SCOHIA PHARMA, Inc.
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Publication regarding a preclinical study of SCO-267, a novel GPR40 agonist

In a new study published in *Journal of Pharmacology and Experimental Therapeutics*, researchers of SCOHIA PHARMA, Inc. and Takeda Pharmaceutical Co., Ltd. have shown that SCO-267, a GPR40 full agonist, is highly effective in improving glycemic and body weight control in rat models of diabetes and obesity.

Research title
SCO-267, a GPR40 full agonist, improves glycemic and body weight control in rat models of diabetes and obesity
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GPR40, a G-protein-coupled receptor (GPCR), couples predominantly with the Gq/11 protein, promoting phospholipase C-dependent hydrolysis of phosphatidylinositol 4,5-bisphosphate into diacylglycerol and inositol 1,4,5-triphosphate. GPR40 is expressed in pancreatic beta-cells and intestinal endocrine cells, and its activation stimulates insulin and incretin secretion. As insulin and incretin are pivotal for glycemic control, GPR40 activation is considered a new option for treating diabetes.

In the current study, treatment with SCO-267 activated down-stream signaling of GPR40 in both high- and low-GPR40-expressing cells. When administered to rats, SCO-267 increased insulin, glucagon, GLP-1, glucose-dependent insulinotropic peptide (GIP), and peptide YY (PYY) secretions. These results show the full agonistic property of SCO-267 against GPR40. In diabetic rats, SCO-267 was highly effective in stimulating insulin and GLP-1 secretions and improving glucose tolerance. Obese rats treated with SCO-267 showed elevated plasma GLP-1 and PYY levels, reduced food intake, and decreased body weight.

In summary, SCO-267 stimulated islet and gut hormone secretion, improved glycemic control in diabetic rats, and decreased body weight in obese rats. These data suggest the therapeutic potential of SCO-267 for the treatment of diabetes and obesity.

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