EuReCa International PhD Program

PhD thesis project

2023 Call for application

Temperature scaling of gene regulatory networks for multicellular development

General information

Call	2023
Reference	2023-05-KEIL_HAMMELL
Keyword(s)	morphogenesis; cell-fate specification; live imaging of transcription, microfluidics; developmental timing;

Director(s) and team

Thesis director(s)	Wolfgang Keil & Christopher M. Hammell
Research team	Quantitative Developmental Biology Team
Research department	UMR168 - Physical Chemistry Curie

Description of the PhD thesis project

One of the most remarkable properties of developing multicellular systems is their ability to generate precise outcomes, e.g., cell fate patterns of morphogenetic events, even in the face of considerable fluctuations in their environment. To maintain developmental precision, organisms have evolved molecular mechanisms to change and adjust their developmental rates or even arrest development and resume at later time points. Combining microscopy, image analysis, mathematical modeling and genetics, our group investigates how this kind of robustness emerges during development, using *C. elegans* as a model organism with powerful genetics, genome-editing, and live-imaging tools.

In this PhD project, we will focus on the development and cell-fate specification of hypodermal stem cells. Using real-time live-imaging of transcription as well as transcription factor dynamics, we will try to uncover how the underlying gene regulatory networks achieve an invariant stem-cell fate-progression over a wide range of temperatures.

International, interdisciplinary & intersectoral aspects of the project

All projects in the lab run at the interface between developmental biology and biophysics with strong emphasis on interdisciplinarity. This project will be developed in close collaboration with the group of Christopher M. Hammell at Cold-Spring Harbor Laboratories which will provide expertise in genetics, biochemistry, and genome engineering. Several lab visits and joint retreats with this group are planned. To develop mathematical and computational methods for modeling cell-fate decisions, we collaborate with groups at Rockefeller University New York City as well as groups in Paris, France.

Recent publications

1. Brian Kinney, Shubham Sahu, Natalia Stec, Kelly Hills-Muckey, Dexter W. Adams, Jing Wang, Matt Jaremako, Leemor Joshua-Tor, **Wolfgang Keil***, Christopher M. Hammell*. Circadian rhythm orthologs drive pulses of heterochronic miRNA transcription in C. elegans. *bioRxiv* (2022)

2. Natalia Stec, Katja Doerfel, Kelly Hills-Muckey, Victoria M. Ettorre, Sevinc Ercan, **Wolfgang Keil***, Christopher M. Hammell*. An Epigenetic Priming Mechanism Mediated by Nutrient Sensing Regulates Transcriptional Output during *C. elegans* Development. *Current Biology* (2021)

3. Michelle A. Attner*, **Wolfgang Keil***, Justin M. Benavidez, Iva Greenwald. HLH-2/E2A Expression Links Stochastic and Deterministic Elements of a Cell Fate Decision during C. elegans Gonadogenesis. *Current Biology* (2019)

4. **Wolfgang Keil**, Lena M. Kutscher, Shai Shaham, Eric D. Siggia. Long-Term High-Resolution Imaging of Developing C. elegans Larvae with Microfluidics . *Developmental Cell* (2017)

5. Lena M. Kutscher, **Wolfgang Keil**, Shai Shaham. RAB-35 and ARF-6 GTPases Mediate Engulfment and Clearance Following Linker Cell-Type Death. *Developmental Cell* (2018)

Expected profile of the candidate

Applicants should have a strong desire to explore cell biological phenomena in an *in vivo* context from a biophysics viewpoint. They should show solid capacity for independent and creative thinking. Background in biophysics, developmental biology and/or cell biology is strongly recommended. The project relies heavily on microscopy and microfluidics techniques for live imaging, as well as quantitative image analysis for which the applicant should have either experience or a strong motivation to learn.