

CRBM external seminar

Thursday, June 29th, 11:00 am Salle Marcel Dorée

Mechanism of Morphogen Gradient Scaling

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Maria's background is in Biochemistry (BA and MSc, University of Geneva) and Developmental Biology/Physics of Biology with a strong focus on quantitative imaging (PhD, University of Geneva). She had fruitful collaborations with organic chemistry labs that yielded in several publications. During her PhD and Postdoc, she has used her expertise in collaboration with theoretical mathematicians and physicists internationally to answer complex biological questions and go to the core of understanding of key phenomena in developing organisms, such as patterning and growth by morphogen gradients. This work has ultimately resulted in a recent publication in Nature.

Abstract

Morphogen gradients are fundamental to establish morphological patterns in developing tissues¹. During development, gradients scale to remain proportional to the size of growing organs. Scaling is a universal gear adjusting patterns to size in living organisms, yet its mechanisms remain unclear. Here, focusing on the Dpp gradient in the *Drosophila* wing disc, we unravel a cell biological basis behind scaling. From small to large discs, scaling of the Dpp gradient is achieved by increasing the contribution of the internalized Dpp molecules to Dpp transport: to expand the gradient, endocytosed molecules are re-exocytosed to spread extracellularly. To regulate the contribution of endocytosed Dpp to the spreading extracellular pool during tissue growth, it is the Dpp binding rates that are progressively modulated by the extracellular factor Pentagone, driving scaling. Thus, for some morphogens, evolution may act on endocytic trafficking to regulate the range of the gradient and its scaling, which could allow adaptation of shape and pattern to different sizes of organs in different species.

Selected publications

- Romanova-Michaelides M***, Hadjivasiliou Z, Aguilar-Hidalgo D, Basagiannis D, Seum C, Dubois M, Jülicher F, Gonzalez-Gaitan M. Morphogen gradient scaling by recycling of intracellular Dpp. **Nature**. 2022 Feb;602(7896):287-293. doi: 10.1038/s41586-021-04346-w. Epub 2021 Dec 22. PMID: 34937053.
- Aguilar Hidalgo, D., Hadjivasilou, Z., **Romanova-Michaelides, M.**, González-Gaitán, M. & Jülicher, F. Dynamic modes of morphogen transport. Preprint at <https://arxiv.org/abs/1909.13280> (2019).
- Romanova-Michaelides M**, Aguilar-Hidalgo D, Jülicher F, Gonzalez-Gaitan M. The wing and the eye: a parsimonious theory for scaling and growth control? *Wiley Interdiscip Rev Dev Biol*. 2015 Nov-Dec;4(6):591-608. doi: 10.1002/wdev.195. Epub 2015 Jun 24. PMID: 26108346.
- Piou T, Romanov-Michailidis F, **Romanova-Michaelides M.**, Jackson KE, Semakul N, Taggart TD, Newell BS, Rithner CD, Paton RS, Rovis T. Correlating Reactivity and Selectivity to Cyclopentadienyl Ligand Properties in Rh(III)-Catalyzed C-H Activation Reactions: An Experimental and Computational Study **JACS** 2017, 139(3)