Proposal of Master Research Project (MRP) for the Academic Year 2026-27

Group Name: Cell-to-Tissue Architecture
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Title of the MRP:
High resolution imaging of secretory and endolysosomal traffic in muscles

Summary of the MRP:

Membrane traffic is central to muscle cell morphogenesis and physiology. Because of their highly organized architecture, specialized endomembrane system and contractile function, muscle cells require particularly precise membrane organization and protein traffic control. However, the mechanisms that organize secretory, endosomal and degradative traffic in muscle tissue remain vastly underexplored. Our laboratory is interested in understanding the structural and functional organization of the endoplasmic reticulum (ER), the Golgi apparatus, the endolysosomal system and their associated trafficking pathways in muscle, including how they contribute to membrane remodeling, proteostasis and cellular specialization. A subject of particular interest is the postsynaptic neuromuscular junction (NMJ), a highly specialized membrane domain (subsynaptic ER) that imposes exceptional demands on local secretory and degradative trafficking for the maintenance of synaptic structure and function. In this research project, we propose to investigate the functional architecture of ER-Golgi and Golgi-endolysosomal interfaces in muscle cells. To achieve this, the applicant will use genetics in *Drosophila* (fruit fly), molecular biology and high-resolution imaging to (1) characterize the structural connectivity among the ER, Golgi and endolysosomal compartments in muscle cells using markers generated through CRISPR knock-in combined with SIM superresolution microscopy and electron microscopy, (2) analyze the dynamics of interactions among the secretory pathway and the endolysosomal system in vivo using spinning disk microscopy and the RUSH system, and (3) genetically screen for determinants of ER-Golgi and Golgi-endolysosomal coordination in muscle cells and at the postsynaptic NMJ. Defects in membrane traffic, autophagy and organelle homeostasis are strongly associated with muscular dystrophies, myopathies and age-related muscle degeneration. Insights obtained from this work may have broad implications for understanding and treating muscle diseases caused by defects in protein trafficking and lysosomal/autophagic degradation.

Relevant publications:

Farhan H, Raote I, Campelo F, Ge L, Hirschberg K, Forrester A, Zanetti G, Lippincott-Schwartz J, Pastor-Pareja JC, Perez F, Saito, Malhotra V.
Towards a unified framework for the function of endoplasmic reticulum exit sites.
Nat Rev Mol Cell Biol (2025) https://doi.org/10.1038/s41580-025-00899-0

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

Methods and technology involved in the MRP:
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).

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