**Interaction of LRRK2 with Rab GTPases *in vivo*.** S. Petridi, C.A. Middleton, A. Fellgett, S. Chawla & *C.J.H Elliott*,

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* Objective(s)

To determine if Rab proteins are required *in vivo* for neurodegeneration induced by expressing the most common Parkinson’s disease related mutation *LRRK2-G2019S*  in dopaminergic neurons.

* Background

*In vitro* experimentshave suggested that Rab proteins interact with LRRK2, but it is not clear which exact Rab is key in dopaminergic neurons

* Methods

All experiments used the fly *Drosophila*, assaying visual and movement phenotypes, and using immunocytochemistry/GFP expression in the CNS.

* Results

Rab10 is the top hit in a gain-of-function screen, in which all the Rabs were tested for interactions with *LRRK2-G2019S* using our electrophysiological, visual assay. In loss of function experiments, knockdown of *Rab10* ameliorates the visual neurodegeneration seen in old flies expressing *LRRK2-G2019S* in their dopamine neurons. Knockdown of *Rab10* also rescues the *LRRK2-G2019S* induced movement deficits in a reaching task, the proboscis extension response. Neither *LRRK2-G2019S* overexpression nor *Rab10* knockdownaffect the circadian pattern.

Localisation with GFP expression/antibody staining suggests that the dopamine neurons innervating the visual system and suboesophageal zone (controlling the proboscis extension response) are Rab10+, but other dopamine neurons (e.g. those controlling sleep/wake/circadian patterns) show no sign of co-localisation.

Thus both physiological and anatomical approaches suggest that not all dopaminergic neurons have an interaction between *LRRK2-G2019S* and *Rab10*.

Rab3 and Rab32 interact with LRRK2 in different subsets of dopaminergic neurons.

* Conclusions

We conclude that not all dopaminergic neurons are equal differences in neurodegeneration between groups of dopaminergic neurons may be the consequence of their palette of Rab proteins.