

Group name: Cell-to-tissue architecture in the nervous system

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Group web: <https://in.umh-csic.es/en/grupos/arquitectura-celular-y-tisular-en-el-sistema-nervioso>

Title of the MRP/TFM:

High Resolution Imaging of Golgi-Endolysosomal Traffic in Neurons

Summary of the Project:

Membrane traffic is central to many aspects of 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 in light and electron microscopy, (2) analyze the dynamics of relations among the secretory pathway, the trans-Golgi and endolysosomal 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:

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):

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