2019-11-20

EuReCa International PhD Program

PhD thesis project

2020 Call for application

‘What big eyes you have’: a systems biology approach to the developmental mechanisms of eye size variation

General information

Call	2020
Reference	2020-06-RAMAEKERS
Keyword(s)	Developmental variation, Temporal regulation of cell fate specification, Single-cell sequencing, Mathematical modeling, Organogenesis

Director(s) and team

Thesis director(s)	Ariane Ramaekers
Research team	Epigenetic plasticity and polarity of the embryo
Research department	UMR 3664 – Nuclear Dynamics

Description of the PhD thesis project

Pervasive morphological variation between individuals, between or even within species, suggests that different tuning of developmental gene regulatory networks (GRNs) modulates the size and shape of tissues and organs without disrupting their fundamental organization and function.

However, the exact mechanisms by which such coordinated – as opposed to pathological - developmental variation occurs in nature remain largely elusive. We tackle this question using variation of Drosophila eye size as a model system. In fruit flies, eye size varies between and within species. We recently demonstrated that inter and intraspecific variation in eye size can be caused by altering the proportion of the head primordium directed towards eye fate at the expense of other head fates, such as antenna or face. Quite unexpectedly, we found out that this is triggered by varying the time of the onset of eye fate specification, caused by different temporal regulation of the highly conserved eye specifying transcription factor, eyeless/PAX6 (Ramaekers et al. Dev. Cell. 2019).

The aim of this project is to decipher how regulatory networks governing head development in fruit flies modulate the temporal dynamics of eye fate specification, ultimately controlling eye size. To this goal, we will first use single-cell transcriptomics to build an atlas of gene expression during the specification of the distinct head fates. Based on this set of data, we will use mathematical modeling to draw hypotheses about the regulation of the temporal dynamics of eye fate specification which will be tested using genome engineering techniques such as CRISPR.

This project asks fundamental developmental biology questions relevant to both biomedicine – i.e. what distinguishes “healthy” vs “pathological” morphological variation and to evolutionary biology – i.e. how is morphological variation generated. It is highly interdisciplinary and lies at the interface between systems biology and developmental genetics.

International, interdisciplinary & intersectoral aspects of the project

This project combines cutting-edge single cell RNA sequencing techniques, mathematical modeling and genome engineering which must combine a broad range of expertise, largely represented within the host team and strengthen by collaborations within the Institut Curie and the nearby ENS.

The selected applicant may also have to spend some time in a collaborating laboratory in Switzerland, a leading expert in microfluidics developing methods for single-cell sequencing on small samples. By contributing to the optimization of pipelines for single cell sequence analyses on small samples, this project should be beneficial to a broad range of biological questions, including in the biomedical field. In the longer term, this could provide support for potential industrial applications.

Recent publications

1. **A. Ramaekers***, A. Claeys, M. Kapun, E. Mouchel-Vielh, D. Potier, S. Weinberger, N. Grillenzoni, D. Dardalhon-Cuménal, J. Jan, R. Wolf, T. Flatt, E. Buchner, Bassem A. Hassan*, 2019. Altering the temporal regulation of one transcription factor drives evolutionary trade-offs between head sensory organs. Dev Cell, 50: 780-792.

2. Lucas T, Tran H, Perez Romero CA, Guillou A, Fradin C, Coppey M, Walczak AM, **Dostatni N**, 2018. 3 minutes to precisely measure morphogen concentration. PLoS Genet. 2018 Oct 26;14(10):e1007676.

3. Tran H, Desponds J, Perez Romero CA, Coppey M, Fradin C, **Dostatni N**, Walczak AM. Precision in a rush: Trade-offs between reproducibility and steepness of the hunchback expression pattern. PLoS Comput Biol. 2018 Oct 11;14(10): e1006513.

4. S. Weinberger, M. P. Topping, J. Jan, N. De Geest, D. Ozbay, T. Hassan, X. He, J. T. Albert, B.A. Hassan*, **A. Ramaekers***, 2017. Evolutionary changes in proneural coding sequence quantitatively regulate sensory organ development and function. Elife 2017 Apr 13;6. pii: e26402.

5. C. Oliva, A. Soldano, N. Mora, N. De Geest, A. Claeys, M.-L. Erfurth, **A. Ramaekers**, D. Dascenco, D. Schmucker, N. Sanchez-Soriano, B. A. Hassan, 2016. Regulation of Drosophila brain wiring by neuropil interactions via a Slit-Robo-RPTP signaling complex. Dev. Cell. 39 (2): 267-278.

Expected profile of the candidate

Applicants should demonstrate a keen interest in fundamental aspects of animal development including from an evolutionary perspective. They should show solid capacity for independent and creative thinking. Applicants with a background in developmental biology, genomics, genetics and/or evolutionary biology are particularly encouraged to apply. Previous practical experience in transcriptomics, genome engineering or/and mathematical modeling is a plus but applicants strongly motivated to learn these approaches will also be considered.