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Elliott, Christopher John Hazell, Chawla, Sangeeta, Hiesinger, Robin et al. (2018)
Interaction of LRRK2-G2019S with Rab GTPases in vivo. In: Biennial International LRRK2
Meeting of the Biochemical Society, 02-04 Sep 2018, The Botanical Garden.

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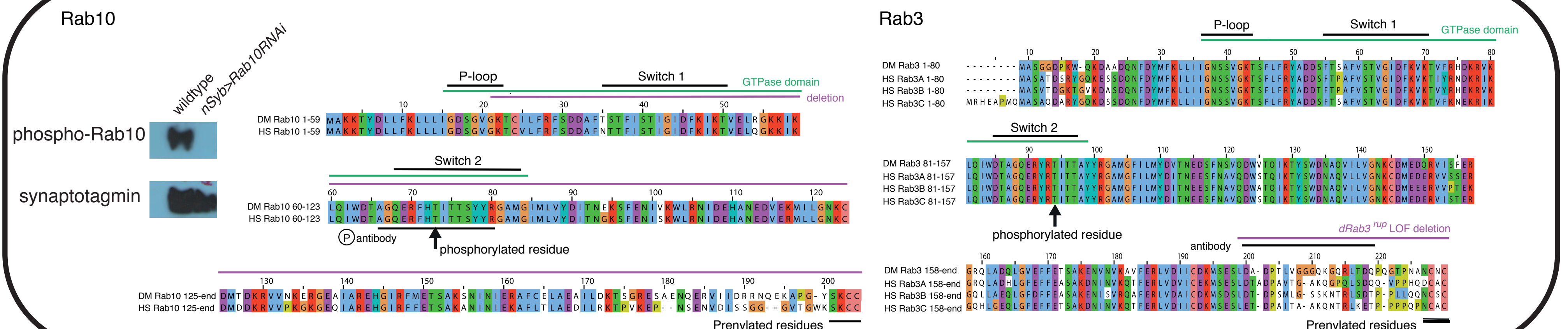
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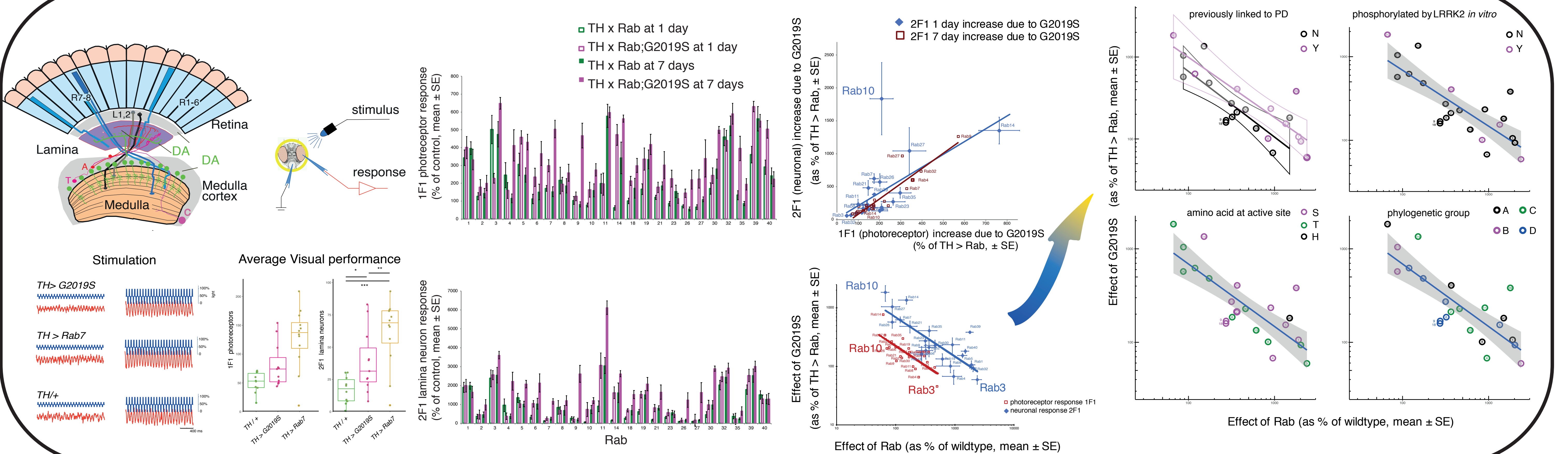
Aim

To test if LRRK2-G2019S interacts with any Rab GTPase in dopaminergic neurons, *in vivo*. We use the conservation of Rab sequence, neuronal circuit, easy genetics of the fly to show an interaction with Rab10 in some (but not all) dopaminergic neurons.

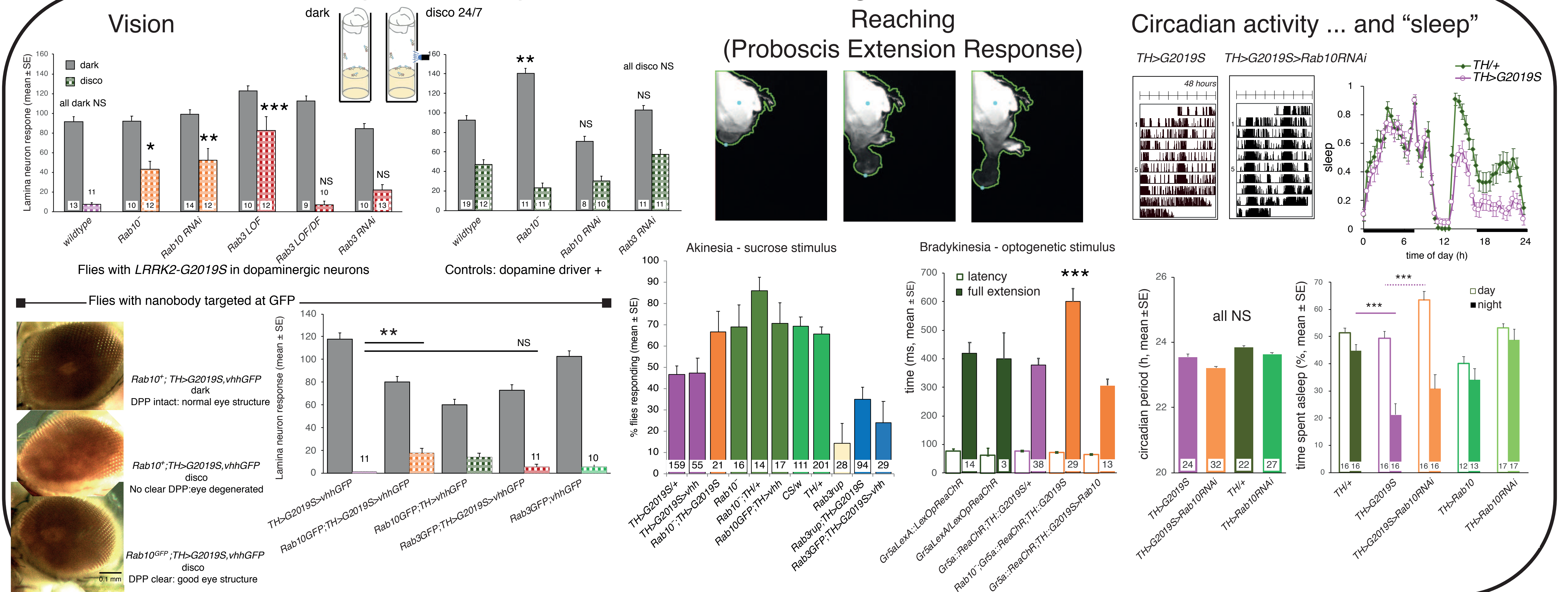
Conservation of Rabs



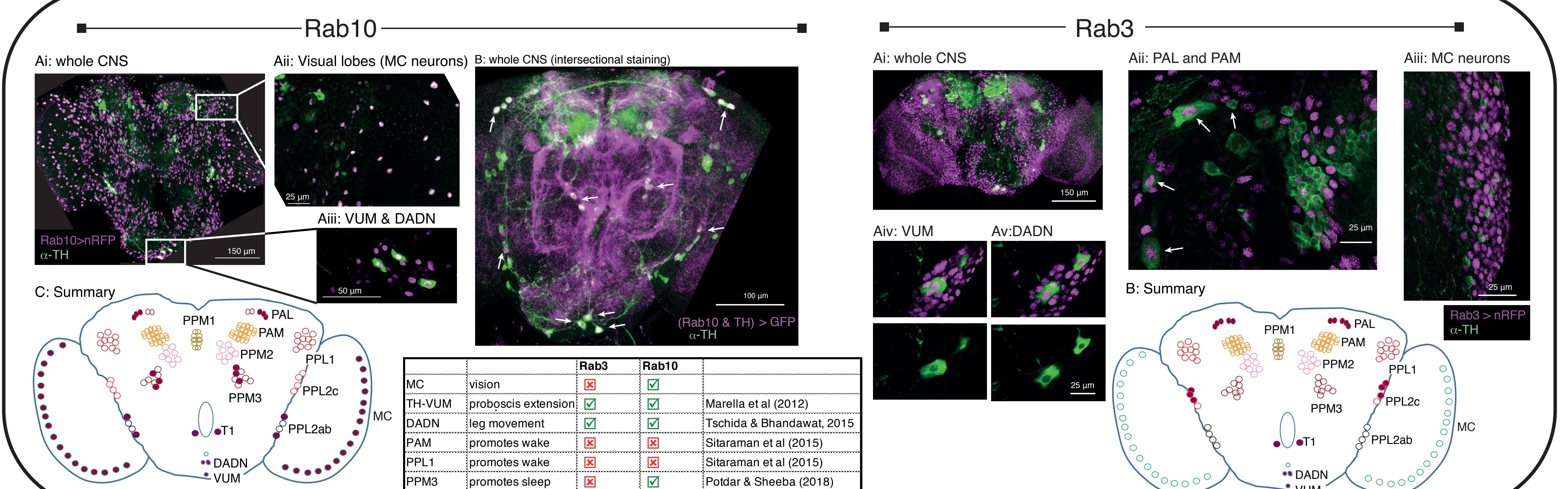
Expression Screen for interaction: Rab10 is top hit and Rab3 the weakest



Knockout of Rab10 (but not Rab3) rescues LRRK2-G2019S degeneration



Morphologically - not all dopamine neurons have the same Rabs



Summary and Conclusion

In vivo, in dopaminergic neurons Rab10 strongly interacts with LRRK2-G2019S, both in overexpression and knockout experiments.
• Global and dopamine-specific knockouts are equally effective
Not all dopamine neurons have the same palette of Rabs

Novel Hypothesis

We suggest the differences in dopamine neuron death (in different parts of the *substantia nigra* or VTA) may be due to the palette of Rabs contained in dopamine neurons

Acknowledgements

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