Abstract

Spatial single-cell metabolomics reveals metabolic cell states

Seminar Series: Current research in Bioinformatics II

Description: Recent discoveries put metabolism into the spotlight. Metabolism not only fuels cells but also plays key roles in health and disease. In parallel, emerging single-cell technologies opened a new world of cell types and states previously hidden beneath population averages. Yet, methods for discovering links between metabolism, cell states, metabolic plasticity and reprogramming on the single-cell level and in situ are crucially lacking. Our research aims to contribute bridging this gap. First, we will present how the emerging technology of imaging mass spectrometry can be used for the spatial profiling of metabolites, lipids, and drugs in tissues. These efforts are enabled by our big data community cloud platform METASPACE which is increasingly used across the world. Next, we will present method SpaceM for spatial single-cell metabolomics. SpaceM detects 100+ metabolites and/or 500+ lipids from thousands of individual cells together with a fluorescence-based read-out and morpho-spatial features. We used SpaceM to characterize how stimulating human hepatocytes with fatty acids led to the emergence of two co-existing subpopulations outlined by distinct cellular metabolic states. Inducing inflammation with the cytokine IL-17A perturbs the balance of these states in a process dependent on NF-κB signalling. The metabolic-state markers were reproduced in a pre-clinical in vivo murine model of non-alcoholic steatohepatitis. We will show how a high-throughput version of the SpaceM method helps discover and characterize metabolic states of activated CD4+ T cells from peripheral human blood. Overall, such methods can open novel avenues for understanding metabolism in tissues and cell cultures on the single-cell level.