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Metabolic rewiring during liver regeneration

Failure of tissue repair and regeneration in patients with liver disease is life threatening. During hepatic regeneration, there is a connection between cell division and metabolism. This is exacerbated in cases with metabolic disorders, where recovery from liver resection is impaired. However, the cross-talk between cell metabolism and division in the liver during response to injury is ill defined. To understand this association, we used integrative analysis of transcriptomic and metabolomic data in combination with advanced molecular imaging. We uncovered that when cell division is blocked, hepatic regeneration after acute liver damage is delayed with a concomitant shift from carbohydrate to amino acid metabolism. These changes are driven by impaired mitochondria oxidation and respiration, together with profound remodeling of the pyruvate flux resulting in increased activity of alanine transaminase (ALT). Our results demonstrate that cell division is essential to maintain metabolic homeostasis in the liver and highlight the capacity of adaptation of metabolic flux in response to injury. These findings shed new light on the use of high-throughput data combined with molecular imaging to study metabolism during liver regeneration, offering new approaches to improve therapy and discovery of biomarkers potentially used in personalized medicine.

Biography

Philipp Kaldis has received his PhD from the Institute for Cell Biology, ETH (Swiss Federal Institute of Technology), Zürich, Switzerland, where he worked on the mitochondrial creatine kinase with Dr. Theo Wallimann and Dr. Hans Eppenberger. He has then joined Dr. Mark Solomon's Laboratory at Yale University School of Medicine, Department of Molecular Biophysics and Biochemistry, New Haven, Connecticut, as a Postdoctoral Fellow/Associate Research Scientist to investigate the activation of cyclin-dependent kinases (Cdks). He has later joined the NCI-Frederick as Tenure-Track Investigator and was promoted to Senior Investigator with tenure in 2006. In 2007, he has joined the IMCB as a Senior Principal Investigator. His main research interests are cell cycle, cancer, metabolism, liver regeneration and cancer.

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