**Interaction of LRRK2-G2019S with Rab GTPases in vivo**

**Stavroula Petridi, Adam Middleton, Alison Fellgett, Laura Covill, Amy Stewart, Friederike Kohrs, Robin Hiesinger, Sangeeta Chawla & *Chris Elliott***

**University of York & Free University Berlin**

Previously, we identified an excitotoxic mechanism by which expression of mutant forms of LRRK2 in the dopaminergic neurons increased visual signalling in young flies, followed by the complete loss of visual response in old flies. We used this assay to screen for Rabs which interact with LRRK2.

Our top hit is Rab10. In young flies, expressing both Rab10and LRRK2-G2019Sincreases the lamina neural response ~20 fold. These changes in the neural response are independent of photoreception.

Knockdown of Rab10 ameliorates the neurodegeneration seen in the visual system of old flies expressing LRRK2-G2019S in their dopamine neurons.

GFP expression/antibody staining suggests that the dopamine neurons innervating the visual system (lobes and lamina) and suboesophageal zone (controlling the proboscis extension response) are Rab10+, but in other dopamine neurons (e.g. those controlling sleep/wake/circadian patterns) Rab10 is undetectable. We therefore tested dopaminergic knockdown of Rab10and found it rescues movement G2019S-induced deficits in the proboscis movement. Neither LRRK2-G2019S nor Rab10-RNAiaffect the circadian pattern.

In dopaminergic neurons, not all Rabs are equal: Rab3 and Rab32 (the fly homolog of Rab29) affect LRRK2 in other ways. Neither are found in visual neurons.

We conclude that differences in neurodegeneration between groups of dopaminergic neurons may be the consequence of their palette of Rab proteins.

Presented at:

Biennial International LRRK2 Meeting of the Biochemical Society

02/09/2018 to 04/09/2018

The Botanical Garden, Padua,Italy