Non-Canonical Metabolic Regulation of Mammalian Organogenesis

Summary

During the last decade, my work has been focused on cellular and molecular characterization of regulatory steps controlling mammalian organ formation in health and disease. To that end, I took advantage of my expertise on use of stem cells-derived organoids and mouse models to dissect those process particularly during eye morphogenesis. As an example of the power of these tools, during my talk I describe my recent work identifying novel functional roles of lactate in organogenesis.

Glycolysis is an evolutionary conserved metabolic pathway necessary to support bioenergetic demands during tissue growth and differentiation. Similar to tumors, retina utilizes aerobic glycolysis and its end product lactate. However, what advantage is conferred by preferential use of the glycolysis in retina morphogenesis is not yet known. By using a combination of eye organoids and mice, I found lactate plays an unexpected role in morphogenesis: organoids and embryos defective in glycolytic enzymes are defective in eye formation. Remarkably, addition of lactate to eye organoids is sufficient to rescue phenotype. I found lactate directly regulates histone deacetylation-mediated epigenetic modifications of eye developmental genes.

These novel results argue that metabolites act as signaling molecules playing diverse physiological signaling processes important during normal and pathological organ morphogenesis.