Neural signaling mechanisms linking overnutrition and obesity

Summary

The brain is long known as a critical regulator of energy balance. In an era of the obesity epidemic, it is of interest whether and how the brain mediates obesity upon excess nutrients. We are particularly searching for neural pathways that actively respond to overnutrition and mediate dietary obesity. Toward this end, employing first our unique ex vivo brain slice model, the primary focus of our research is the identification of critical pathways that induce hypothalamic hallmarks of obesity. We will then validate plausible candidates in genetic mouse models in vivo to determine whether they have a role in dietary obesity. In this seminar, I will present our recent findings that illuminate a novel hypothalamic signaling mechanism involving two previously unrelated obesity susceptibility genes. Based on our findings, I will also propose a gut-derived hormone GIP (Glucose-dependent insulino tropic polypeptide) as a long-sought signal that arises from excessive caloric intake, regulates hypothalamic metabolic circuitry and drives leptin resistance and obesity. Through these multidisciplinary approaches, our study will shed light on the neurobiological causes of obesity.