PARKINSON'S UK, EDINBURGH BRANCH

NOTE OF MEETING OF RESEARCH INTEREST GROUP, EDINBURGH, SATURDAY, APRIL 22, 2017, 10.30-12.30.

A record audience attended the latest meeting of the Edinburgh Research Interest Group at the Scottish Centre for Regenerative Medicine to hear a talk by Dr Esther Sammler, entitled **'200 years on: genes, genetics and signalling pathways in Parkinson's Disease.'** After initial training in medicine and neurology in Munich and Heidelberg, Esther has worked and studied in Scotland since 2008, and is currently consultant neurologist and honorary senior lecturer at Ninewells Hospital, Dundee, and also a postdoctoral researcher in Professor Dario Alessi's laboratory, the Medical Research Council Protein Phosphorylation and Ubiquitylation Unit at Dundee University. She explained how she values this dual role, in the lab and on the ward, giving her the opportunity to undertake research which will be of use 'from bench to bedside'.

Esther has kindly made the slides from her talk available on our website. Consideration of the diagrams and references contained in these will lead to a far deeper understanding of the research than this brief report can hope to convey.

She began by explaining the concept of **protein phosphorylation**, for the discovery of which Krebs and Fisher received the Nobel Prize as recently as 1992. Abnormal phosphorylation has been identified as the cause or consequence of many human diseases, including Parkinson's. Esther outlined the **historical eras** of the treatment of Parkinson's since its identification by James Parkinson in 1817, suggesting that we have now moved from the 'genetic era' which began in the 1990s with the discovery of gene mutations in families with Parkinson's, into the 'biochemical era', in which research is directed towards understanding the functions of genes – in particular, those which affect the loss of dopaminergic neurons in the substantia nigra.

Since changes and mutations in alpha-synuclein were first discovered in 1997, many more genes implicated in Parkinson's have been identified: Esther's focus is on **LRRK2**, which genetically links idiopathic and familial forms of Parkinson's. It has been shown to function as a protein kinase, and Professor Alessi's lab, together with international collaborators, has recently shed light on LRRK2 associated Rab

phosphorylation. Changes in the LRRK2 gene have been shown to be the greatest genetic contributor to the development of Parkinson's.

So the labs have been busy, but how do we move **from the bench to the bedside?** As a clinician, Esther is interested in the potential for LRRK2-mediated Rab phosphorylation to act as biomarker for LRRK2-associated Parkinson's, and in exploring ways to monitor LRRK2 pathway activity in patients with Parkinson's. In association with colleagues, a 'robust assay' to assess quantitatively LRRK2-mediated Rab phosphorylation in peripheral blood samples has been developed, and pilot studies are now underway in Dundee and Tubingen. The assay provides a tool to monitor LRRK2 pathway activity in a human blood sample, and - most importantly for people with Parkinson's - can also assess how well drugs administered to inhibit that activity are working. It has potential to help clinicians monitor the progress of the disease in their patients, and also to help those who design new drugs to test their efficacy.

This was a complex topic to cover in an hour, and a complex one for the lay audience to grasp, but while we may not have understood every little detail, the audience was enthusiastic about the broad and positive messages which Esther conveyed so clearly. The many questions asked indicated our considerable interest in the potential value of her research for monitoring – and hopefully, eventually slowing - the progress of Parkinson's. We also appreciated her willingness to respond to questions during the talk, and to stay on to talk more to us over a sandwich lunch.