Dear Friends and Supporters,

This summer, as the wild flowers on SITraN’s rooftop garden are in full bloom, I am pleased to report one of our long-term projects has reached fruition. The Head-Up collar co-developed with our first patient involvement group SMNDRAG has finally hit the shelves and been made available through the NHS to benefit patients with neck weakness from motor neuron disease and other conditions. Coming up the pipeline more projects are beginning to blossom: The first hit compound to come out of our drug screening programmes for Parkinson’s Disease is entering a clinical trial currently in set-up. We have reached a new stage to take hit compounds for the Nrf2 pathway forward for MND with funding for drug and biomarker development secured. The foundations are being laid for a new PET-MRI facility that will take our ability to measure biomarkers to new levels.

With partnerships now in place to help pull-through the translational work of SITraN such as with the Sheffield BRC, I look forward to seeing many more successful developments to come.

With kindest regards,

Professor Dame Pamela Shaw
**Highlights**

### Patient input improves Quality of Life in MND

Progress has been made in addressing quality of life issues for patients with MND this year. Partnering with orthotics company based in Chesterfield, (TalarMade), has made the Head-Up collar available on the NHS and for sale worldwide following the soft launch of the collar at the ENCALS meeting in Boston in December 2017. The myTube website, also co-developed with patients and carers in the Sheffield Motor Neuron Disorders Research Advisory Group won awards as a nutrition information resource and a programme grant, High-CALS continues this area of research. More on pages 10-11.

### Spin-out company Keapstone Therapeutics to develop Nrf2 activator

Dr Richard Mead (above) and Prof Pamela Shaw have founded a spin-out company Keapstone Therapeutics to develop a new class of drug-like molecules they found activate a pathway in the cell called ‘Nrf2’ that is dysregulated in MND. The Nrf2 pathway, sometimes referred to as the cell-life pathway regulates a host of protective genes involved in the antioxidant response to oxidative stress. The lead compound received orphan drug designation from the European Medicine Agency. Orphan drugs for rare diseases lack the market base to make their clinical development commercially viable for pharmaceutical companies. Academically led drug discovery can overcome this impasse. Parkinson’s UK recognised the funding gap in early stage drug discovery and invested £1 million in Keapstone Therapeutics to enable promising products to be fast-tracked into clinical trials. Prof Shaw and colleagues have now secured a Centres of Excellence in Neurodegeneration (CoEN) award to develop biomarkers to support a clinical trial for Nrf2 activators. More on the CoEN award on page 6. Feature on SITraN’s drug screening laboratories on pages 12 &13.
Translating discoveries with the NIHR Sheffield Biomedical Research Centre

At the end of the 1st year of operation of the NIHR Sheffield Biomedical Research Centre (BRC), we feature headline stories taking discoveries made in SITraN through to experimental medicine and beyond. The progress made this year has been celebrated with a short film available on the BRC website and youtube highlighting: 1) A clinical trial of UDCA in Parkinson’s Disease ready to recruit later this year arising from a drug hit from SITraN screens in Parkinson’s patient tissue 2) The high profile Stem Cell Treatment for multiple Sclerosis as reported by BBC earlier this year 3) Clinical adoption of the Head up Collar, and more Read the feature (pages 8 and 9).

C9ORF72: The hunt for a cure continues

Research into the commonest known genetic cause of MND continues apace. Dr Guillaume Hautbergue (right) has been awarded an MRC New Investigator research grant to work on a new therapeutic strategy for C9ORF72 (page 4) and also obtained a Royal Society International Exchange Grant to collaborate with the University of Taiwan (page 17) to investigate mechanisms in how the C9ORF72 mutation causes MND. Dr Adrian Higginbottom describes developing a drug screening assay for C9ORF72 (page 12) to test compounds targeting toxic mechanisms for therapeutic effect. Finally, we report the first gene therapy clinical trial for C9ORF72 using an antisense oligonucleotide beginning later this year on page 5.

Organising for optimum research efficacy

The formation of new working groups along four translational themes (right) is encouraging researchers to think more strategically and work together to achieve “pull-through” of SITraN discoveries into the clinic. Collaborative teams of Academic staff including Basic Scientists and Clinicians, Grant Proposal and Business Managers and the BRC Management team are meeting monthly in order to select projects for further development. The working groups help to increase collaboration along strategic alignments, share knowledge and best practice of working with Industrial partners, and to agree on areas which could most benefit from support from BRC resources and from across the Sheffield research landscape.
extensions of a short repeated sequence of DNA in a gene called C9ORF72 are the most common changes causing both frontotemporal dementia (FTD) and MND. Approximately 10,000 individuals suffer from MND and FTD at any time in the United Kingdom. In the past year SITraN researchers have published 2 major papers on the disease biology of C9ORF72 mutations.

First, Callum Walker, a PhD student jointly supervised by Prof Minoun Azzouz and Prof Sherif-El-Khamisy published a Nature Neuroscience paper showing that DNA damage and compromised DNA repair are important mechanisms in the C9ORF72 expansion mutation driving 10% of all MND cases.

In a Nature Communications paper, led by Dr Guillaume Hautbergue (top right), a potential new therapeutic approach for C9ORF72 was revealed which could be developed into a new experimental gene therapy treatment in the future. Dr Hautbergue has studied the biology of RNA — the messenger molecule that transmits genetic information from DNA in the cell nucleus out to the cellular machinery that forms proteins from active genes – looked into how RNA from the C9ORF72 mutation is actually transported.

A surprising feature of C9ORF72-MND is that the mutation is in a region of DNA that is not normally made into protein at all. Yet the RNA messenger molecules some how override normal control processes, exit the nucleus and direct the cellular machinery to make abnormal, toxic ‘dipeptide repeat (DPR)’ proteins which show up in motor neuron cells from C9ORF72 model animals and patient-derived cells. The presence of DPRs are even more unusual because they lack a chemical signal previously thought to be essential for protein manufacture in the cell. As the basic biology of C9ORF72 is so fundamentally different at a molecular level, Dr Hautbergue is beginning a long-term collaboration to study how the mutation operates (more page 17) in addition to working on potential new therapeutic approach (more on p. 13).

Findings from this research may also be directly applicable to other fatal and incurable DNA repeat expansion disorders including Huntington’s disease, spinocerebellar ataxias, myotonic dystrophy, Friedreich’s ataxia, Fragile X-associated Tremor/Ataxia Syndrome and some forms of cancer.

**Genetic knowledge of MND expands**

The MNDA UK MND DNA bank continues to contribute to the worldwide Project MINE effort to understand the genetic basis of the disease. This year another new causative gene, KIF5A has been discovered and is associated with a slower disease progression. Mutations in different regions of this gene are already known to be causative of Hereditary Spastic Paraplegia (SGP10) and Charcot-Marie-Tooth type 2.
SOD1 gene therapy trial continues to open label extension

Although the majority of patients suffer from sporadic ALS (without family history), approxi-
mately 2%, have an inherited, or familial, form caused by a variety of genetic mutations in a gene called superoxide dismutase 1 m (SOD1). A investigational gene therapy trial which uses a drug called an ‘antisense oligonucleotide (ASO) reduces the levels of the toxic SOD1 protein has been underway across the United States, Canada, and Western Eu-

Parkinson’s disease UDCA trial in set up

A drug repurposing trial using ursodeoxycholic acid (UDCA) in Parkinson’s disease will start recruitment later this year. The study protocol has been co-
developed with patients on the Parkinson’s UK patient and public involvement (PPI) group who will continue to help steer the research. This trial is a direct pull-through from the first unbi-
ased drug screen conducted in Parkinson’s patient tissue in SITraN (more on page 9). The trial contains several novel aspects. Daily activity will be objective monitored with wear-
able sensors. A cutting edge medical imaging technique, ‘31-
Phosphorous Magnetic Resonance Spectroscopy will be used to assess brain energy status in response to the drug. Overall, this study will determine if a Phase III, definitive trial would be safe, feasible and justified.

AMBRoSIA: A multicentre biomarker resource strategy in ALS

AMBRoSIA is the first large scale, long-term systematic observational study in ALS collecting biosamples coupled with clinical information to find biomarkers that can track progression of the disease. Clinical trials often fail if there is no reliable way to monitor response to treatment so biomarkers are extremely important for drug development. The study aims to 900 MND pa-
tients and 450 control volunteers and collect samples over 3 sites, London, Oxford and Sheffield. One year into recruitment 242 participants in total have taken part in the study. Dr Nick Verber, a Clinical Research Fellow who has been collecting samples on the project at SiTriN has now started a PhD looking for bi-
omarkers in the samples. AMBROsIA is a model template for systematic biosample collection that is being used as a template for other disease areas such as Parkinson’s Disease in the BRC.

Introducing:

Dr Emily Mayberry

The Sheffield MND Care Centre expanded its interdisciplinary team to include a Clinical psychology service to help patients to cope with diagnosis and direct the care of cases of Fronto-
temporal Dementia. Dr Emily Mayberry conducts cognitive screening and the neuropsychology clinical pathway and will be helping on research pro-
jects like COMMEND an NIHR funded Health Technology Assessment pro-
gramme to improve psychological health in MND (more on page 10).
Centre of Excellence in Neurodegeneration (CoEN) Award

The NIHR Sheffield Biomedical Research Centre (more on page 8) make us eligible to apply for new funding streams like the network of Centres of Excellence in Neurodegeneration. CoEN is an international initiative to drive collaboration between national centres of excellence to accelerate progress in understanding neurodegenerative disease mechanisms and advance new therapeutic approaches. Prof Pamela Shaw and a cross-Faculty team applied for a CoEN award to develop biomarkers for the master antioxidant Nrf2 pathway. Drugs that target oxidative stress in neurodegeneration (e.g. edaravone in ALS), are being investigated in clinical trials but without reliable biomarkers to monitor whether oxidative stress is reduced. Taking a multi-pronged approach the Sheffield CoEN award will measure antioxidant capacity in the brain with an Advanced Imaging method and look for a panel of oxidative stress markers in body fluids.

**SITraN has attracted over £25 m research funding since 2010**

Some other examples of recent grant funding and research awards

- **Prof Chris McDermott**
  - Leads a £2,364,069 NIHR Programme grant ‘HighCALS’ to develop and evaluate a complex intervention to achieve a high calorie diet for people with ALS

- **Prof Chris McDermott**
  - Was awarded £198,30 for a multicentre evaluation of post-gastronomy management in patients with ALS, from MNDA

- **Dr Esther Hobson and Haris Stavroulakis** were awarded a £216,228 grant under the NIHR Research for Patient Benefit scheme to optimise the delivery of Non-Invasive Ventilation in MND.

- **Prof Chris McDermott** was awarded £249,456 for ‘Pro-Sec’ continuing assessment of effective treatments for secretion problems in MND patients by Marie Curie and the MNDA

- **Prof Dame Pamela Shaw**
  - leads a Centres of Excellence in Neurodegeneration award Developing preclinical and clinical biomarkers of NRF2 pathway activation for therapeutic application in neurodegenerative diseases for £553,959

- **Dr Guillaume Hautbergue**
  - awarded £435,000 MRC New Investigator grant to work on manipulating the RAN translation of C9ORF72 repeat transcripts as a therapeutic strategy of neuroprotection in C9ORF72-ALS/FTD.

- **Professor Dame Pamela Shaw, Dr Laura Ferraiuolo and Dr Richard Mead** join an EU funded consortium ‘Euroneurotrophins’ training network with €273 288 apportioned to Sheffield.

- **Prof Arshad Majid**
  - was awarded £800,000 under the MRC asset sharing scheme with AstraZeneca for MMP 9/12 inhibition in experimental stroke

- **Prof Oliver Bandman**
  - was awarded £272,119 from the JP Mouton foundation for a drug re-purposing trial of UDCA in Parkinson’s disease

- **Dr Laura Ferraiuolo**
  - was awarded £125,560 from BenevolentBio industrial sponsorship for continued collaboration drug screening for neurodegeneration

- **Dr Guillaume Hautbergue**
  - was awarded £169,358 from the MNDA for Novel therapeutic strategies to prevent toxicity in C9ORF72-related MND
UK’s 8th combined PET-MRI scanning facility breaks ground in Sheffield this summer

An appeal has been ongoing for the past year to bring the future of medical imaging to South Yorkshire which will help research into MND, stroke, Parkinson’s and other diseases tremendously. PET-MRI combines two powerful imaging techniques into one scan bringing precise functional metabolic information from PET imaging into the high visual resolution of MRI. This gives an unprecedented level of detail about the physiological state allowing for early diagnosis and treatment even before overt symptoms appear. New biomarkers to track disease processes and see whether a person is responding to a given treatment are possible with PET-MRI.

Dr Tom Jenkins has been working with collaborating PET-MRI facilities in Manchester and Cambridge to conduct pilot work with MND patients from Sheffield travelling to participate or patients recruited from other clinics for the time being. With only 7 other PET-MRI centres around the country, the addition of the Sheffield Scanner will be very significant for patients nationally.

Directly connecting with the Royal Hallamshire hospital, the new facility is close to the Neurology clinic

The scanner appeal has received widespread support from staff, current and former students, members of the local community and friends of the University. The Big Walk 2017, walking 50 miles in 24 hours proved a popular event raising £115,000 through 272 sponsored participants (118 of whom made it to the finish line). The Big Walk 2018 will happen on the 22nd of June with a slightly more gentle 26 mile stroll through the Peaks.

The Big Walk 2017: SI TraN staff Guillaume Hautbergue and Erica Lin were among a large team sponsored to walk through the Peak District.

DARE office raise £1.5 of £2 million goal

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Sheffield BRC

What is a BRC?
The National Institute for Health Research (NIHR) commands a 10% equivalent of the whole Department of Health budget for health research with the mission to improve the health and wealth of the nation. NIHR fund 13 different types of infrastructure of which Biomedical Research Centres (BRCs) are one. BRC awards to University-Hospital partnerships help to pull through scientific advances into early phase clinical trials and experimental medicine, predominantly by providing infrastructure including funding personnel that can be strategically allocated to support research objectives. In the Sheffield BRC these so far include a clinical trials manager, research nurse, data manager, postdoctoral scientists and 8 trainees (PhD students and Clinical Research Fellows). BRC Manager Jodie Keyworth oversees the centre operationally and Prof Dame Pamela Shaw is the Director.

Translational Neuroscience for Chronic Neurological Disorders
There are 20 BRCs around the country but Sheffield is the only one with the sole focus on Neurology. This standing has been achieved on the basis of SITraN’s research excellence and the BRC functions to bridge the gap between the translational findings at SITraN and early phase clinical trials. There are many projects going on simultaneously across the Sheffield BRC in 3 main areas of neurology research: Neurodegeneration, Neuroinflammation and Cerebrovascular Disease. Supporting themes of Advanced Medical Imaging, Genomic Medicine and the NIHR Sheffield Clinical Research Facility support the neurology research. Across the board, standardised protocols for collecting clinical and biological information are being developed so that data can be integrated, shared, and translational research become streamlined.

Opportunities
Having the BRC status enables University of Sheffield and Sheffield Teaching Hospitals NHS Foundation Trust researchers to apply for different types of awards from bodies such as the network of Centres of Excellence in Neurodegeneration (CoEN) and Innovate UK. A raised profile and access to new business initiative is stimulating new commercial partnerships too.

Sheffield BRC binds Neuroscience with Engineering, Bioinformatics & Imaging
Major achievements in the first year

HeadUp: Novel neck collar commercially and clinically adopted
5 years ago in SITraN, Professor Chris McDermott and our first patient and carer involvement in research panel, the Sheffield Motor Neuron Disorders Research Advisory Group (SMNDRAG), began addressing the issue that there were no orthotic devices that gave adequate neck support while allowing enough movement and comfort to be worn for daily life. This year licensing and manufacture with local company TalarMade has made the collar available through the NHS and to buy worldwide. The journey taking an idea through to having a revolutionary new product on the market goes to show what can be achieved through cross-disciplinary research and true partnership with patients. More on page 10 overleaf.

Drug discovery from bench to bedside for Parkinson’s Disease
Parkinson’s disease (PD) affects over 6 million people worldwide and there are no disease modifying treatments available. L-Dopa only partially manages symptoms and fails to slow the progression of the disease. In the drug screening laboratories here at SITraN High Content Imaging equipment rarely seen outside of the pharmaceutical industry is used to study patient derived models of neurodegenerative diseases like PD. Skin biopsies from patients provided fibroblasts to screen a library of 2000 compounds in the first ever drug screen in PD tissue in 2013. Ursodeoxycholic acid (UDCA) emerged as a lead candidate that rescued mitochondrial dysfunction, an important pathogenic mechanism in the neurodegeneration of PD. Already licenced for use in other diseases, UDCA is now entering a drug repurposing clinical trial for PD led by Prof Oliver Bandmann (more on page 5).

Advanced Therapy Stem Cell Treatment for MS breakthrough
Autologous Haematopoietic Stem Cell Treatment (AHSCT) is a novel therapeutic strategy based on deleting autoreactive lymphocytes with the use of various ‘conditioning regimens’ and restarting a new immune system, using patients own haematopoietic stem cells, in a non-inflammatory environment without co-stimulatory signals. The treatment received worldwide attention with a BBC Panorama programme following Prof Basil Sharrack’s patient on the treatment. The interim results of a long-term 3-site study following up AHSCT have just been published (Neurology, 2018; 90, S36.004) confirming it the most effective treatment for MS to date and setting the stage for Sheffield to become a centre for excellence for AHSCT for neuroinflammation.
Symptom management research gathers momentum under Prof Chris McDermott

This year has seen a host of successes and a slew of new investment in research for the symptomatic management of MND at SITraN. The Head Up collar, co-developed with the Sheffield Motor Neuron Disorders Research Advisory Group, launched on to the market and into NHS practice with the BBC interviewing Philip Brindle about the difference the device has made to his life. The myTube patient information website was recognised through several awards for its value to patients making PEG feeding choices (more page 18). A range of new studies are starting from the large programme grant HighCALS to those on service delivery for NIV and oral secretion management to improve the care that patients receive. Prof Chris McDermott reflected at his Inaugural Head of Department lecture (page 21) that putting patients at the centre of clinical practice is essential to improve their quality of life while we look for a cure.

Non-Invasive Ventilation (NIV) methods such as wearing a mask or more discrete nasal clips to support breathing during waking hours or at night is recommended to assist respiration in MND. To enhance the efficacy of NIV use Dr Esther Hobson (left) and Haris Stavroulakis are working on a Research for Patient Benefit’ grant to conduct a systematic review to identify factors influencing the optimal use of NIV (patient, equipment and service factors). A UK wide survey of NIV use will be conducted to map the current practice standards at different sites. Focus groups with policy makers, respiratory management staff, patients and carers will help to co-design an online tool and information resource to help service providers deliver NIV in the most effective way for patients.
Malnutrition is a frequent problem in MND affecting up to half of all patients. Difficulty in preparing and consuming food compounded by the frequent observation that ALS patients have a raised metabolic rate explain why two separate studies have found that caloric intake is insufficient to meet the needs of up to 94% of MND patients. The HighCALS programme is led by Christopher McDermott in collaboration with a number of colleagues at the Sheffield School of Health and Related Research (ScHARR), the University of Leeds, University of Oxford and King’s College, London. Understanding the current national service model and evaluating the effects of complex nutritional interventions as compared to standard dietary management aims to positively impact the survival, function and quality of life for the 6000 people living with ALS in the UK. Once these methodologies are established they may well prove useful in other neurological disease areas as well. Patients with Parkinson’s disease are liable to weight loss that is associated with accelerated disease progression. The possibility of using an advanced MRI technique, 31-phosphorous MR Spectroscopy to objectively measure the energy status of patients has been discussed to complement HighCALS. 31-Phosphorous Spectroscopy will be used in a clinical trial in Parkinson’s disease (page 5) on a drug that improves mitochondrial functioning. Multiple drug screening projects focus on mitochondrial function as a known mechanism in neurodegeneration (more on page 24).

Evaluating Gastrostomy Feeding in ALS

ProGas was a landmark UK multi-centre observational nutritional study which looked into the optimum method and timing for gastrostomy insertion in 323 people with MND. The findings provided evidence to show that people with MND might benefit from early gastrostomy, before substantial weight loss. Its recommendations for clinical practice have been included in the latest NICE guideline NG42 (Feb 2016) on the assessment and management of MND. PostGas is a UK multi-centre observational study, building on the success of ProGas, looking into the effect of gastrostomy feeding on the nutritional status of people with MND. The plan is to follow-up 200 patients for 9 months after gastrostomy, assess their nutritional status and identify factors that might influence this outcome. The aim is to provide evidence-based guidance on how to improve nutrition and limit weight loss in people with MND after gastrostomy. Progress so far: 17 confirmed sites; 8 open to recruitment and 9 in set-up.
Dr Adrian Higginbottom has been liaising with Quanterix, a US based company specialising in precision laboratory equipment about a system to help look for biomarkers in clinical samples. In particular, blinded samples of cerebrospinal fluid from MND patients and control volunteers have been shipped over to see whether a digital biomarker detection system can differentiate between the groups from levels of Neurofilament (NF). The returned results were unblinded by Adrian and there was a significant difference between groups. Having a system capable of detecting biomarkers in the femptogram range with a binary yes/no reporting system would be a great asset for investigating precious samples from clinical studies.

Feature: Drug Screening

Artificial Intelligence looks for candidate drugs
90% of the world’s data has been produced in the last 2 years! British artificial intelligence company BenevolentAI is using machine learning to have computers do the reading for us, conducting unbiased literature searches and scouring chemical databases to suggest compounds that could have a therapeutic effect in diseases like MND. Dr Richard Mead and Dr Laura Ferraiuolo tested one such candidate emerging from BenevolentAI in patient cell models and found that it delayed the onset of the disease and prevented death of motor neurons. Dr Richard Mead said: “This is an exciting development in our research for a treatment for ALS. BenevolentAI came to us with some newly identified compounds discovered by their technology - two of which were new to us in the field and, following this research, are now looking very promising. Our plan now is to conduct further detailed testing and continue to progress promising findings toward new treatments”.

The collaboration continues and Mark Rackham, a drug discovery scientist with BenevolentAI travelled with Richard Mead to an Industry Showcase hosted by the Northern Health Science Alliance for the 4 Northern Biomedical Research Centres (Sheffield, Leeds, Manchester and Newcastle) to take part in panel discussions on the challenges and opportunities of partnering industry with academic in the life sciences. Mark said that it had been wonderful working with Richard and Laura and stressed the importance of openness in science.

BenevolentAI

Investigating new Equipment
Dr Adrian Higginbottom has been liaising with Quanterix, a US based company specialising in precision laboratory equipment about a system to help look for biomarkers in clinical samples. In particular, blinded samples of cerebrospinal fluid from MND patients and control volunteers have been shipped over to see whether a digital biomarker detection system can differentiate between the groups from levels of Neurofilament (NF). The returned results were unblinded by Adrian and there was a significant difference between groups. Having a system capable of detecting biomarkers in the femptogram range with a binary yes/no reporting system would be a great asset for investigating precious samples from clinical studies.

Collaboration with Oncology heavyweight
Professor Thomas Hellday, Sweden’s pre-eminent cancer scientist will be joining the Faculty with a team of medicinal chemists from the Karolinska Institute. Prof Hellday made one of his major discoveries while working as a post-doctoral researcher in Sheffield, leading to a new drug, Lynparza, licenced for several cancers. It is often said that cancer and neurodegeneration are two sides of the same coin, on the one hand cells proliferate out of control, on the other, cells degenerate in the opposite direction along the same molecular pathways. A biological yin and yang that may share therapeutic targets. Many drug screening methods used at SITraN originated in cancer research. Prof Hellday plans to undertake some drug screening in SITraN, where the two teams stand to learn a lot from one another.

Prof Thomas Hellday
Developing a drug screen for C9ORF72 Motor Neuron Disease

For 7 years now researchers in the field of motor neurone disease (MND) and fronto-temporal dementia (FTD) have been trying to understand why the most common genetic cause, found to date, for MND is caused by a large repetitive DNA expansion in a gene called C9orf72. The fact the gene is simply a genetic location showed we were starting with little information about the gene’s function. In SITraN, we have helped with the global understanding of C9orf72 function (Webster et al), showing a role in autophagy (the cells waste disposal route for removing damaged proteins), which may help with future therapies. However, we do know that the mutation, a large expansion, quite common in several neurodegenerative conditions, gives rise to two different pathological hallmarks. Firstly, the expansion gets copied into RNA sufficiently that RNA foci form, which it should not, as it is located in a non-coding region and should not be long lived enough. Then even more surprisingly, not only does it exist, but it escapes the nucleus where it is made and then gets translated in the cytoplasm of the cell to generate novel proteins (dipeptide repeat (DPR) protein), due to the nature of the repetitive expansion). Both of these processes could alter normal cell function, such that over time these unwanted products compete for the cells normal basic function, and with the normal ageing process this becomes a burden too big to handle. We have generated stable cell models that express the DNA expansion as RNA, with the plan to perform drug screens to identify compounds that help the cell remove these unwanted products. However, this model, due to the instability of the DNA construct generated, took a long time to generate (2 yrs) and proved to be too variable (dynamic) for a robust drug screen. So we developed a model that produces the expansion, in such a way that all the DPR protein produced by it has a small tag, to be readily detected. In that way we can find compounds that will act on any of the aberrant cell processes that lead to the RNA being produced, or how it escapes the nucleus through to how it gets made into protein. The previous model generated will then be useful in understanding at which point in the process any hit compounds are acting.

Everything in red are abnormal macromolecules, competing with the cells normal processes. Causing cellular dysregulation that eventually, combined with time, leads to the loss of motor neurons.

Our current tagged DPR model possesses all these represented features. All the arrows in red represent potential points in the biology we could find “drugs” to modulate these processes.
Diversity in a dish; patient cell models

Scientists strive to make experimental conditions as uniform as possible to control variability. However disease models that are made to be as similar to each other as possible do not reflect the clinical reality of patient populations. By genetically reprogramming skin cells back into stem cells, scientists have been able to make patient-derived brain cells to study diseases like MND in a dish. This process erases some of the age-related changes that are acquired by the age of disease onset. Dr Laura Ferraiuolo and team having been working on a new technique to directly convert skin cells to brain cells that retain age-dependent changes, taking us closer to personalised medicine.

SHEF-1 Stem Cell Lines

Autologous Stem Cell treatment for multiple sclerosis was (page 9) was not the only advanced therapy to receive press attention this year. Patients with macular degeneration hit headlines when embryonic stem cell treatment restored their eyesight. The stem cell line ‘SHEF1.3’ that was used in the treatment is a success story for Sheffield stem cell scientists. Dr Zoe Hewitt (left) ran quality management for the team who took a vial of the original line through to Good Manufacturing Practice (pharmaceutical grade) production. The creation of the clinical grade line, bought by Pfizer in 2010, demonstrated that GMP production can be achieved by academic groups.

GMP Manufacturing Centre for Gene Therapy: Consultancy Sought

Prof Mimoun Azzouz is engaging industry leaders in GMP consultancy to provide in depth market analysis, costing and feasibility work around the proposal to establish a centre for gene therapy in Sheffield that will help take novel candidate gene therapies into clinical trials. There is a worldwide shortage of GMP manufacturers for viral vectors for gene therapy. The consultants will provide a business case for Sheffield GMP centre.
New biomarker for early diagnosis and potential therapy target

Prof Annalena Venneri and Dr Matteo De Marco published a study that received worldwide press attention as the findings could revolutionise screening for Alzheimer’s disease. They discovered that a loss of cells that use dopamine – a neurotransmitter that has a number of functions including regulating movement and emotional responses – may cause the part of the brain responsible for forming new memories to function less effectively. Prof Venneri said, “Our findings suggest that if a small area of brain cells, called the ventral tegmental area, does not produce the right amount of dopamine for the hippocampus, a small organ located within the brain’s temporal lobe, it will not work efficiently. The hippocampus is associated with forming new memories, therefore these findings are crucial to the early detection of Alzheimer’s disease. The results point at a change which happens very early on, which might trigger Alzheimer’s disease. This is the first study to demonstrate such a link in humans.” MRI scans were acquired on 51 healthy adults, 30 patients with a diagnosis of mild cognitive impairment, and 29 patients with a diagnosis of Alzheimer’s disease. The results showed a key link between the size and function of the ventral tegmental area, the size of the hippocampus and the ability to learn new material. The findings could lead to the potential to change or halt the course of the disease very early, before major symptoms manifest.

Prestigious Wellcome Trust fellowship

Dr Simon Bell has been awarded a Wellcome 4ward North Clinical Fellowship for his work “Characterising astrocyte metabolic deficits in sporadic and familial Alzheimer’s Disease to identify new therapeutic targets”. Simon’s work within SITraN focuses on metabolism in astrocytes, the main support cells of the central nervous system and how deficits in energy production contribute to Alzheimer’s disease. He uses a model in which skin biopsies from patients with Alzheimer’s disease are taken to provide fibroblasts. These connective tissue cells are then reprogrammed into astrocytes and neurons. His work also looks for ways of correlating the findings in patient-derived cellular models with clinical imaging (MRI) markers of Alzheimer’s disease.
EuroNeurotropin: a Europe-wide drug discovery training network

SITraN joined a collaboration of 10 academic institutions and 8 pharmaceutical organizations from across Europe to develop small drug agents that mimic substances made by the body called neurotrophins that sustain nerve cells. The consortium will work on natural and chemically synthesised candidate compounds. SITraN lead on high throughput drug screening Dr Laura Ferraiuolo will supervise the use of a co-culture of motor neurons and astrocytes derived from skin biopsies donated by MND patients that has been developed in her laboratory. To see whether the compounds have any neuroprotective effects in vivo, we will contribute to training a student to take forward the most promising compounds into animal and zebrafish models of Motor Neuron Disease, Multiple Sclerosis and Alzheimer’s Disease, to check whether they reach the brain and evaluate their effects. The project aims to create a new generation of young scientists with a skill set in chemical biology and drug discovery underpinning the neurotrophins work. The consortium will train 14 early stage career researchers who have been appointed.

Dr Laura Ferraiuolo (3rd from left) represented SITraN at the kick start meeting in Athens, January 2018

Industrial Partnerships

Several industrial collaborations flourished this year. BenevolentAI teamed up with Drs Richard Mead and Laura Ferraiuolo to test artificial intelligence predictions of drug screens in validated disease models. Through 2017 this collaboration has blossomed into a series of sponsored research agreements and studentships attracting £81K of research income to date, providing several jobs as well as training opportunities for the next generation of Sheffield biomedical scientists. Prof Pamela Shaw and Dr Laura Ferraiuolo entered a collaborative research project with Pfizer using patient-derived cellular models of MND for drug screening. Student Sian Heledd Brown-Wright is completing her Heptares sponsored PhD on a pharmacological therapeutic approach in MND and discussions of a clinical trial stemming from the work are underway.
Collaborations

The Jeff Wadsworths Fellowship programme

The University of Sheffield in 2017 was awarded $1.5 million to support international research partnerships and early career research fellowship exchanges by the global science and technology research organisation Battelle, based in Columbus, Ohio, USA. The gift was used to establish the Jeffrey Wadsworth Fellowships - an early career fellowship exchange programme between the University of Sheffield, Battelle and Ohio State University. The ambition for the Fellowships is to provide an outstanding educational experience for early-career researchers and to advance the academic programmes and values of the institutions involved. Battelle’s vision is to translate knowledge into innovative applications that have significant societal and economic impacts. Dr Jeffrey Wadsworth visited the Department of Neuroscience and SITraN in 2016 and highlighted it as a key area for research collaboration with the Ohio/Battelle partnership, alongside projects in engineering.

The first Jeff Wadsworths Scholar

SITraN PhD student Joe Scarrott supervised by Profs Mimoun Azouz and Pamela Shaw travelled to the Meyer lab at Nationwide Children’s Hospital Columbus, Ohio continuing a long standing collaboration between the two groups to bring viral vector mediated gene therapy for MND into human use. In Ohio Joe learnt new techniques including laser capture microdissection to isolate motor neurons from surrounding tissue. He has published his work in “Translating gene therapy for SOD1 silencing towards the clinic: A highly efficacious, off-target free and biomarker supported strategy for familial ALS” Molecular Therapy Vol 12, 7 September 2018, Pages 75-88.

Royal Society International Exchange with Taiwan on C9ORF72 biology

Dr Guillaume Hautbergue was awarded a UK-Taiwan International Exchange Programme grant from the Royal Society. From February next year, he and a colleague will kick start a series of exchange visits between SITraN and Professor Kung-Yao Chang’s laboratory at the National Chung-Hsing University in Taiwan. Researchers will collaborate on investigating the biologically unusual mechanism found in the MND linked C9ORF72 gene (more on page 4) whereby a repeating pattern of DNA from a region that does not normally form protein in healthy individuals, is expanded and made into a pathological protein via an unorthodox cellular route in the disease state. A similar mechanism operates in several other neurodegenerative diseases including Huntington’s and myotonic dystrophy. The long stay exchange visits of multiple researchers are expected to foster long-term collaborations between the Chang and Hautbergue groups.
A new collaboration with Bangladesh

On the 25th of March, a memorandum of understanding between the University of Sheffield UK, Dhaka Shishu Hospital and Barisal Biotechnology UK Ltd was signed to cooperate to improve health in Bangladesh by developing training opportunities for scientific and clinical staff and programs in teaching, research and clinical care provision.

Prof Dame Pamela Shaw, Prof Paul Ince and Prof. Ann Dalton, Director of Sheffield Diagnostic Genetics Service at the Sheffield Children’s Hospital travelled to Bangladesh to meet with the Director of Dhaka Shishu Hospital, Prof. Abdul Aziz and Dr. Sanjan Das, the founder of Barisal Biotechnology to discuss a potential new collaboration.

Opportunities such as with the Global Challenges Research Fund (below) encourage new partnerships with low to middle income countries on health related research. Barisal Biotech is a life sciences company with a focus on transferring UK healthcare, science knowhow, products, and knowledge based services into developing countries and worldwide, whose current focus is on Bangladesh.

Global Challenges Research Fund

The Global Challenges Research Fund (GCRF) is a £1.5 billion fund announced by the UK Government in late 2015 to support cutting-edge research that addresses the challenges faced by developing countries. The fund is advised by UK Research and Innovation (UKRI) and includes initiatives to reduce mortality from non-communicable diseases in addition to other health related schemes. Transferring aspects of clinical care, providing specialist research training and exchange studentships are some of the ways that SiTraN could help to improve the lives of patients suffering with diseases like MND in countries like Bangladesh. Developing transformational healthcare through multidisciplinary and multi-country collaborations is part of The University of Sheffield’s ‘Think Global’ strategy.
**New Appointments**

**Dr Haris Stavroulakis** Haris has worked at SiTraN since its inception in the area of symptom management for MND in Prof Chris McDermott’s team. Continuing his work on the impact of gastrostomy nutrition in MND through the Post-Gas study (more on page 11), Haris has achieved a Lectureship in Clinical Neuroscience. Qualified as a nurse in his home country of Greece, Haris will also be contributing to teaching at The School of Nursing and Midwifery in addition to his research activities. His main research interest is the development of new clinical interventions for optimising symptom palliation in patients with neurological illnesses and translating the findings of research into tangible benefits for patients.

**Dr Matteo De Marco** began a Non-Clinical Lectureship in the Neuroscience of Dementia. His research interests range from cerebral connectivity, the genetics of neural structure and function, machine learning in cognition and MRI.

**Vice Chancellor’s Fellow** Dr Alison Twelvetrees studies axonal transport as a mechanism in neurodegeneration. She aims to make her work translate into drug discovery for neurological diseases by expanding her team of researchers at SiTraN. www.twelvetreeslab.co.uk

Two new appointments for Genomic Medicine and Bioinformatics: **Dr Mark Dunning** (right) joins as Director of the Sheffield Bioinformatics Core which runs training courses and offers analysis support for all researchers in Bioinformatics techniques. Mark was Senior Bioinformatics Analyst at the Cancer Research UK Cambridge Institute. **Dr Matt Parker** (left) joins us from the Sheffield Children’s Hospital as one of the country’s few Clinical Bioinformaticians.

**Dr Esther Hobson** Joining as an NIHR Clinical Lecturer in Neurology, Esther’s work focuses on the area of optimising service delivery for patients with MND. Previously an NIHR Academic Clinical Fellow, Esther has extensive experience with patient and carer involvement in research and has published on digital health technology to improve access to specialist care in MND. Recently she secured an NIHR Research for Patient Benefit scheme award together with Dr Haris Stavroulakis to optimise the delivery of Non-Invasive Ventilation in MND (more on page 10).
Awards

myTube is a winner!

Video information website myTube, by patients for patients, was named ‘Nutrition Resource of 2017’ by top public health & primary care nutrition publication Complete Nutrition, (left) and won several BMA patient information awards (below). The website was made by patients and carers sharing their insights into difficult care decisions they have faced in living with Motor Neuron Disease. A pragmatic, honest and personal video resource website to inform others thinking about tube feeding in case of compromised eating and swallowing was the result making the research done at SITraN by Prof Chris McDermott’s team real and relevant to a wider audience than ever of people facing similar challenges. The myTube team included patients and carers and past members of the South Yorkshire MND Association and members of the Sheffield MND Research Advisory Group. Registered Nurse and filmmaker, Cathy Soreny recorded patient stories about having a Percutaneous endoscopic gastrostomy (PEG) tube fitted. From thinking about it, deciding to have it, deciding not to have it, and the practical reality of living with and caring for someone with a gastrostomy feeding tube, a wealth of lived experience is conveyed in the collection of short videos on the user-friendly website. A reviewer at the BMA awards said, “I was very impressed by this resource. I admired its ambition and clearly stated objective to use patient stories to encourage change. The involvement of parents and their carers has been exemplary. Patients and carers were involved throughout the process; all key choices on the content and design of the resource were user-led, with the design and clinical teams enabling this.”
Double win for Translational Neuroscience MSc. graduate Theo Wing

Jude Sellmeyer commissioned a sculpture for the award in honour of her son, Jody de Vos who passed away from MND. Jody’s love of sunflowers inspired the design for the award by scrap metal artist Jason Heppenstall. The unique piece sits in the lobby for the next round of Masters projects in MND to be assessed.

Theo’s project centred around the C9ORF72 subtype of MND which accounts for 40% of all familial cases and features an unusual process of protein production (described in more detail on page 4). Theo investigated the effect of an anti-cancer agent, Episilvestrol, and an enzyme inhibitor to prevent the unusual toxic protein from forming in cells that had been engineered to express the C9ORF72 mutation. Theo learnt many molecular biology techniques on the project including cell culture, protein analysis, immunofluorescence microscopy and cell viability assays to find concentrations of both agents that would inhibit the toxic protein forming with a high degree of sensitivity thanks to his careful work.

MSc awards

SITraN offers four taught Masters (MSc) programmes; Translational Neuropathology, Genomic Medicine, Clinical Neurology, and Translational Neuroscience which also offers an integrated PhD programme. Prizes for the best Master’s projects are awarded annually:

- The Irene and Richard Beard prize for Clinical Neurology
- The Jonathan Stone prize for Translational Neuroscience
- The Professor Paul Ince prize for Translational Neuropathology

Winning students receive £100 in vouchers.

More information on our postgraduate taught courses can be found on: www.sheffield.ac.uk/neuroscience/
Events

WISC challenge pays homage to the Ice Bucket Challenge of 2014

Whipped, iced or squirty cream went into a fun #pietaN pies in the face challenge raising £764 in the process for the Ian Pratt foundation. Carl Dundas from Barnsley propositioned Prof Dame Pamela Shaw to receive the first shot from himself and then challenge 3 more people, leading to a cascade of messy faces one hot day last July.

The 2nd International Symposium on Stem Cell Treatment in Multiple Sclerosis

Prof Basil Sharrack and colleagues received world-wide press attention following the interim results of a long-term study of autologous haematopoietic stem cell treatment for MS, announced this March (more on page 9). Just prior to the announcement SITraN hosted a conference bringing MS specialists from across the globe together to discuss the therapeutic approach. Dr Richard Burt leading the long-term trial gave a ‘hitchhiker’s guide’ to the treatment, and a care pathway for NHS patients was put forward by Prof Alisdair Coles.

SITraN Open Day

Our annual public Open Day gives all our friends and supporters the opportunity to get a behind-the-scenes look at our research. The day offers short talks with research updates, as well as guided tours and laboratory demonstrations. Last year we increased the interactive opportunities for our guests with group activities including a biosampling demonstration taking a skin biopsy from willing volunteer, Kevin Corke, porcine brain dissection and extracting DNA from strawberries. This year activities will include a mock clinical trial water taste test to show the principals involved and other attractions.

Look out for information on the next:

SITraN Open Day
Friday 6 July 2018

Entry is free, however registration is required.

Please email sitran@sheffield.ac.uk or phone 0114 222 2230

International delegates network over lunch
Sheffield Biomedical Research Centre Public Launch December 2017

Emphasising opportunities for patient and carer involvement in research, the Sheffield BRC extended invitations through research advisory groups and charitable organisations to a launch event featuring a wide range of neurological research. A live demonstration of wearable sensors for monitoring movement disorders and genomic games were among the sessions offered. Find out more on [www.sheffieldbrc.nihr.ac.uk](http://www.sheffieldbrc.nihr.ac.uk) @SheffieldBRC

Dementia Futures 2018

The University of Sheffield's Dementia Futures 2018 is a conference for members of the public who are affected by dementia and for organisations who represent or offer support to persons affected by dementia. PhD students will be communicating their research in an accessible way for this fully booked event, for some their first experience of patient and public engagement.

Prof Chris McDermott inaugural lecture as Head of Department

Prof Paul Ince retired from the University having served as Head of Department for Neuroscience since 2011 and became Emeritus Professor as well as continuing his pathology work with Sheffield Teaching Hospitals. Succeeding him as Head of Department, Prof Chris McDermott gave a lively inaugural lecture titled ‘Helping Patients to Survive the Experts’. Giving insight into developing the evidence base for delivering supportive and symptomatic care for patients living with motor neuron disease, he highlighted the advantage of allowing people living with MND to have direct and collaborative input into research. The HeadUp collar for neck weakness, award winning patient information website myTube, and evidence based guidelines for non-invasive ventilation and tube feeding are among his substantial contributions to the field.

NHS70: 5th July 2018

Look out for stalls and exhibits on the past, present and future of healthcare at Sheffield Cathedral this July marking 70 years since the NHS formed.
Events

Wilko staff raise £4,225 for MND research

Gemma Middleton (2nd right) who was diagnosed with MND at just age 29, presents a cheque raised through a staff karting event organised by her Father’s (Nigel, left) colleague Martin Talyor. The funds will be allocated to new laboratory equipment (page 12).

Taking to the skies for MND research

Sue Rawdings who’s Father sadly passed away from MND raised over £6000 with a skydive and family fun day she organised to support research. Also taking to the skies, Yvonne Foster (right) at the age of 86 following her diagnosis of MND successfully completed a gliding challenge from Sutton Bank gliding club (and back) raising an incredible £18,000 in the process.

SITraN collections at the Rugby League

On a freezing night in February 2017, a small team of SITraN staff attended the Leeds Rhinos vs the Salford Devils game. Standing at the gates with their buckets and SITraN tee-shirts, they raised awareness among our regional neighbours and collected £520 in donations in the process.
Golden Globe Race 2018; a non-stop solo sail race around the world is supporting SiTraN this year

To celebrate Sir Robin Knox-Johnston’s historic 1968/9 world first solo non-stop circumnavigation in the Sunday Times Golden Globe Yacht Race, a new race will be staged to mark the 50th Anniversary, starting from Falmouth on 14 June 2018. The SiTraN Challenge race will be the first part of this epic adventure, taking the skippers from Falmouth to Les Sables-d’Olonne.

Like the original event, the 2018 Golden Globe Race is very simple. Depart on 1 July 2018 and sail solo, non-stop around the world, via the five Great Capes and return to Les Sables-d’Olonne. Entrants are limited to sailing similar yachts and equipment to what was available to Sir Robin in that first race. That means sailing without modern technology or the benefit of satellite based navigation aids.

19 sailors will be taking part in the 30,000 mile unassisted voyage including 5-time circumnavigator and father figure of French solo sailing Jean-Luc van den Heede.

Don McIntyre, Australian Adventurer and Explorer is the founder and Race Chairman of the 2018 Golden Globe Race which will be sailed under the auspices of the Royal Nomuka Yacht Club in the Kingdom of Tonga. His Royal Highness, Crown Prince Tupouto’a Ulukalala is Patron of the Race and plans to officiate at the start of the Race in Falmouth. Our kind friend and supporter, Stuart Keane will be travelling down to Falmouth for the start of the race.
Selected Publications


**Nature Communications** July (2017)  

**Nature Reviews Disease Primers 3, 17071 (2017)**  
**Amyotrophic Lateral Sclerosis.** O Hardiman, A Al-Chalabi, A Chio, EM Corr, G Logroscino, W Robberecht, PJ Shaw, Z Simmons, L Van der Berg.

**Neurology** 04 Oct (2017)  
**Meta-analysis of pharmacogenetic interactions in amyotrophic lateral sclerosis clinical trials.** RPA van Eijk, AR Jones, W Sproviero, A Shatunov, PJ Shaw, PN Young, CE Shaw, G Mora, J Mandrioli et al.

**Brain** 140(6):1611-1618 Jun (2017)  
**A comprehensive analysis of rare genetic variation in amyotrophic lateral sclerosis in the UK.** S Morgan, A Shatunov, W Sproviero, AR Jones, M Shoai, D Hughes, A Al Khlefat, A Malaspina, KE Morrison, PJ Shaw et al.

**A data-driven approach links microglia to pathology and prognosis in amyotrophic lateral sclerosis.** J Cooper-Knock, C Green, G Altschuler, W Wei, JJ Bury, PR Heath, M Wyles, C Gelsthorpe, JR Highley, A Lorente-Pons, K Doyle, K Otero, B Traynor, J Kirby, PJ Shaw, W Hide.

**Human Molecular Genetics** 26(6):1133-1145 (2017)  
**C9ORF72 hexanucleotide repeat exerts toxicity in a stable, inducible motor neuronal cell model, which is rescued by partial depletion of Pten.** M Stopford, A Higginbottom, GM Hautbergue, J Cooper-Knock, PJ Mulcahy, KJ De Vos, A Renton, H Pliner, A Calvo, A Chio, B Traynor, M Azzouz, PR Heath, ITALSGEN consortium, NeurOX consortium, J Kirby, PJ Shaw.

**Dis Model Mech** 26 May (2017)  

**Sleep** 1:40(8) Aug (2017)  
**Prodromal Parkinsonism and Neurodegenerative Risk Stratification in REM Sleep Behavior Disorder.** T Barber, M Lawton, M Rolinski, S Evetts, F Baig, C Ruffmann, A Gornall, JC Klein, C Lo, G Dennis, O Bandman, et al.

**The Lancet** 15 Aug (2017)  
Selected Publications

**Neuron** 97(6):1268-1283 March 2018


**Molecular Therapy Nucleic Acids** (2018)


**The Lancet Neurology** (2018)


**Therapeutic Targets for Neurological Diseases** 4:15 Jan 2018


**Frontiers in Molecular Neuroscience** 10:09 Nov 2017


**Ergonomics** 61(2):329-338 01 Feb 2018


**FEBS Letters** 17 Dec 2017

*Translational approaches to restoring mitochondrial function in Parkinson's disease.* Mortiboys H, Macdonald R, Payne T, Sassani M, Jenkins T, Bandmann O.

**The Lancet Neurology** 16(9):701-711 Sep 2017


**Journal of Neurology, Neurosurgery, and Psychiatry** Feb (2018)


**Journal of Alzheimer's Disease** 63(1):167-180 10 Apr 2018

*Volume and Connectivity of the Ventral Tegmental Area are Linked to Neurocognitive Signatures of Alzheimer's Disease in Humans.* De Marco M, Venneri A

27
Michael Hickman, Chairman of the Sheffield Motor Neurone Disorders Research Advisory Group 2017-2018

Michael worked with British Tele- coms before he retired and used his background in IT and communica- tions to set up the MNDA South Yorkshire branch’s first website. He was their publicity officer and last year received a long-service medal recognising his 10 year’ service to the branch. Michael was tremendously help- ful in terms of advice on fund rais- ing and research. He co-edited the SYMNDAs newsletter and Chaired the SMNDRAG. He was instrumental, together with Gor- don Harrison, in securing the MNDA as one of the charities to benefit from the Sheffield Half Marathon event and he was in- volved with the planning of it be- tween 2009 -2012 and gave his time as a Marshall for the event helping to man the water station together with friends and family. Michael cared for his wife, Chris- tine who died of MND in June 2005. He became a member of the MNDA and South Yorkshire branch committee member from 2007. In 2009 he joined SMNDRAG and chaired this group from 2017. He offered to help fur- ther with patient and public in- volvement (PPI) for the Sheffield Biomedical Research Centre. Mi- chael fundraised and donated regularly for St Luke’s Hospice in tribute to his late son, Christo- pher. He had also been a Cycling club Secretary, a Scout group Treasurer, a Church Finance Sec- retary and was involved in brass band concerts at Woodseats Methodist Church and Loxley silver band. In the summer 2017 MNDA newsletter, Michael wrote of the special link and relationship between the South Yorkshire MNDA, SITraN, Sheffield Teaching Hospitals and the SMNDRAG in helping to bring about improve- ments in the quality of life to peo- ple suffering with MND. It cannot be underemphasised today how important Michael was himself to these links and getting people together for a cause.

Interested in helping to inform MND research?

Sheffield Motor Neurone Disor- ders Research Advisory Group (SMNDRAG) are a group of pa- tients, carers, past carers and family members affected by MND who meet quarterly in SITraN and hear from clinical and basic sci- ence researchers working on a wide range of MND projects. SMNDRAG aim to enable patient and carer perspectives to be in- cluded in research proposals and help to identify and prioritise re- search topics important to pa- tients and their families. The group welcomes new members. More details about the role of membership can be found online (http://smndrag.group.shef.ac.uk) or by contacting Annette Taylor Tel: 0114 222 2289 or email: annette.taylor@sheffield.ac.uk
Irene Beard was told in 2003, at the age of 61, that she had motor neurone disease. Having met Professor Pamela Shaw at a dinner she decided to become her patient, despite the distance from London to the Sheffield MND clinic. One day in 2005 Beard asked Professor Shaw what she would do if she was given £20 million for research into the complex disease. Shaw told her that she would develop the first European research institute and attract the best clinicians and scientists from all over the world. “Well, I am going to help you to do that,” said Beard. She applied her energy and considerable charm to the task. Quite unabashed about ringing up millionaires, within a year Beard had helped to raise £12 million in donations from supporters in Yorkshire and London, and had persuaded the Duke of Devonshire to be the patron of her Sheffield Institute Foundation. More money was forthcoming from the University of Sheffield and from the government’s matched-funding scheme. So in 2010 SITraN was opened by the Queen. Born Irene de Marotte de Montigny in Paris 1942, she was named Irene Victoire (for peace and victory) by her resistance parents. She settled in London in 1972 where she soon found she had a talent for helping her fellow new arrivals to negotiate with untrustworthy builders when doing up their houses. Her first building project was for John Stefanidis, who was doing up a Holland Park house for Lord Glenconner. She found herself running a building company that eventually became Eaton Gate Builders, working with designers such as Alidad and Nicky Haslam, and managing renovations for clients who included Madonna and Princess Chantal of Hanover. Her death happened the day after Stephen Hawking’s. They were almost the same age, and she had just discovered that she was losing the ability to drink champagne from an elegant glass, which would not do at all.

Read her full, fascinating obituary in The Times March 24 2018.

London’s first ‘lady builder’ who helped raise £20 million for MND
Addendum

SITraN high content imaging  OperaPhenix Picture Competition

Last year a major equipment wish was fulfilled for the SITraN drug screening facility with patron’s donations funding an OperaPhenix high content imaging system. This automated confocal microscope can image overnight what would take 100 days to image on a manual microscope, vastly speeding up results obtained from our drug screening experiments. Researchers have been using the machine on a variety of projects across 7 academic groups, reflected in the diverse entries for a picture completion profiling the imaging system (below). Experiments range from relatively simple single-cell imaging of cells in culture that can be labelled, for example for mitochondria, through to more complex co-cultures of 2 or more cell types where specific cells may be counted or parts of them quantified for their neuronal like structures. In particular, the the Opera Phenix™ is used to identify potential new treatments for both MND and Parkinson’s disease. Cells taken from a small skin biopsy from a patient can be studied or reprogrammed into neurons and their support cells; helping to match the most suitable treatment to particular groups of patients.

*Parkinson’s brain cells*  
*by Aurelie Schwartzentruber*  

*Whole brain Imaging in Zebrafish by Dr Alex McGowan*

*Bone Marrow Tumour cells*  
*by Mohammed Karami*  

*Copper in Parkinson’s mitochondria, Ruby MacDonald*  

*MND patient astrocytes*  
*by Noemi Gatto*  

*Parkinson’s patient skin cells*  
*by Dr Chris Hastings*
A special “Thank You”

to everyone who has supported us through their fundraising and donations over the last year!

We are immensely grateful to all our supporters who so generously give their time and money to support our research at SITraN.

A special thank you also to the following groups and organisations

Academy of Medical Sciences
ALS Association
ALS Worldwide
Alzheimer’s Research UK
Alzheimer’s Society UK
Barlow Small Well
Basil Samuel Charitable Trust
Bet365 Foundation
Bridlington Lions Club
British Academy
British Medical Association
Brookfield Aviation Foundation
Castleford Christadelphian Ecclesia
Charles Wolfson Charitable Trust
Chesterfield & Scarsdale Rotary Club
Deafness Support Network (DSN)
DLA Piper UK LLP
Department of Health - DeNDRoN
Dransfield Novelty Company Ltd
European Commission Framework 7
European Commission Horizon 2020
European Research Council (ERC)
EU-JPND Programme
Ex-Parkside RL Players
Flow Foundation
Frick Foundation for ALS research
Gordon Bramah Charitable Settlement
GS & GL Brown Fund
Hemingbrough Bowls Club
Hereditary Neuropathy Foundation
Hunslet Hawks Rugby League Club
Hutton Collins Foundation
Inner Wheel Club of Sheffield
Irene Beard
John Greenwood Trust
Jonathan Stone
Kings Heath Christadelphian Church
Ladies Eastwood Probus Group
Lions Intl. District Charity Trust
Longley Community College
L6ve Life Charity
Marie Curie Fellowships
Maris Street Motors Ltd.
Medical Research Foundation
Mills & Reeve Charitable
MND Association (MNDA)
National Institute for Health Research
Neurocare
Parkinson’s UK
Retail Computer Solutions Ltd.
Resource New Jersey
Richard Nagy Ltd.
Rotherham United Football Club
Royal Society
ReNeuron
Ryder Briggs Trust
SI Foundation for MND
Sigma (Leeds) Ltd.
Sound Leisure Ltd.
Skelton Ltd.
Spastic Paraplegia Foundation
Sterling Hydrotech Ltd
Stocksbridge Hydrotech Ltd
The Streaking Meerkats
Stroke Association
Stuart Keane
Target ALS
Technology Strategy Board - Innovate UK
The Wellcome Trust
The Wolfson Foundation
Thierry Latran Foundation
Universal Steels & Aluminium Ltd.
UK research councils: BBSRC, EPSRC, ESRC, MRC, RCUK
Waites Mechanical Services Ltd.
Walter Dawson and Son
Welton Foundation
Westfield Health Trust
Wilkos
York and District against MND
The Zegarelli Foundation
SITraN is a reality thanks to our loyal patrons and supporters. We would not have come this far without your help!

Thank you so much for your kind support!