S08-6 BOSS as a membrane GPCR receptor to regulate energy homeostasis

◯Yoshio HIRABAYASHI[1,2]

[1]RIKEN Brain Science Institute, [2]CREST, JST

Lipid (triacylglycerol) and glucose serve as energy sources, and the latter exerts many hormone-like regulatory effects in a wide variety of eukaryotic cell types. However, it is not fully elucidated how organisms respond to circulating glucose to control nutrient and energy homeostasis. Drosophila shares the common basic metabolic functions present in vertebrate. G-protein coupled receptors (GPCRs) are a large superfamily of membrane proteins that respond to a variety of extracellular molecules playing important roles in physiological events such as cell-cell communication, sensory perception, chemotaxis, neurotransmission, etc. Understanding ligand-receptor relationships represents a critical step in developing drugs for GPCR-related diseases. We found that an orphan *Drosophila* GPCR, BOSS, formally identified as a ligand for the receptor tyrosine kinase Sevenless, is expressed in the fat body (the fly equivalent of the liver and adipose tissues in mammals) and is required for proper insulin signaling (Kohyama *et al.,* PNAS, 2008). This receptor responded to glucose in a concentration dependent manner but did not respond to other sugars. Deletion of the *DGR1* gene caused down-regulation of the insulin/PI3K signaling cascade, perhaps due to decreased secretion of insulin, leading to an increase in circulating lipid and glucose levels. Our findings provide insights not only into the conserved mechanisms of metabolic regulation but also into the pathological basis for diabetes and obesity.