Title Seminar: Gut epithelial metabolism as a key driver of intestinal dysbiosis

Abstract: In high-income countries, the leading causes of death are non-communicable diseases, such as obesity, cancer and cardiovascular disease. An important feature of most non-communicable diseases is inflammation-induced gut dysbiosis characterized by a shift in the microbial community structure from obligate to facultative anaerobes such as Proteobacteria. This microbial imbalance can contribute to disease pathogenesis due to either a microbiota-derived metabolite being depleted or produced at a harmful concentration. However, little is known about the mechanism by which inflammation mediates changes in the host physiology to induce disruption of the microbial ecosystem in our large intestine leading to disease. Recent work by our group suggests that during gut homeostasis, epithelial hypoxia derived from PPARγ-dependent β-oxidation of microbiota-derived short-chain fatty acids limits oxygen availability in the colon, thereby maintaining a balanced microbial community. During inflammation, disruption in gut anaerobiosis drives an expansion of facultative anaerobic Proteobacteria, regardless of their pathogenic potential. Therefore, our research group is currently exploring the concept that dysbiosis-associated expansion of Proteobacteria can thus be viewed as a microbial signature of epithelium dysfunction and has further consequences in different models of non-communicable diseases, including diet-induced obesity and inflammation-associated colorectal cancer.