13:15-15:00 Lunch offered and Lab tour (posters will be up)

Chair person: Juan Cabello

15:00-15:15 **Ester Dalfo**

The Small GTPase RAC1/CED-10 Is Essential in Maintaining Dopaminergic Neuron Function and Survival Against α-Synuclein-Induced Toxicity

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Parkinson's disease is associated with intracellular α-synuclein accumulation and ventral midbrain dopaminergic neuronal death in the Substantia Nigra of brain patients. The Rho GTPase pathway, mainly linking surface receptors to the organization of the actin and microtubule cytoskeletons, has been suggested to participate to Parkinson's disease pathogenesis. Nevertheless, its exact contribution remains obscure. To unveil the participation of the Rho GTPase family to the molecular pathogenesis of Parkinson's disease, we first used C elegans to demonstrate the role of the small GTPase RAC1 (ced-10 in the worm) in maintaining dopaminergic function and survival in the presence of alpha-synuclein. In addition, ced-10 mutant worms determined an increase of alpha-synuclein inclusions in comparison to control worms as well as an increase in autophagic vesicles. We then used a human neuroblastoma cells (M17) stably over-expressing alpha-synuclein and found that RAC1 function decreased the amount of amyloidogenic alpha-synuclein. Further, by using dopaminergic neurons derived from patients of familial LRRK2-Parkinson's disease we report that human RAC1 activity is essential in the regulation of dopaminergic cell death, alpha-synuclein accumulation, participates in neurite arborization and modulates autophagy. Thus, we determined for the first time that RAC1/ced-10 participates in Parkinson's disease associated pathogenesis and established RAC1/ced-10 as a new candidate for further investigation of Parkinson's disease associated mechanisms, mainly focused on dopaminergic function and survival against α-synuclein-induced toxicity.