

Mon, 22 Feb 2021 | 9 am | Online Zoom Session

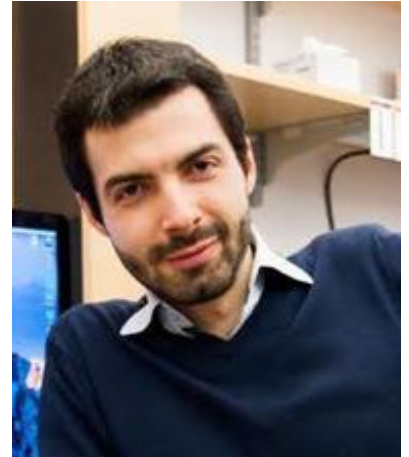
Hosted by Assoc Prof Toyama Yusuke

Listening to the scale-beat: Erk activity waves in zebrafish scale regeneration

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By **Alessandro DE SIMONE**

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About the Speaker

Dr. De Simone investigates the morphogenesis of regenerating tissues in zebrafish. To this end, he applies a quantitative approach at the intersection of cell biology, developmental biology and physics. Dr. De Simone studied theoretical physics at the University of Turin. At the time, he became interested in the collective behaviour of biological systems and in the possibility of investigating it with quantitative methods. To follow this interest, he performed his graduate studies in cell biology at EPFL, advised by Prof. Pierre Gönczy. There, he researched how dynein forces position centrosomes and nuclei in mitosis in the *C. elegans* early embryo. This early work at the interface of cell, developmental biology and imaging inspired an interest on how cellular events are orchestrated in multi-cellular systems, in particular during adult regeneration. Thus, he joined the Di Talia and Poss groups at Duke University, where he is studying the interplay of signals and cell behaviours in regeneration using a quantitative live imaging approach.

Regeneration is a complex chain of events that restores a tissue to its original size and shape. How are cells coordinated across the large sizes of regenerating adult tissues for proper morphogenesis? Signalling gradients established by diffusible morphogens regulate cell behaviour in myriad multicellular systems and contexts and have been proposed to direct regenerative events. In addition, feedbacks in biochemical pathways can provide an effective mechanism of communication. However, how these feedback mechanisms might regulate tissue regeneration remains largely unresolved, owing to difficulties in imaging, analysing and conceptualizing these complex systems. To overcome those barriers, we developed a quantitative platform to study morphogenesis in the regenerating scale of adult zebrafish, a simple bone disk amenable to live imaging. We discovered concentric traveling waves of Erk activity, broadcasted from a central source, that instruct hypertrophic growth of the regenerating osteoblast tissue. Using a combination of theoretical and experimental analyses, we find that Erk activity propagates as an excitable wave and traverse the entire millimetre-sized scale in approximately two days. Erk activity waves induce patterned tissue expansion and the frequency of wave generation controls the rate of scale growth, thus orchestrating scale morphogenesis. Furthermore, periodic induction of synchronous, tissue-wide, Erk activation in place of travelling waves impairs tissue growth, indicating that wave-distributed Erk activation is key to regeneration. Our findings reveal trigger waves as a regulatory strategy to coordinate cell behaviour and control tissue morphogenesis during regeneration.

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