Research Theme
Metabolic Disorders

Research Project Title
PPARγ in the Intestine as a Whole Body Metabolic Sensor

Principal Investigator
Professor Walter Wahli, LKCMedicine

Co-supervisor
Professor Sven Pettersson, LKCMedicine

Collaborator
Dr Kalina Duszka, LKCMedicine

Project Description
The aim of the project is to explore the influence of diet on the gut flora and the impact of gut flora on metabolic organs. Firstly, we propose to investigate the impact of gut microbiota on the gene expression profile of the intestine and other organ systems. Secondly, we will study the interaction and interdependence between the discovered eukaryotic gene targets and the microflora. Among many potential targets, attention will be paid to members of the Peroxisome Proliferator Activated Receptor subfamily (PPARα, PPARβ/δ, and PPARγ). It has been shown that PPARγ has anti-inflammatory properties in Intestinal Bowel Disease (IBD) and prevents colon cancer progression. Moreover, PPARγ is associated with intestinal microbiota composition. PPARα and PPARβ/δ were reported to modulate inflammation, too.

Up to now we have concentrated on PPARγ as a factor playing a role in the crosstalk between diet, gut flora and inflammation. The questions we are asking are now are: does PPARγ, known to be activated by polyunsaturated fatty acids (PUFA) and other dietary lipids serve as "metabolic sensor" in the intestine, and what are the consequences of its activity? How are PPARγ and its target genes affected by gut flora? In turn, how does PPARγ influence gut flora composition? What is the connection between the regulation by PPARγ of gut flora composition and its role in inflammation?

So far we showed that deletion of PPARγ in intestine epithelium lowers fatty acid and triglyceride plasma levels compared to wild type (WT) mice after lipid intake. Under certain conditions PPARγ in the intestine influences whole body fat content. Preliminary gut microbiota composition analysis revealed differences in the Clostridium coccoides group of bacteria between PPARγ mutant mice and their WT littermates. Furthermore, there is a downregulation of the number of bacteria in WT compared to mutated mice for all examined bacterial strains. The student will be involved in a study on how absence of bacterial flora (germ free mice) influences mouse metabolism and inflammatory parameters, particularly in PPARγ-null mice.
Contact Us
If you have questions regarding this project, please email the Principal Investigator.
Professor Walter Wahli
Walter.Wahli@ntu.edu.sg