CCR – Lecture Series

Monday, March 11th 2024, 13:00

Leif S. Ludwig

Max Delbrück Center

Clonal dynamics and mitochondrial genetics via the lens of single-cell multi-omics

Mitochondria are special organelles central to metabolism and carry their own genetic information in the form of a small circular and multi-copy number genome. Here, I will introduce concepts and single-cell multi-omic technologies for leveraging the high mutational rate of mitochondrial DNA (mtDNA) that enable inferences of clonal population dynamics of native human cells in vivo. In the context of hematopoiesis and immunity, we leverage these approaches to longitudinally follow hundreds to thousands of mtDNA mutations to study fundamental aspects of hematopoietic (stem) cell biology during homeostatic, regenerative, and perturbed blood production to ultimately attain a more quantitative understanding of these processes. Further, mutations in the mitochondrial genome are associated with a clinically diverse spectrum of human phenotypes collectively known as mitochondriopathies. Curiously, we recently described the purifying selection of pathogenic mtDNA variants in select T cell populations suggesting unique cell-state-dependent metabolic vulnerabilities. Via the identification of a mosaic synonymous mtDNA variant in a healthy donor, we further suggest the limited diversity of the mitochondrial transfer RNA pool and variable codon affinity in mtDNA to shape evolutionary and somatic fitness, collectively demonstrating yet poorly appreciated aspects of mitochondrial genetics and its contribution to human phenotypic diversity and disease.

Venue: Lecture Hall B1, Borschkegasse 4a
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Host: Bernhard Englinger

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