PARKINSON'S UK, EDINBURGH BRANCH

NOTE OF MEETING OF RESEARCH INTEREST GROUP, EDINBURGH, SATURDAY, JANUARY 14, 2017, 10.30-12.30.

Around thirty members of the Research Interest Group came to the Scottish Centre for Regenerative Medicine to hear a talk entitled **'A potential new diagnostic test for Parkinson's Disease: real-time QuIC of alpha-synuclein'** by Alison Green, Reader in Biochemistry at the National Creutzfeldt Jakob Disease Research and Surveillance Unit at the University of Edinburgh.

Her work on Parkinson's has developed out of a longstanding research interest in the development of diagnostic tests for dementia and her internationally acclaimed work on a protein aggregation test for Creutzfeldt Jakob Disease (CJD) called Real-Time Quaking Induced Conversion (RT-QuIC). These techniques have now been adapted to investigate the aggregation of the protein alpha-synuclein in the cerebro-spinal fluid, the results of which could aid diagnosis of Parkinson's which hitherto has been so difficult to diagnose in the early stages.

Alison 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 highlighting that Parkinson's is only one of several neurological diseases, including Huntington's and Alzheimer's, which are associated with protein misfolding and subsequent aggregation, which occurs when the misfolded proteins 'stick together'. She then used the example of well-tested research into **CJD**, showing us diagrammatically how the introduction of fluorescent markers to the misfolded proteins – a process referred to as 'seeding' – then allows researchers to trace the subsequent aggregation throughout RT-QuIC, as the misfolded proteins begin to stick together. This has permitted a robust and reliable test for diagnosis of CJD, a very disease which develops very rapidly and needs a rapid and certain diagnosis.

Moving on to her work on **Parkinson's**, Alison described some similarities with the CJD research in that cerebro-spinal fluid may contain misfolding proteins. In the case of Parkinson's, misfolding alpha-synuclein may lead, through aggregation, to Lewy body dementia. As in

the case of CJD, ‘seeding’ with fluorescent markers provides evidence of aggregation. One significant difference is the time required for the RT-QuIC process: tests on alpha-synuclein need much longer than the tests for CJD - up to 80 hours of quaking to produce results.

There are still **further advances** to be made in this field of research: for example, the current process does not distinguish between Parkinson’s and Lewy Body Dementia. As more samples are examined, it may become possible to assess the relationship between RT-QuIC results and disease duration, disease severity and the gender and age of the patient at the onset. Our recent Parkinson’s Lecturer, Bas Bloem and colleagues at Nijmegen, are working on atypical PD samples and controls. Alison also noted that the use of cerebro-spinal fluid, acquired through a lumber puncture, is not without risk, and the use of other tissues, such as olfactory mucosa and blood, is being explored. Dr Gianluigi Zanusso in Verona is working on olfactory mucosa samples. Blood would be much easier to collect than cerebro-spinal fluid, but the presence of so many other proteins in blood complicates its use in this process. Alison’s colleague here in Edinburgh, Graham Fairfoul, is working to develop an alpha-synuclein RT-QuIC test for blood. There are also plans to use similar methods to explore motor-neurone disease.

In the course of a lively question and answer session, Alison clarified that this research does not point directly to a cure for Parkinson’s. It is possible to disrupt the process of aggregation, but not to stop it. It does, however, mark a great potential advance in the diagnosis of Parkinson’s, and may also in future help monitor the progress of the disease.