Title: Functional characterization of autophagosome populations by single event microscopy and proteomic approach

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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 of 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.