BP 3: Focus Physics of Stem Cells

Time: Monday 9:00–11:00 Location: BPc

BP 3.1 Mon 9:00 BPc

How Tissue Microenvironment Impacts Pluripotent Cell Differentiation — •Allyson Quinn Ryan[1,2], Diana Alves-Afonso[1], Jacqueline M. Tabler[1], and Carl D. Modes[1,2] — [1]Max Planck Institute for Molecular Cell Biology and Genetics — [2]Center for Systems Biology Dresden

The importance of stem cell population maintenance throughout both development and adulthood has been evident for several decades. Classically, how these populations are regulated is investigated through genetic and cell biological studies. However, work in recent years has shown forces exerted by and through tissue microenvironments to be of equal importance as molecular and transcriptional profiles to cell potency and identity. Here we show that collagen organization and tissue stiffness of the midline suture, a stem cell like niche in the cranial mesenchyme, is distinct from that of adjacent tissues. Surprisingly, Lamin A/C nuclear envelope expression is higher in suture than bone, despite the soft nature of the tissue. When collagen crosslinking is perturbed, Lamin A/C localization patterns, nuclear morphology and neighbor relationships within the suture are significantly altered. These results point towards a framework of noncellular tissue entities and collective organization influencing the maintenance of potency in developmental tissues.

BP 3.2 Mon 9:20 BPc

Robustness and timing of cellular differentiation through population based symmetry-breaking — Angel Stanoev[1], Dhruv Raina[1], Christian Schröter[1], and •Aneta Koseska[2] — [1]Department of Systemic Cell Biology, Max Planck Institute of Molecular Physiology, Dortmund — [2]Cellular computations and learning, caesar, Bonn

During mammalian development, cell types expressing mutually exclusive genetic markers are iteratively differentiated from a multilineage primed state. The current dynamical framework of differentiation, single-cell multistability, however requires that initial conditions in the multilineage primed state are appropriately controlled to result in robust proportions of differentiated fates.

We propose a fundamentally different dynamical treatment in which cellular identities emerge and are maintained on population level, as a novel unique solution of the coupled system. We show that the subcritical organization of such a coupled system close to the bifurcation point enables symmetry-breaking to be triggered by cell number increase in a timed, self-organized manner. Robust cell type proportions are thereby an inherent feature of the resulting inhomogeneous solution. In accordance with this theory, we demonstrate experimentally that a population-based mechanism governs cell differentiation in an embryonic stem cell model for an early lineage decision of mammalian embryogenesis. Our results therefore suggest that robustness and accuracy can emerge from the cooperative behavior of growing cell populations during development.

BP 3.3 Mon 9:40 BPc

Inference of emergent spatio-temporal processes from single-cell sequencing reveals feedback between de novo DNA methylation and chromatin condensates — •Fabrizio Olmeda[1], Tim Lohoff[2], Stephen Clark[2], Laura Benson[2], Felix Krueger[2], Wolf Reik[2,3], and Steffen Rulands[1,4] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]The Babraham Institute, Cambridge, UK — [3]University of Cambridge, Cambridge, UK — [4]Center for Systems Biology Dresden, Dresden, Germany

Recent breakthroughs in single-cell genomics allow probing molecular states of cells with unprecedented detail along the sequence of the DNA. Biological function relies, however, on emergent processes in the three-dimensional space of the nucleus, such as droplet formation through phase separation. Here, we use single-cell multi-omics sequencing to develop a theoretical framework to rigorously map epigenome profiling along the DNA sequence onto a description of the emergent spatial dynamics in the nucleus. We show how DNA methylation patterns of the embryonic genome are established through the interplay between spatially correlated DNA methylation and topological changes to the DNA. This feedback leads to the predicted formation of condensates of methylated DNA. Our work provides a general framework of how mechanistic insights into emergent processes underlying cell fate decisions can be gained by the combination of single-cell multi-omics and methods from theoretical physics.

BP 3.4 Mon 10:00 BPc

Competition for stem cell fate determinants as a mechanism for tissue homeostasis — •David J. Jörg[1,2], Yu Kitadate[3,4], Shosei Yoshida[3,4], and Benjamin D. Simons[1,2,5] — [1]Cavendish Laboratory, University of Cambridge, Cambridge CB3 0HE, UK — [2]Gurdon Institute, University of Cambridge, Cambridge CB2 1QN, UK — [3]Division of Germ Cell Biology, National Institute for Basic Biology, National Institutes of Natural Sciences, Okazaki, Japan — [4]Department of Basic Biology, School of Life Science, Graduate University for Advanced Studies (Sokendai), Okazaki, Japan — [5]Department of Applied Mathematics and Theoretical Physics, Centre for Mathematical Sciences, University of Cambridge, Wilberforce Road, Cambridge CB3 0WA, UK

Stem cells maintain tissues by generating differentiated cell types while simultaneously self-renewing their own population. The mechanisms that allow stem cell populations to control their density, maintain robust homeostasis and recover from injury remain elusive. Motivated by recent experimental advances, here we develop a robust mechanism of stem cell self-renewal based on competition for diffusible fate determinants. We show that the mechanism is characterized by signature dynamic and statistical properties, from stem cell density fluctuations and transient large-scale oscillation dynamics during recovery, to scaling clonal dynamics and front-like boundary propagation. We suggest that competition for fate determinants provides a generic mechanism by which stem cells can self-organize to achieve density homeostasis in an open niche environment.

30 min. Meet the Speaker