Bile acid receptor in the gut: potent therapeutic strategy for the treatment of type Ⅱ diabetes

Sungsoon Fang, Ph.D.
Department of Severance Biomedical Science Institute
Gangnam Hospital, Yonsei University College of Medicine, Seoul, Korea

Farnesoid X receptor (FXR) has been known to be a key component in regulating metabolic homeostasis including glucose and lipid metabolism as well as bile acid (BA) homeostasis. Previously we demonstrated that Fexaramine (Fex) is a gut-specific FXR agonist to reduce diet-induced weight gain, body-wide inflammation and hepatic glucose production, while enhancing thermogenesis and browning of white adipose tissue. In the present study, we report that Fex restores pancreatic β-cell functions with robustly enhanced glucose-stimulated insulin secretion (GSIS) in diabetic mice without body weight changes. We found that Fex potentiates bioenergetics to enhance GLP-1 secretion in enteroendocrine L cells. Concomitantly, Fex increases gene expression of Glucagon-like peptide-1 receptor (GLP-1R) in pancreatic β-cells, resulting in restoration of GSIS in β-cells to ameliorate hyperglycemia in ob/ob mice. Our findings propose that enteroendocrinal FXR activation would be promising therapeutic strategy to treat type Ⅱ diabetes.