Proposal of Master Research Project / Proyecto fin de Master for the academic year 2025-26

Group name:
IP name:
Group web:

Title of the MRP/TFM:
High resolution imaging of secretory/endolysosomal traffic in neurons

Membrane traffic is central to neuronal morphogenesis and physiology. Because of their branched morphologies and extreme functional polarization, neurons require particularly precise membrane organization and protein traffic control. However, the mechanisms that organize secretory, endosomal and degradative trafficking in neurons are poorly understood. Our laboratory has recently discovered that degradative organelles called lysosomes closely associate with the secretory pathway (trans-Golgi-associated lysosomes). The implications for local traffic control and secretory-endolysosomal coordination of this close Golgi-lysosome relation are yet to be explored. In this research project, we propose to investigate the structural and functional architecture of the Golgi-endolysosomal interfaces in neurons. For this, the applicant will use genetics, molecular biology and high-resolution imaging to (1) characterize Golgi-endolysosomal structural connectivity in neurons using markers generated through CRISPR knock-in through SIM superresolution microscopy and electron microscopy, (2) analyze the dynamics of relations among the secretory pathway, the trans-Golgi and endolysosomal system using spinning disk microscopy and the RUSH system, and (3) genetically screen for determinants of Golgi-endolysosomal coordination in neurons. Defective traffic in the endolysosomal and autophagic pathways is strongly associated with Alzheimer's, Parkinson's and Huntington's disease. Given the conservation of traffic machineries, insights obtained here may have broad implications for the understanding and treatment of neural diseases caused by defects in protein traffic and lysosomal/autophagic degradation, including congenital and age-related diseases.

Relevant publications:

Yang K, Feng Z, Pastor-Pareja JC.
p24–Tango1 interactions ensure ER–Golgi interface stability and efficient transport.
J Cell Biol (2024) https://doi.org/10.1083/jcb.202309045

Zhou L, Xue X, Yang K, Feng Z, Liu M, Pastor-Pareja JC.
Convergence of secretory, endosomal, and autophagic routes in trans-Golgi-associated lysosomes.
J Cell Biol (2023) https://doi.org/10.1083/jcb.202203045

Yang K, Liu M, Feng Z, Rojas M, Zhou L, Ke H, Pastor-Pareja JC.
ER exit sites in Drosophila display abundant ER-Golgi vesicles and pearled tubes but no megacarriers.
Cell Rep (2021) https://doi.org/10.1016/j.celrep.2021.109707

Methods and technology involved in the MRP/TFM Project:

This research project will involve the use by the applicant of the following main sets of techniques/laboratory skills: (1) basic cloning and molecular biology, (2) fruit fly genetics, (3) light imaging (laser scanning, spinning disc, super-resolution), and (4) electron microscopy imaging (APEX-TEM and FIB-SEM).

Member/s of the lab who will act as tutor/co-tutor of the project (if different from the group IP; PhD required to be tutor / co-tutor):

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