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Physiological functions of GPCRs sensing Long-chain Free Fatty Acids

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A strategy to deorphanize G-protein-coupled receptors (GPCRs) identified a series of receptors, which are activated by Free Fatty Acids (FFAs). Hence, FFAs are now recognized as not only essential nutritional components but also signaling molecules in various physiological processes. A number of previous studies showed that GPCRs sensing FFAs play significant roles in nutritional regulation. In this free fatty acid receptor family, FFAR1 (GPR40) and FFAR4 (GPR120) are activated by long-chain FFAs. FFAR1 regulates insulin secretion in pancreatic beta-cells. FFAR4 promotes the secretion of glucagon-like peptide-1 (GLP-1) in the intestine, mediates anti-inflammatory effects of docosahexaenoic acid in macrophages and acts as a lipid sensor in adipose tissue to sense dietary fat and control systemic energy homeostasis. Furthermore, we recently found novel roles of these fatty acid receptors in the relationship between gut microbiota and host energy metabolism via the metabolites of dietary fatty acids. In this symposium, I will introduce recent advances in the physiological roles of FFAR1 and FFAR4, and I further present a summary of current understandings of their pharmacological characterization and their potential as drug targets.