Title of presentation**: Interplay between LRRK@ kinase and Rab GTPases in Parkinson's diseasae**

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Dario Alessi -Biographical Note and Topic Discussion

Dario is biochemist whose research work has contributed to our understanding of several disease relevant signal transduction pathways including PDK1 (diabetes and cancer), LKB1 (cancer), WNKs (blood pressure). Autosomal dominant missense mutations that hyperactivate the LRRK2 protein kinase are a common cause of inherited Parkinson's disease and therapeutic efficacy of LRRK2 inhibitors is being tested in clinical trials. I will overview the nuts and bolts of current research that has revealed that LRRK2 phosphorylates a subset of Rab GTPases within their Switch-II motif controlling interaction with a new set of effectors such as RILPL1/2 and JIP3/JIP4. I will discuss a new protein complex that we have identified interacts with the pRAB8A:RILPL1 complex. I will consider how mutations in other components linked to Parkinson's such as Rab29 and VPS35 promote LRRK2 mediated Rab protein phosphorylation as well as characterization of the PPM1H phosphatase member that counteracts LRRK2 signalling by dephosphorylating Rab proteins. I will discuss the implications that this work has for the diagnosis and treatment of Parkinson's disease. If time permits, I will also present data that indicates that the LRRK2 paralog termed LRRK1 is directly activated by PKC isoform phosphorylation and functions as a Rab7A kinase.