Speaker: Filipa Simões
Affiliation: Institute of Developmental and Regenerative Medicine, University of Oxford, UK
Host: Pedro Simas
Title: Macrophage function in the regenerating heart.

Abstract:
The damage caused by myocardial infarction (MI) leads to a permanent loss of cardiac tissue in adult mammals. Following MI, large numbers of monocyte-derived macrophages are recruited to the injured heart. Macrophages are integral to both repair by scar formation and tissue regeneration; however, the local environmental cues and cell-cell interactions that control distinct macrophage functions across the damaged heart are largely unknown. I will describe recent findings where we reveal that macrophages directly contribute collagen to the forming post-injury scar. Unbiased transcriptomics shows an upregulation of collagens in both zebrafish and mouse macrophages following heart injury. Adoptive transfer of macrophages, from either collagen-tagged zebrafish or adult mouse GFPtpz-collagen donors, enhances scar formation via cell autonomous production of collagen. In zebrafish, the majority of tagged collagen localises proximal to the injury, within the overlying epicardial region, suggesting a possible distinction between macrophage-deposited collagen and that predominantly laid-down by myofibroblasts. Our findings contrast with the current model of scarring, whereby collagen deposition is exclusively attributed to myofibroblasts, and implicate macrophages as direct contributors to fibrosis during heart repair. A comprehensive understanding of the regenerative microenvironment in which the innate immune response persists but is permissible for regeneration, alongside targeting of macrophage-induced pro-fibrotic pathways, may ultimately contribute to the development of therapeutic strategies aimed at harnessing pro-regenerative responses within the injured mammalian heart.

Biography:
Filipa Simões is a Group Leader and British Heart Foundation Research Fellow at the Institute of Developmental and Regenerative Medicine, University of Oxford, UK. Her research is focused on understanding how immune cells, in particular macrophages, can be programmed by their neighbouring cells to repair the damage caused by a heart attack. Her team uses genomics, spatial transcriptomics and functional *in vivo* and *in vitro* assays to dissect the spatiotemporal dynamics of cellular microenvironments, identify intercellular signalling networks and decipher how these converge to define macrophage identity, plasticity and function in the healthy and diseased heart.

Filipa has a degree in Microbiology and Genetics from the Faculty of Sciences, University of Lisbon, Portugal, and a PhD in Biochemistry from the Faculty of Sciences and Technology, University of Coimbra, Portugal, which research was undertaken at the Weatherall Institute of Molecular Medicine, University of Oxford, UK. Here she used the zebrafish embryo to uncover the molecular cues driving cardiovascular specification and differentiation. Filipa did her postdoctoral work at the Department of Physiology, Anatomy and Genetics, University of Oxford, UK, where she identified distinct functional cell subpopulations in the developing and the regenerating epicardium, an essential lineage for heart development across species. Through a British Heart Foundation Centre of Research Excellence Transition Fellowship, Filipa identified macrophages as direct collagen contributors to the forming scar during both

zebrafish heart regeneration and mouse heart repair. This seminal work reveals paradigm-shifting insights into the source of collagen deposition during cardiac scar formation and is likely applicable across organ systems and fibrotic disease.