff as a major international centre for delivering advanced therapies to the human brain.

Work package leads: *Professor William Gray and Professor Anne Rosser*

The BRAIN Unit funding has been crucial for developing essential infrastructure for advanced therapy trials.

The BRAIN Unit is one of the first centres worldwide to deliver antisense oligonucleotide (ASO) , and RNAi therapies into CSF and gene therapies directly into the brain for for people with Huntington's disease (HD). Over the past five years in particular, we have consolidated our unique expertise in first-in-human (FIH) trials, delivery technology, and bespoke clinic trial design.

Our reputation has attracted several high-profile clinical trials to Wales:

- We were selected as one of a small number of global sites for the first potential disease-modifying HD treatment (Ionis therapeutics intrathecal ASO), continuing as a site for the Phase 3 Tominersen (Roche) trial
- We are an active site for WAVE therapeutics allele-specific ASO (intrathecal) and an RNA splicing agent trial (PTC therapeutics) for Huntington's Disease
- Cardiff is one of only five sites globally performing intracranial delivery of the AMT-130 gene therapy into the striatum of early-stage HD patients using advanced MRI-guided stereotactic surgery—the only UK site with this capability
- One of three centres delivering the AskBio PD5_CS201 trial for Parkinson's Disease using AAV2-GDNF therapy
- One of three worldwide centres delivering the AviadoBio PGRN-001 ASPIRE trial for frontotemporal dementia—the first Advanced Therapy Medicinal Product (ATMP) developed by the UK Dementia Research Institute
- Globally one of the first three sites recruiting for the first-in-human Phase 1 trial of Alnylam's investigational RNAi therapy (ALN-HTT02) for Huntington's disease.

This progress has been supported by establishing the dedicated Neurosciences Research Unit (NRU) at the University Hospital of Wales.

The NRU is now financially self-sustaining and supports two clinical fellows, six research nurses and 26 clinical trials across neurological disorders including Huntington's Disease, Multiple Sclerosis, Parkinson's Disease, Motor Neurone Disease, Migraine and Epilepsy.

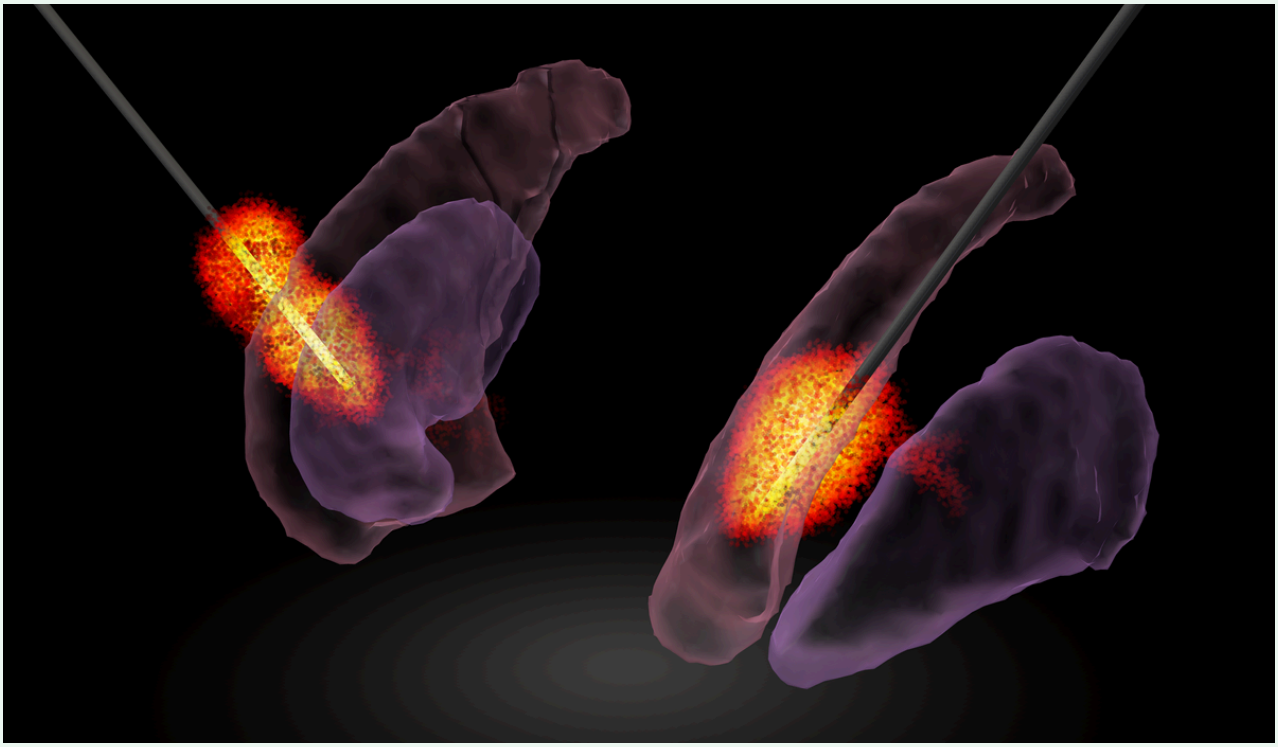
In the past two years, we've built on this foundation by securing external funding to expand our capacity for delivering neurosurgical advanced therapy clinical trials.

Thanks to additional funding from Advanced Therapies Wales and Midlands Wales ATTC, we now have a team dedicated to new ATMP trial set up and execution including a Senior Research Nurse, Research Nurse and Locum Consultant Neurosurgeon.

In addition to developing a global reputation for our ability to deliver advanced therapies intracranially, we are also leading research in this field, focussing on solving known challenges associated with delivery.

For example, in November 2024, we finalised a data sharing agreement with UniQure to analyse a globally unique dataset of MRI scans during ATMP infusion from over 30 participants and have begun analysis of this data.

This offers a huge step forward in understanding the delivery science behind the clinical trials and how we can improve the delivery of gene therapies for neurological and neurodegenerative diseases, a key focus as we move forward.



This schematic image demonstrates ATMP (fiery blobs) administration into the caudate heads (taupe coloured deep brain structures affected in Huntington's disease) via thin surgical catheters. Ideally, this should be contained to the target structure, and the small degree of ATMP leak outside of the caudates as seen on these images represents an ongoing challenge in ATMP delivery

Providing human adult neural tissue to model disease and validate novel therapies and advanced MR imaging

Work package aim: To support and expand a previously funded unique human adult (hA) tissue facility to perform 2D & 3D culturing of primary brain tissue (Gray, Zaben), for disease modelling and extend this to developing 3D cultures to support brain tumour research.

Work package lead: *Professor William Gray*

Our focus has been on optimising human tissue processing output and improving 3D hi-spot culture models of living human brain tissue, allowing longer-term tissue culture to enable studying long-term effects and conditions.

The improved protocols, collaborations, and new organotypic slice and hi-spot models have enhanced tissue processing capabilities, enabling broader research opportunities, preserved brain microstructure studies, traumatic brain injury insights, and potential for increased collaborations within and outside Cardiff University.

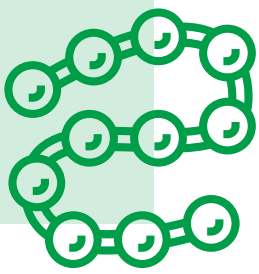
This is evidenced through increased research projects using living human tissue to test methodologies across a range of diseases:

Dr Florian Siebzehnrubl

Our project investigates differences in proteins between more aggressive and less aggressive glioblastoma cells to find new ways for treating glioblastoma by stopping more aggressive cells from growing.
We want to understand how protein production is conducted in each glioblastoma cell type, and we will combine different ways of investigating proteins inside glioblastoma cells.

As part of this study, we are using a new type of microscope for measuring protein amounts inside glioblastoma cell types and this is exciting because this technology has the potential to readily identify more aggressive glioblastoma cells, with increased sensitivity and quicker than ever before.

We will test this in living human patient material, provided by the BRAIN Unit to evaluate its diagnostic/prognostic value. This new technology could help other scientists and clinicians in the future by making it easier to identify and study more aggressive cancer cells.

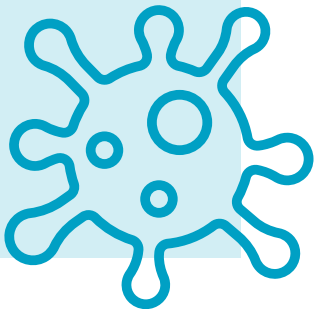


Dr Alan Parker

Our funding from Cancer Research Wales focusses on the development and assessment of “smart viruses” engineered to only recognise and infect glioma (brain cancer) cells.

Once inside glioma cells, these viruses replicate and eventually burst the glioma cell, spreading daughter virions to surrounding cells to repeat the process. To make them even more effective, we alter the viral DNA further so that they additionally force the infected cells to produce anti-cancer immunotherapies. These medicines, produced by infected glioma cells, signal to immune cells to recognise and kill the tumour cells.

So far, we have only been able to test these “smart viruses” in commercially available cell lines, which – whilst useful – fail to recreate the complexity of primary patient tumours. Our new funding will allow us to rest how well these agents work in material immediately derived from patients undergoing glioma resection, which is surgically removed and processed by the human tissue team at the BRAIN Unit. This represents the most relevant pre-clinical module we can use before progressing towards clinical trials in patients.



Professor Derek Jones

With our MRC funded collaboration with Professors Gray & Hamandi, Dr Marco Palombo and investigators at UCL and in the USA, we are examining the microstructure of the human brain in patients with focal cortical dysplasias using both advanced MRI and histology on human brain tissue.

This will help us to develop new MRC scanning sequences to reveal lesions currently invisible to clinical MRI for patients being worked up for epilepsy surgery.

Biobanking

Work package aim: To develop and expand our comprehensive bio-resources of clinical and biological data to facilitate translational, and clinical research across a wide range of neurological diseases, allowing efficient participant engagement and recruitment to study-ready cohorts.

Work package lead: *Professor Neil Robertson (Welsh Neuroscience Research Tissue Bank - WNRTB) and Professor Owain Howell (Swansea Neurology Biobank - SNB)*

Cardiff

The Wales Neuroscience Research Tissue Bank (WNRTB) has secured ethical approval until at least 2029, allowing it to continue collecting, processing, storing, and distributing biosamples for neuroscience research.

Since 2014, the WNRTB has received 104 applications from 63 research collaborations, with a 97% approval rate. Of the 18,254 requested samples, nearly 10,341 have been provided to researchers as of March 2025.

After a four-month closure during early COVID-19 lockdowns, the biobank implemented changes including postal recruitment. The Multiple Sclerosis (MS) research project, SNOWDONIA, obtained 235 consents primarily through this method.

Whilst epilepsy research was severely impacted by the pandemic and was slow to recover with no access to healthy volunteers, neurosurgery cases continued to provide direct recruits.

The remote study COVID19-DREAM dry blood spot study was particularly successful, collecting over 1,700 samples, from 761 participants during lockdowns. This research produced several published papers on COVID-19 vaccine response in people with Multiple Sclerosis

The biobank has successfully secured significant equipment funding, including a cutting-edge SiMOA platform (£250k) through Cardiff University's Research Infrastructure Fund, which is now operational for analysing biomarkers like Neurofilament light chain levels.

This technology has enabled several funded projects and publications, including an MRC-funded Biomarkers in MS paper and DEVISE-HD study. Additionally, recent Voluntary Scheme for Branded Medicines Pricing and Access (VAPG) HCRW Equipment Call 2025 funding allowed purchase of two incubators and a centrifuge to support the laboratory's clinical trial work.

***SNOWDONIA is an epidemiology for Multiple Sclerosis study, and Epilepsy-Bio is an epidemiological study of epilepsy. Participants are consented to these projects with the option of depositing half of their samples to the WNRTB.**

Swansea

The Swansea Neurology Biobank has secured approval to operate until 2027 and continues to collect and share valuable brain tissue samples. Research using these samples has been published in top science journals like Nature Genetics and Nature Communications.

Over the past five years, with BRAIN Unit support, Swansea researchers have won significant funding, such as:

- **2020-21:** Funding for Huntington's disease research, studying fats in the brain that might help diagnose the disease. This success led to a follow-up project in 2024-25 examining potential markers in body fluids (CHDI Foundation)
- **2021-22:** Two-year Fellowship awarded to Dr. Angelini to study special fats important for brain cell connections (MRC/AMS Springboard Fellowship Award)
- **2022-23:** £2.49 million in grants, including money for a specialized machine to study brain chemistry (various, including MRC)
- **2023-24:** Funding to develop better ways to diagnose rare diseases using fat and chemical analysis (MRC)
- **2024-25:** £385,618 grant to Professors Griffiths and Wang to find markers for motor neurone disease (MRC MND Accelerator grant)

These research efforts are already making a real-world difference. The rare disease diagnosis project has helped patients at the SWAN Clinic by providing unique chemical information about their conditions.

Additionally, Multiple Sclerosis Society funded PhD studentships in 2022-23 and 2024-25, creating valuable partnerships between Swansea University, the NHS, and universities in the UK and Europe.

The team's reputation continues to grow internationally. In 2024, Swansea researchers started collaborating with global teams on understanding how brain "white matter" becomes damaged in disease, using brain inflammation patterns to measure disease severity, and studying genetic factors that might predict MS severity.

Central to this progress has been Dr. Lauren Griffiths, supported by BRAIN funding, who has helped secure grants and create new research partnerships, strengthening Swansea's position as a growing centre for neuroscience research.

Patient and Public Involvement and Engagement (PPI)

Work package aim: To continue our work on PPI and engagement with patients, the public, the third sector, NHS and industry.

Work package lead: *Dr Cheney Drew and Mr Peter Roberts*

Understanding the mechanisms of how diseases develop and progress is key to discovering new treatments. However, another critical factor in therapy development is the patient voice.

It is vital that we include the views of people with lived experience of disease in the development process to make sure what we are doing is relevant and will make a fundamental difference to their lives (largely referred to as public involvement).

It is also important for us, as researchers, to communicate how and why we do things to improve trust and understanding within communities and to improve awareness across the general public (commonly referred to as engagement).

Public Involvement describes a bidirectional exchange of information, as people living with disease work alongside researchers to guide research projects or clinical trials, bringing their unique understandings together to provide a more effective pathway to delivering successful research.

We believe this is essential in the development of advanced therapies, where the nature of the treatments and their delivery add a greater degree of complexity than occurs in the development of traditional medicines.

Cardiff has been leading the way in listening to the patient voice in cell and gene therapy. This work started back in 2017 with extensive patient involvement in the design of the TRIDENT cell transplantation trial in Huntington's disease which included embedding a process evaluation as a fundamental objective of the study.

This comprised comprehensive, interviews with trial participants and trial delivery staff about their experiences through the trial. This approach evolved, with the award of funding from the leading charities Parkinson's UK and Cure Parkinson's to conduct similar interviews with people with Parkinson's who participated in a therapeutic trial which involved neurosurgical delivery. (The LEARN study).

Findings from this study have been used to create resources that will support future trial participants as they consider trial participation in advanced therapies and to determine how best to support trial participants as they go through the rigours of a challenging trial. Further funding from the Michael J Fox Foundation aims to expand the impact of these resources, by including contemporaneous interviews from people currently taking part in a stem cell therapy trials. This is alongside additional work on understanding the wider views and knowledge of the PD community surrounding advanced therapies, with a particular focus on improving inclusivity and diversity in ATMP research.

As part of our work to support widening knowledge of cell and gene therapies, Cardiff University and the BRAIN Unit are partners in the **EuroGCT** project, providing reliable and accessible information on the use of cell and gene therapies for the public, patients and researchers. www.eurogct.org.

Similarly, our PPI lead is a long-standing member of the ATMP Engage group, which brings together UK-based stakeholders with an interest in ATMPs to discuss and collaborate on PPIE activity. This has led to enhanced collaboration with Midland and Wales Advanced Therapy Treatment Centre, where we are leading on the development of a comprehensive PPI strategy for ATMP research and delivery within the UK, with a spotlight on issues of equity of access and public awareness of ATMPs.

The PPIE activities of BRAIN ensure that the patient voice is centred in the work that we do to bring novel treatments to people where disease modifying therapies do not yet exist.

The depth and breadth of HD research in Wales has recently been recognised by the launch of the new Huntington's disease Centre in Wales network, which aims to bring together multidisciplinary researchers across the translational pipeline and provide a platform for developing and supporting world leading HD research, including that into advanced therapies for HD.

In April 2024, we were pleased to co-deliver a public facing event called *Working together for better brain health* with the National Centre for Mental Health.

Professor Liam Gray was interviewed by public contributor Jacqui Campbell about the importance of PPI in clinical trials during our Working together for better brain health engagement event.

The engaging and interactive programme saw 45 members of the public enjoy talks from some of our research partners and learn more about how those leading research value the dedicated contributions from the public.

Attendees were also treated to a range of interactive stalls and games, explaining some of the scientific principles behind the work we do.

At the event, one attendee remarked:

"My father had Parkinson's and there wasn't much out there in the way of support or involvement, it felt like a lonely experience for us as a family. I can see from this event that things have changed since 1990."

Meet the researcher

Dr Nicholas Bennion

Early Career Researcher, School of Engineering, Cardiff University

About me

I am a biomedical engineer with experience in both industry and academia. My PhD at Cardiff University focused on modelling soft tissue mechanics during neurosurgery, and I have since contributed to the design, development and Intellectual Property protection of multiple medical devices in regulated settings. My work bridges clinical need with technical innovation, with a focus on translation into real-world health impact. I am currently supported by funding from Advanced Neurotherapies Centre and Neuroscience and Mental Health Innovation Institute of Cardiff University, and the European Huntington Disease Network.

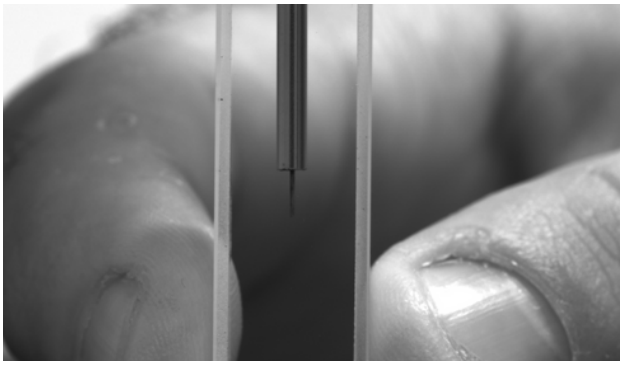
The research

I'm working on the development of a novel medical device to improve the delivery of advanced therapies directly to the brain.

These Advanced Therapy Medicinal Products (ATMPs) include cutting-edge gene and cell-based treatments that are showing real promise in tackling conditions such as Parkinson's and Huntington's disease. However, delivering them to precise locations in the brain remains a challenge, with current methods often resulting in incomplete or inconsistent delivery.

My research addresses this delivery challenge by designing and testing an innovative device aimed at improving the accuracy and reliability of ATMP administration, while ensuring the therapy stays in the intended region. The work involves close collaboration between engineers, clinicians, and imaging specialists to ensure the device is suitable for preclinical evaluation and future clinical translation.

Early testing has been promising, with further work ongoing to refine the approach and gather the data needed to support larger-scale funding bids.



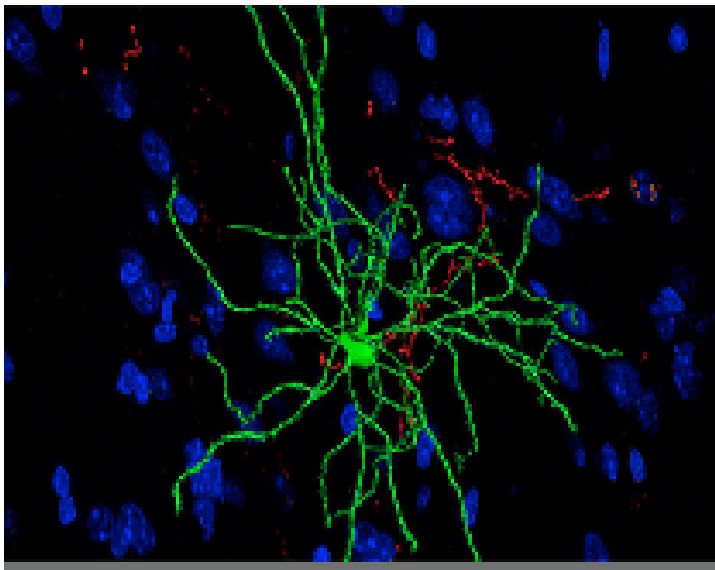
Research implications

We anticipate that the project will soon progress to preclinical trials and ultimately improve the delivery of ATMPs in first-in-human studies.

By improving the precision of therapeutic delivery, the research aims to improve clinical trial effectiveness, reduce treatment variability, and support the safe introduction of next-generation neurological treatments. It may also contribute to broader advances in digital surgical planning, regulatory pathways for novel therapies, and more consistent outcome prediction.

Spotlight on
Cell product development

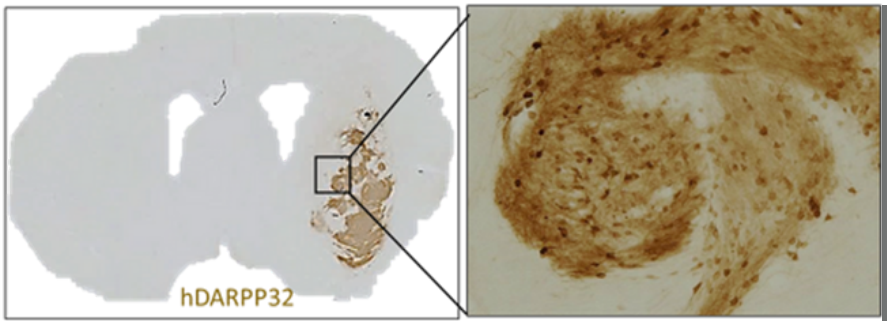
Neurodegenerative diseases, such as Huntington's (HD), Parkinson's and Alzheimer's diseases, result in progressive death of specific groups of neurons in the brain. This prompted interest in cell transplant therapies in which healthy cells are transplanted into the area of degeneration, where they can mature, make synapses with downstream brain regions, and take over the function of the cells that have been lost.



Medium spiny neurons (MSNs) are the principle projection neuron of the striatum and are the neuronal cell type that degenerates in Huntington's disease.

For such a therapy to be successful, it is essential that the transplanted cells are primed to develop into the exact neuronal subtype lost in the disease. Most groups globally who work on such therapies generate such cells from pluroipotent stem cells (embryonic stem cells (ESCs) and induced Pluripotent stem cells (iPSCs)).
Generating cells with the right characteristics has not been easy. We have been working for many years to generate cells from human ESCs for HD, in which medium spiny neurons (MSNs) the striatum degenerate.

We led an EU consortium that produced a differentiated protocol for making MSNs suitable for transplanting into humans. We have shown that these cells survive transplantation into animal models of HD and that they are capable of restoring damaged neuronal circuitry.
Over the last couple of years we have worked with the UK cell and gene catapult to work out the pathway to a first-in-man clinical trial. In March of this year, we met with MHRA to discuss the design of a Good Laboratories Practice (GLP) toxicity study, which will probably be the last preclinical study needed, and in parallel we have been designing the clinical trial that we hope will be at the end of this particular journey.



A graft of hESCs directed to a medium spiny neuron fate using our differentiation protocol, and transplanted into the rodent brain. The graft is stained with human specific DARPP32, which is an MSN marker.

International Collaborations

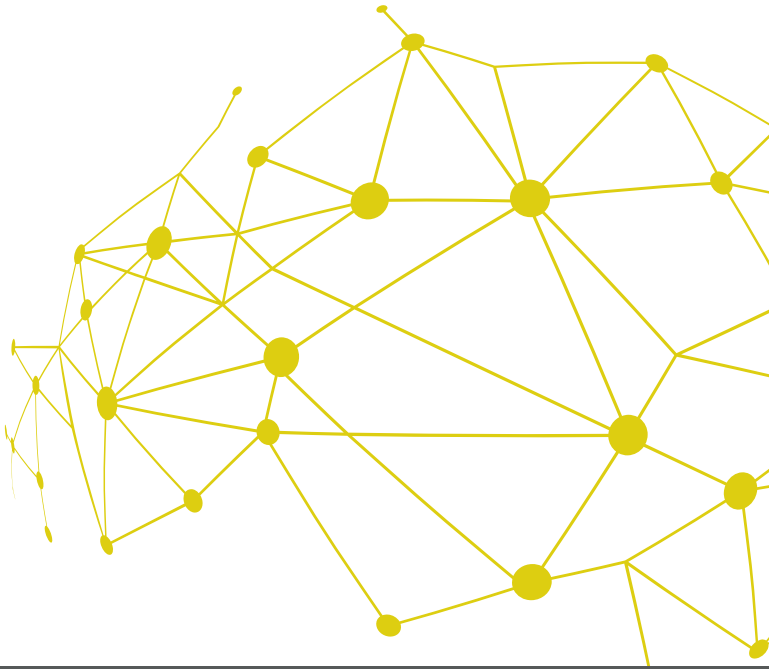
Many of the most potent disease-modifying treatments that are being considered for use in brain diseases are advanced therapeutic medical products (ATMPs, ie gene or cell therapies) or interfere with gene function, such as antisense oligonucleotides or interfering RNAs. The reason for this is that they are often the best method for directly targeting disease mechanisms. However, getting these products safely and effectively into the brain is complex and poses several challenges.

These challenges include multiple issues relating to surgical instrumentation, trial design, the selection of suitable and sensitive primary and secondary outcomes and compliance with regulatory regulations. In addition, production of clinical-grade cell and gene medicinal products requires adherence to regulatory standards with extensive quality control of the protocols across different laboratories and production centres.

Currently, there is no consensus on how best to address these challenges, so we formed two international consortia to address these issues for Huntington's Disease (HD); "Stem cells for Huntington's Disease (SC4HD)" (*https://www.sc4hd.org/*) and the "Advanced Therapies Working group (ATWG)", which is under the umbrella of the European Huntington's Disease Network (*https://ehdn.org/advanced-therapies-wg/*). The ATWG covers issues related to both cells and genes and the SC4HD picks up the additional cell-specific challenges.

Both groups comprise researchers and clinicians who are working to develop guidance and greater standardization for the HD field, in the hope that this will also provide a template for other neurodegenerative diseases. Both groups were established in 2018 and have held a series of international face-to-face meetings across Europe and North America (co-hosted by BRAIN Unit leads Prof Anne Rosser and Dr Cheney Drew, funded by the European Huntington's Disease Network, the California Institute of Regenerative Medicine and CHDI), in addition to regular online discussions.

Together we have published several papers that are starting to provide guidance for the field. This work is ongoing and in order to provide more depth of discussion to address the most difficult issues, we have formed several task forces. One example of a task force is the Neurosurgical Task force, which is holding a workshop in Venice in Autumn 2025, led by Profs Liam Gray, Anne Rosser in Cardiff and Romina Aron Badin in Paris, as part of the "Neuroscience School of Advanced Studies" series.



Conclusion

Sustained funding from Welsh Government, through Health and Care Research Wales, has enabled the BRAIN Unit to refine its research focus over the past five years. The unit now concentrates on optimising the direct delivery of advanced therapy medicinal products (ATMPs) to the human brain. By investigating both the mechanisms of therapeutic delivery and treatment efficacy, the unit is advancing translational research in neurological interventions as we transition into our new identity of the Advanced Neurotherapies Centre.

We are actively working with Cardiff Health Partners, the Cell & Gene Therapy Catapult and wider industry partners to identify investment opportunities to build our Centre of Excellence, allowing us to expand our capabilities and attract research opportunities. Meanwhile, our portfolio of first-in-human trials continues to grow, with the first surgery (of up to 20) for the AskBio Parkinson's Disease trial scheduled for Q2 2025. We are also conducting feasibility assessments to become a designated site for antisense oligonucleotide (ASO) trials in myotonic dystrophy.

We continue to build our translational research around the advanced therapy clinical trial activity, advancing the field by understanding the delivery science behind the clinical trials and how we can improve the delivery of gene therapies for neurological and neurodegenerative diseases. We have several projects underway and more coming on board as we move into the new award period.

Engagement with public representatives remains central to our mission, focusing on expanding equitable access to ATMP research and treatments. Our collaboration with the Midlands-Wales Advanced Therapies Treatment Centre and industry partners has secured additional funding streams dedicated to this vital work, reflecting our commitment to combining scientific excellence with social responsibility.

Finally, I would like to thank you for your support over the past five years and I hope you have enjoyed reading this report. I look forward to sharing our continued successes with you over the coming years.

Professor William Gray
BRAIN Unit Director

Interested in getting involved?

Help influence research by joining our public and patient involvement group, BRAIN Involve.

Please contact us for more information:

antc@cardiff.ac.uk

Stay in touch

In April 2025, the BRAIN Unit will be rebranded as the Advanced Neurotherapies Centre (ANTC). Connecting with us on social media is the best way to keep up-to-date with the latest activity from the ANTC.

Advanced Neurotherapies Centre
Cardiff University
Hadyn Ellis Building
Maindy Road
Cardiff
CF24 4HQ

antc@cardiff.ac.uk
@advancedntc
brain.wales
advancedntc

Cardiff University | Prifysgol Caerdydd
Swansea University | Prifysgol Abertawe
GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
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