PARKINSON'S UK, EDINBURGH BRANCH

NOTE OF MEETING OF RESEARCH INTEREST GROUP, EDINBURGH, SATURDAY NOVEMBER 7, 2015, 10.30-12.30.

Nearly thirty members of the Research Interest Group came to the Scottish Centre for Regenerative Medicine on a wet and windy Edinburgh morning, to welcome Maria Doitsidou, recently appointed Chancellor's Fellow at the University of Edinburgh, and hear about her research. Maria's distinguished international career in developmental research has taken her from Greece, where she first graduated, to Germany, where she gained her doctorate, and on to post-doctoral work in the USA, at the University of Columbia, and in Norway, at the University of Stavanger. She came to the Centre for Integrative Physiology in January 2015, and is in the early stages of new study of dopaminergic neurons in health and disease, working with tiny Caenorhabditis elegans (*C. elegans)* worms, seeking answers to questions about how an undifferentiated cell develops into a specialised dopamine-producing neuron and what happens, in cases of disease such as Parkinson's, when these neurons begin to degenerate.

The presentation was entitled: *A C. elegans model of dopaminergic neuron development and degeneration: what can a tiny nematode teach us about human disease?* The subject area is complex and inherently difficult for a non-specialist audience to grasp, but Maria had worked hard to make it accessible to us all. Because the slides used in her presentation are now available on the Branch website, this report aims only to highlight key elements.

Her introduction paid homage to the pioneering work of Sydney Brenner, who, in 1963, saw the potential value of study of a small organism and laid the foundations of developmental neurobiology by his work on cell development in the *C. elegans* worm. John Sulston's work on the cell lineage and Bob Horvitz's work on the genetics of programmed cell death (also known as apoptosis) and the similarities of genes and gene pathways in simple worms and in humans, which he termed 'the principle of biological universality', have led to an exponential growth of *C. elegans* research in recent years. The value of this work has been acknowledged by the award of Nobel prizes to six of these researchers, including Brenner, Sulston and Horvitz.

Next, Maria explained her own research questions, about how neuronal diversity is generated, what cell fate programs co-ordinate neuronal

differentiation and which molecular mechanisms govern neuronal degeneration. She demonstrated the value of using a simple model organism such as *C. elegans* for this study, with its small size, rapid three-day generation time, one thousand offspring (which compares impressively with the human average of 2.4 children) and only eight dopaminergic neurons, as opposed to up to 600,000 dopaminergic neurons in the human brain. The search for mutations in *C. elegans* neurons is speeded by the availability of technology, the COPAS Biosorter, which can identify and isolate mutants far more rapidly than a human researcher could. While few, if any, of us could claim to have grasped fully the detail of the complex science, Maria made clear the broad principles behind her research into mutations which stop or slow down neurodegeneration. Mutagenesis is used to make changes to the genome of worms which have lost their dopamine neurons; a search is then made for those mutants which have developed some resistance to neurodegeneration for further examination of their genome. The underpinning question is whether the protective mechanism is relevant for human disease too.

The closing section of the presentation turned to the implications for people with Parkinson's. A collaborative project with the Stavanger University Hospital in Norway, is using exome sequencing and looking at the transient receptor potential (TRP) channels in the substantia nigra of Parkinson's patients and matched controls. They have found rare protein changing mutations; introducing human TRP channel variants in the worm may lead to further findings with implications both for the diagnosis and the treatment of Parkinson's. Although her own current research is still in the early stages, Maria promised to keep us informed of her team's progress.

Finally, Maria dealt with a surprisingly wide range of questions about her work from an audience which had clearly enjoyed a very stimulating morning.