

Our laboratory investigates the reverse sides of two well-accepted theories related to the development of metabolic diseases: increased inflammation and uncontrolled production of reactive oxygen species (ROS). Thus, the focus of our research is the decrease of anti-inflammatory signals and the lack of regulated production of ROS in the development of diabetes and obesity.

Within these two topics we investigate the role of a prominent anti-inflammatory cytokine, interleukin-4 (IL-4) and its signal transmitter transcription factor, STAT6 in the regulation of lipid flux between adipose tissue and liver. In this context we demonstrated that mice deficient in STAT6 are prone to develop liver steatosis but stay relatively lean. The current focus of our research project is to understand the molecular mechanisms linking the IL-4/STAT6 axis to lipid metabolism both in liver and in adipose tissue.

The second main line of our research is related to the production of reactive oxygen species. ROS are highly reactive molecules that are produced both during normal cellular metabolism and under varying conditions of stress. In regular, physiological state the production and elimination of these radicals are in balance. If, for any reason, this balance is perturbed, ROS will accumulate in the cell and will trigger the onset of oxidative stress leading to the damage of cellular function and hampering cell survival.

More recently, however a novel concept emerged: ROS, when produced in a tightly regulated manner and present in small amounts, play vital and positive roles in cell growth, gene regulation and diverse signaling events. These positive/signaling ROS are generated by a specific class of enzymes, termed the NADPH oxidases (NOX-es). Our research focuses mainly on two specific NOX enzymes: NOX4 and NOX5 and investigates their role in the context of obesity and adipose tissue development, as well as in diabetes, with a particular focus on their role in the function of pancreatic islets.

For translational research, our objectives are to determine the therapeutic potential that may represent molecules that modify the signaling of the anti-inflammatory IL-4/STAT6 axis or enhance the activity of NOX enzymes. Indeed, molecules explicitly targeting NOX-es might prevent risks caused by taking anti-oxidants that eliminate ROS regardless of their sources of production, thus exert negative effects on cell functions, and beyond, the health of patients.

Our laboratory participates in the research network of the “Diabetes Center” of the University of Geneva.