

Decoding the ATG8 code

Membrane biophysics of autophagy

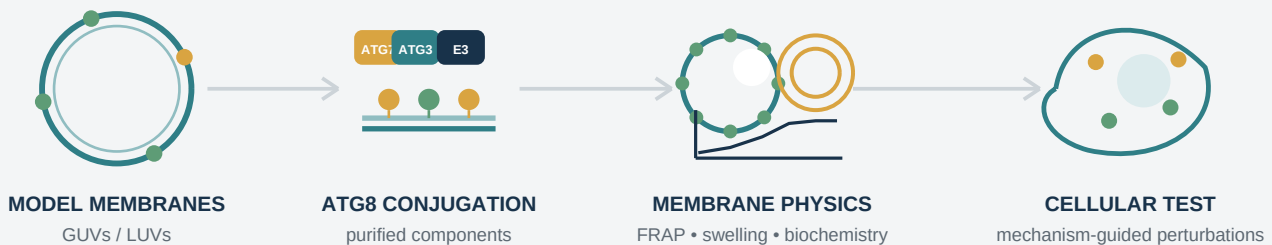
MASTER PROJECT

Master project at the interface of cell biology, membrane biochemistry and physics

Background and scientific question

Autophagy is a conserved cellular pathway that captures and degrades cytoplasmic material in lysosomes. It is essential for cellular homeostasis and stress adaptation, and its dysregulation is linked to infection, neurodegeneration and cancer. A central step in autophagosome biogenesis is the covalent attachment of ATG8-family proteins (LC3 and GABARAP paralogs) to membrane lipids by an E1-E2-E3-like conjugation cascade involving ATG7, ATG3 and the ATG12-ATG5-ATG16L1 ligase complex. Membrane-bound ATG8 proteins recruit cargo receptors and regulatory factors, but they can also organize and remodel membranes. Why mammalian cells maintain several ATG8 paralogs, and whether their distinct cellular functions arise from different physical effects on membranes, remains a major open question. This project addresses this 'ATG8 code' from a quantitative biophysical perspective.

Experimental concept



The project

The student will establish a bottom-up system in which defined membranes are decorated with selected ATG8 proteins and their physical responses are measured. The work will include preparation of model membranes in the test tube, expression and purification of recombinant proteins, and reconstitution of ATG8 lipid conjugation on membranes using purified components. We will then quantify how different ATG8 paralogs alter membrane organization and material properties. Key readouts will include FRAP to measure protein mobility and scaffold dynamics, osmotic membrane-swelling assays to probe membrane mechanics, and biochemical assays to quantify membrane binding and conjugation. Biophysical results will guide defined manipulations of ATG8 function in cells, allowing physical properties measured in vitro to be correlated with membrane behavior and autophagic function in a cellular context.

What you will learn

This project provides hands-on training across disciplinary boundaries. You will learn membrane biochemistry, recombinant protein purification, quantitative in vitro reconstitution and fluorescence-based biophysics, while connecting these measurements to mechanistic cell biology. The project is particularly suited to students interested in how molecular interactions generate emergent physical properties of biological membranes. A background in cell biology, biochemistry, biophysics or physics is welcome; curiosity, quantitative thinking and motivation to work experimentally across fields are most important.

Central question How do distinct ATG8 proteins encode different physical properties at membrane surfaces, and how do these properties contribute to their specialized functions in autophagy?