Association of British Neurologists

Clinical Research Training Fellowship Scheme

ABN Clinical Research Training Fellowships

Following the introduction of the Clinical Research Training Fellowship fund in 2015 we appointed 5 fellows in 2015 and 4 in 2016 all of whom have now begun their fellowship. Individual posters from these fellows may be found in the exhibition.

Mark Ellul, Liverpool **2016** **Association of British Neurologists**
Improving the diagnosis of encephalitis through examining whole proteome and host gene expression

James Hrastelj, Cardiff **2016** **ABN/Guarantors of Brain**
Investigation of gene expression regulation in CSF-derived $CD4^+$ T-cell dysfunction in multiple sclerosis.

Anne-Catherine Huys, London **2016** **ABN/Patrick Berthoud Charitable Trust**
Attention and functional movement disorders: its role in symptom generation and sense of agency

Thomas Massey, Cardiff **2016** **ABN/Patrick Berthoud Charitable Trust**
The role of DNA repair in Huntington's Disease pathogenesis: towards new therapeutic targets

Thomas Cope, Cambridge **2015** **ABN/Patrick Berthoud Charitable Trust**
MEG reveals Speech Processing Delay in Progressive Non Fluent Aphasia

Ingrid Hoeritzauer, Edinburgh **2015** **ABN/Patrick Berthoud Charitable Trust**
The Clinical Features and Prognosis of Scan Negative Uro-Neurological Disorders

Nazia Karsan, London **2015** **ABN/Guarantors of Brain**
Investigating the premonitory stage of NTG-triggered migraine attacks using fMRI

James Varley, Oxford **2015** **ABN/Guarantors of Brain**
The role of adaptive immunity in Parkinsonian syndromes

Grace McMacken, Newcastle **2015** **ABN/Guarantors of Brain**
Adrenergic Signalling and Congenital Myasthenic Syndromes

We are delighted to introduce the new 2017 Clinical Research Training fellows. 3 ABN fellowships were awarded for 2017 supported by the Multiple System Atrophy Trust, the Guarantors of Brain and the Patrick Berthoud Charitable Trust.

The scheme and applications were advertised, peer reviewed and selected, following interview, by a panel consisting of ABN members, lay, charity and scientific representatives.

We are grateful to the ABN members, individual donors, charitable trusts and industry partners whose generosity made this possible.

What is the ABN clinical training fellowship scheme?

Set up in 2009 the ABN clinical research training fellowship scheme's objective was to promote research and to develop new links between the funders of research and clinical trainees. It has been successful in supporting several clinical fellowships in collaboration with funding partners. However, charitable funds are inevitably limited and there are excellent trainees who find it difficult or impossible to obtain research funding. Our aim is to strengthen and extend the fellowship scheme by adding ABN funding to that provided by the neurological charities.

What does the CRTF fund involve?

Our aim is to fund at least one fellowship per year at the cost of approximately £60,000 per fellow per year, plus university fees and consumables. Applied to three year research projects, the annual cost should plateau at around £210,000 by the third year. This level of investment cannot be sustained with our current income, hence the need for additional fundraising.

How is the scheme funded?

Following the formal launch of the ABN Clinical Research Training Fellowship Fund we have been encouraged by the understanding and commitment to the fellowship fund demonstrated by our members, our industry partners and by other friends of the fellowship in addition to the longstanding support from other neurological charities.

A fundraising committee, chaired by Prof Dafydd Thomas, was set up to manage the various routes to support for the fellowships. Following a review of the ABN's fundraising capabilities, facilitated by the Patrick Berthoud Charitable Trust, a fundraiser was appointed in September 2016. We are grateful for the generous donations already received and, with others promised and additional resource in place, believe that we have a good base upon which to build a successful fellowship programme.

How can I support the scheme?

At the 2015 AGM, ABN members voted to allocate an increase in subscriptions rates (which had not increased in 3 years) to the fellowship fund. This was treated as a voluntary contribution and supported by almost 90% of members. Members are encouraged to complete a gift aid form (available from the ABN stand) to optimise any monies donated.

Additional support may be given in many ways. Individual members may be interested in the 2 following tools.

Viorica Chelban	ABN/Multiple System Atrophy Trust Clinical Research Training Fellow 2017 UCL Institute of Neurology, London

Defining clinical and genetic biomarkers in MSA

Multiple System Atrophy (MSA) is a rapidly progressive, devastating neurological disease that affects 4 adults in 100,000 and is currently incurable. MSA is caused by the death of brain cells from specific areas that have important role in controlling movement and coordination but also breathing, swallowing or blood pressure. Because of the complexity of this disease, a definite MSA diagnosis is only possible after the patient died. This leads to severe disability in sufferers and significant health, social and economic impacts.

The mechanism that causes the death of brain cell in MSA is not known but we know that the accumulation of an abnormal protein called alpha-synuclein in on type of brain cells is the hallmark of MSA. During this Fellowship I plan to study what genes lead to the accumulation of these abnormal proteins and therefore the target-pathways that can be used to find treatment. I will initially measure the abundance or the lack of genes from different brain parts from patients that died as a result of MSA and compare them with exactly the same regions from normal healthy controls. I will perform similar experiments using cerebrospinal fluid and blood. Identifying genetic markers in brain tissue and validating in blood samples will potentially reveal important clues on the cause of MSA and in combination with clinical and imaging analysis can improve our ability to diagnose the disease early, monitor progression and response to treatment. This approach could be used in the future to study similar neurological diseases.

Robert Hurford	ABN/Patrick Berthoud Charitable Trust Clinical Research Training Fellow 2017 University of Oxford

Utility of second-line investigations in TIA and non-disabling ischaemic stroke at older ages: clinical and health economic considerations

Stroke is the second leading cause of death worldwide and the biggest cause of long-term neurological disability in adults. Medical investigation following a 'mini-stroke' or major stroke is important for identifying the cause and preventing further strokes; especially in the elderly, due to a higher risk of recurrent stroke, particularly after a 'mini-stroke'.

However, evidence shows that in real-life practice elderly patients are often not fully investigated. Such investigations include detailed ('MRI') brain scans, heart rhythm and blood pressure monitoring, assessment of fatty-plaques in head and neck blood vessels and heart imaging.

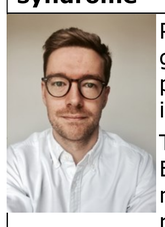
Decisions about what investigations to perform are made on the basis of whether they are clinically useful and whether the cost can be justified. In an age of increasing demands on health care services, it is important therefore that routine practice is based on strong evidence. Unfortunately, however, there have been very few studies of the clinical usefulness and cost-benefit of the various different investigations for stroke in older patients.

The Oxford Vascular Study (OXVASC) includes a large cohort of patients with 'mini-stroke' and stroke and is best placed to address questions about appropriate investigation of older patients for several reasons: all patients with mini-stroke or stroke are recruited from a single population, irrespective of age; all patients are thoroughly investigated, irrespective of age; the investigation results are assessed by a group of clinical researchers with relevant expertise; and all patients are followed-up long-term to identify all recurrent strokes.

The OXVASC study will allow us to identify the best panel of investigations to perform in older patients, from the perspectives of clinical usefulness and cost.

Stephen Keddie	ABN/Guarantors of Brain Clinical Research Training Fellow 2017 Institute of Neurology, London

Investigating the pathological mechanisms underlying the neuropathy in POEMS syndrome



POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, Skin disorder) is characterised by a plasma cell disorder and polyneuropathy. It causes some of the most significant disability and mortality of any inflammatory neuropathy.

The pathophysiology of POEMS neuropathy is unknown. The cytokine Vascular Endothelial Growth Factor (VEGF) may be an important clue to pathogenesis. It is markedly elevated in POEMS and correlates with disease activity. VEGF cannot be solely responsible, as trials of anti-VEGF therapy are ineffective. Other pro-inflammatory molecules play a role; Interleukin-1β, Interlukin-6 and Tumour Necrosis Factor-α are raised in POEMS sera compared to multiple myeloma (a similar plasma cell disorder). Whether such cytokines cause nerve damage remains to be discovered.

My aim is to investigate the pathological mechanisms causing neuropathy in POEMS.

- A database of deeply phenotyped patients will be completed and their pre-treated, treated, and relapsed sera classified.

Samples will

- be tested for a range of 30 cytokines and compared to Waldenström's and Myeloma (plasma cell disorders), CIDP, paraproteinaemic neuropathy (inflammatory neuropathies) and healthy controls to establish a POEMS cytokine fingerprint.
- be analysed by mass spectrometry and SiMOA to produce a detailed proteomic fingerprint of inflammatory markers (the inflammasome). We hypothesise the pathogenic candidates will change with treatment and relapse.

Whole sera and single or grouped cytokines will be tested against Human Induced Pluripotent Stem Cell (HiPSC) derived neurones in a myelinating co-culture system to ascertain which markers cause nerve tissue dysfunction, and by what process.

Novel techniques developed in this research may be utilised to study pathophysiology in other neuropathies, and potential novel therapies.

JustGiving The ABN JustGiving account **www.justgiving.com/A-B-N**, also known as **BRAIN-DR** (British Appeal Into Neurology Dedicated Research) allows people to make immediate donations and also to nominate the Clinical Research Training Fellowship fund as their target charity for running, swimming, cycling events.

easyfundraising.org.uk feel good shopping

Online shoppers may be interested to learn of our **www.easyfundraising.org.uk/causes/abn** link whereby major companies (see overleaf) will donate a percentage of everything you spend via the portal to the CRTF fund.

To learn more about how you could become involved please visit the ABN stand in the exhibition hall. Information may also be obtained via the ABN newsletter and website **www.abn.org.uk**