Laboratoire de Physico-Chimie Curie,
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M2 thesis internship proposal

Molecular Mechanisms for Systemic Coordination of Cellular Stress Responses in *C. elegans*

Start Date: January 2027
Duration: 6 months
Keywords: *C. elegans*, microfluidics, stress granules, heat-shock response, neuronal activity
Location: Paris, 75005, France Institut Pierre-Gilles de Gennes (IPGG)

Project

Cells respond to environmental stress with various organized molecular responses, including the formation of stress granules and the heat shock response (HSR). Both play crucial roles in preventing protein misfolding, aberrant aggregation and the heat shock proteins are major therapeutic targets for cancer cell therapy.

While the regulation of cellular stress responses is well-studied in single cells, their coordination at the cell, tissue, and systemic levels of a multicellular organism is poorly understood. This internship project aims to elucidate the interplay between systemic and cell-autonomous responses to temperature stress, using the nematode *C. elegans* as a model organism.

Our group has established an experimental setup in which animals can be live-imaged at high resolution in a microfluidic device, while:

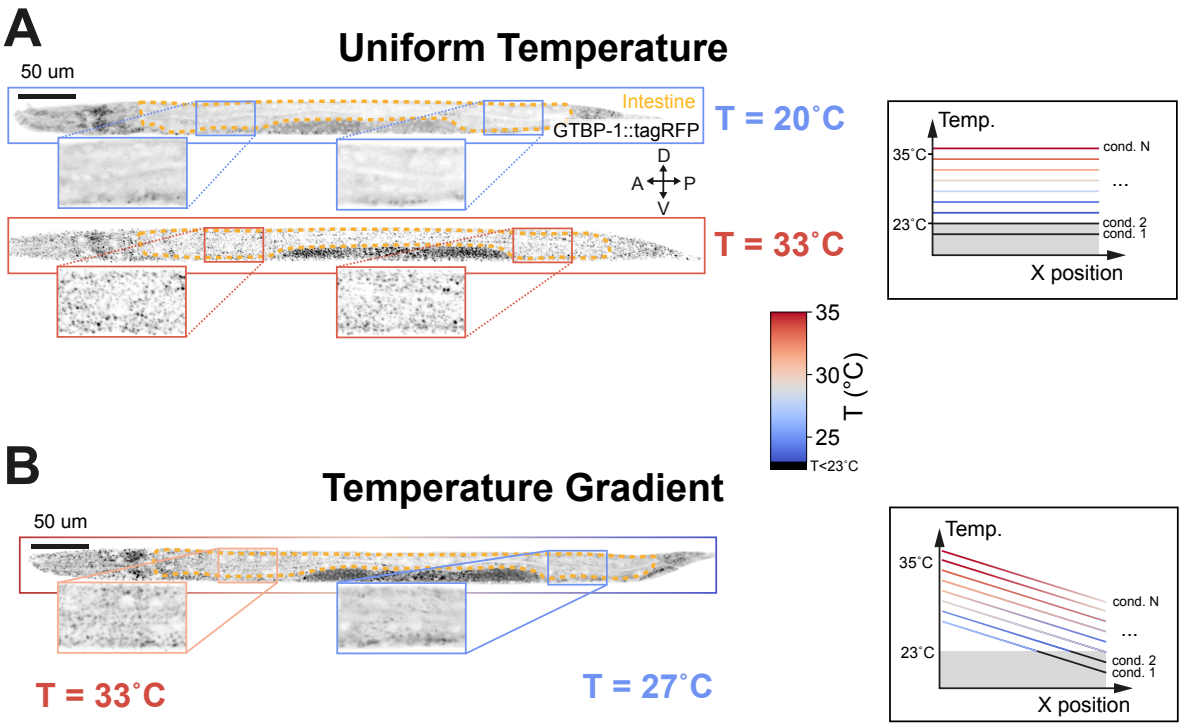


Figure 1: (A) A live *C. elegans* animal expressing a stress granule reporter, mounted in a microfluidic channel at 20C (top) and 33C (bottom). Insets show magnified views of the anterior and posterior intestinal cells. Dashed line outlines the intestine. Stress granules form body wide at high temperatures. (B) Same experiment in a steep temperature gradient of 10C/mm. The anterior of the animal is exposed stress-inducing temperatures, the posterior is not. Yet stress granules form even in the cold animal side.

(1) fast global temperature changes are applied and/or
(2) temperature can be raised **ONLY** in the head or tail region of the animal

Our preliminary data indicates that localized heating of either head or tail of the animal induces the formation of stress granules in a systemic fashion, even in the cold side of the animal, within minutes, suggesting a role for fast inter-tissue communication in organizing a body-wide cellular stress response. The molecular mechanisms mediating this communication are completely unknown.

In this internship, by imaging fluorescent reporter lines for the HSR as well as the formation of stress granules, and subsequent quantitative image analysis, we will explore how localized heat can be translated into the organism-wide activation of stress responses and how the dynamics of this activation differs from a scenario in which the entire organism is exposed to the temperature stress. To determine what role neuronal activity and secretion plays in this process, we will perform these experiments both in wild-type animals and animals in which neuronal secretion pathways are blocked.

Requirements

Candidates for this interdiscplinary project should have a background either in Cell & Developmental Biology or Microfluidics and Microfabrication with a strong interest pursuing fundamental biological questions.

Prior experience with handling *C. elegans* is a plus. Most importantly, candidates should be motivated to pursue interdisciplinary fundamental research and have a passion to see life in action. To apply, candidates should email us at wolfgang.keil@curie.fr.

Environment

The Keil lab at Institut Curie uses an interdisciplinary strategy to study transcriptional regulation, cell-fate patterning and morphogenesis in the model organism *C. elegans*. We are particularly interested in how developing system achieve robustness and precision in the face of environmental variability and molecular noise. To tackle this question, we develop and apply novel techniques for obtaining quantitative high-resolution dynamic gene expression data. We also develop theoretical approaches to conceptualize mechanisms of development and uncover general principles of developmental patterning. Check out https://curie.fr/equipe/keil for more information and feel free to contact us directly.

The Research Center at Institut Curie is a major player in the field of cancer research. It comprises a Hospital and a Research Center with over 1000 employees covering a wide range of nationalities. The Curie Institute Research Center aims to develop opened-ended science to progress in knowledge while exploiting arising possibilities to improve cancer care by stimulating synergies between research, training and innovation to support patients and serve our society.

Team references

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