Funded PhD position in Autophagy and Development
Institute for Integrative Biology of the Cell, University Paris-Saclay

Title	**Functional characterization of autophagosome populations by single event microscopy and proteomic approach**
Team and Institute	Autophagy and Development, Institute for Integrative Biology of the Cell CNRS, Avenue de la Terrasse 91198 Gif-sur –Yvette, France
PhD Supervisors	Christophe Lefebvre and Renaud Legouis
E-mail	renaud.legouis@i2bc.paris-saclay.fr

Summary: Autophagy is a major cellular mechanism of degradation of cytoplasmic constituents. It is an essential mechanism used by the cell to resist adverse conditions, nutritional, physical or chemical stress, by eliminating non-essential or damaged proteins and cellular organelles. Autophagy is also involved in many developmental processes and during aging, and its deregulation is linked to many pathologies (infections, cancer and neurodegenerative diseases). This process focusses on the formation of specialized vesicles called autophagosomes that sequester the cellular constituents to be recycled and then fuse with the lysosomal compartment for their degradation. Our team uses the nematode *Caenorhabditis elegans*, to characterize autophagic functions under physiological, stress or pathological conditions.

The production of autophagosomes is a complex, versatile and highly plastic dynamic process, mobilizing various membrane compartments. This PhD project aims to characterize *in vivo* and at the scale of single events the different autophagosome populations to dissect their specificities. It focuses on specific autophagic processes, characterized by our team, during development or adaptation to stress (1, 2). Our previous studies of the LC3/GABARAP ubiquitin-like proteins showed the existence three autophagosome populations whose functional specificities are unknown. The ambition of this project is to make an experimental leap from global autophagy to individual autophagosome analysis. This project is based on the recent development of new tools to analyze autophagosomes:

- A 4D microscopy approach followed by a tracking image analysis method will allow to characterize single events during the autophagic flux and perform quantitative analyses.
- In parallel, the use of specific LC3 and GABARAP traps (3), will allow to purify the different autophagosome populations and then to characterize their content by a proteomic approach.

Application: We are seeking for highly motivated candidates with an initial background in Cell Biology or Development and a strong aptitude for experimental work. The PhD support is fully funded from an ANR project. More details about the project are available upon request.

Candidates should send a motivation letter, a CV, and Master grades to Renaud Legouis (renaud.legouis@i2bc.paris-saclay.fr). Additional recommendation letters will be highly appreciated. The PhD project is supposed to start in September 2024.

1) Leboutet, R., Largeau, C., Müller, L., Prigent, M., Quinet, G., Rodriguez, M. S., Cuif, M. H., Hoppe, T., Culetto, E., Lefebvre, C., & Legouis, R. (2023). *LGG-1/GABARAP lipidation is not required for autophagy and development in Caenorhabditis elegans.* **eLife**, 12, e85748. https://doi.org/10.7554/eLife.85748

2) Chen, Y., Leboutet, R., Largeau, C., Zentout, S., Lefebvre, C., Delahodde, A., Culetto, E., & Legouis, R. (2021). *Autophagy facilitates mitochondrial rebuilding after acute heat stress via a DRP-1-dependent process*. **The Journal of cell biology**, 220(4), e201909139. https://doi-org/10.1083/jcb.201909139

3) Quinet, G., Génin, P., Ozturk, O., Belgareh-Touzé, N., Courtot, L., Legouis, R., Weil, R., Cohen, M. M., & Rodriguez, M. S. (2022). *Exploring selective autophagy events in multiple biologic models using LC3-interacting regions (LIR)-based molecular traps*. **Scientific reports**, 12(1), 7652. https://doi-org/10.1038/s41598-022-11417-z