Investigating the impact of microbiota on tanycyte barrier controlling food intake

Introduction: An adequate balance between energy supply and expenditure is essential to ensure a healthy life. To maintain this homeostasis, the brain is engaged in continuous dialogue with peripheral tissues to regulate the fraction of energy that enters (i.e., food intake) and leaves the organism (i.e., energy expenditure). In the last decade, it has become clear that tanycytes –peculiar hypothalamic glial cells lining the bottom of the third ventricle– are in a prime position at the blood/hypothalamus interface to control blood/brain exchanges. Indeed, tanycytes assume the role of a plastic blood-brain barrier to modulate the access of metabolic hormones and nutrients into the brain; thus, during fasting, this access is facilitated to induce food intake (Langlet *et al.*, Cell Metab, 2013). However, the mechanisms underlying such plasticity remain largely unexamined.

Preliminary results: Microbiota has an impact on food intake by modulation of hypothalamic orexigenic neuron expression. Indeed, chronic administration of oral butyrate (*i.e.*, a short-chain fatty acid produced by the degradation of fibers by anaerobic bacteria) reduces food intake in mice (Li *et al.*, Gut 2018). As butyrate can enhance the intestinal barrier function, we hypothesize a similar event occurs at the tanycyte barrier to modulate hormone and nutrient access to the hypothalamus and consequently control neuronal functions and energy balance.

Approach: This project aims to elucidate the impact of microbiota on tanycyte barrier plasticity and their involvement in regulating energy balance. A multidisciplinary approach, including neuroanatomy, molecular biology, microbiology, and physiology, will be implemented to achieve this goal.

Significance: The elucidation of tanycyte barrier plasticity will be essential to explain the regulation of energy balance and to allow the development of new therapeutic strategies for type 2 diabetes and obesity.