



SCOHIA PHARMA, Inc.

September 10, 2020

Publication regarding medicinal chemistry research on a GPR40 full agonist (SCO-267)

The research group of SCOHIA PHARMA, Inc. has published research results on the medicinal chemistry leading up to the discovery of SCO-267, a GPR40 full agonist. The results have been published online in the *Journal of Medicinal Chemistry* and in the EFMC-ISMC & EFMC-YMCS Virtual Poster Session on September 9, 2020.

Article title:

Design and Identification of a GPR40 Full Agonist (SCO-267) Possessing a
2-Carbamoylphenyl Piperidine Moiety

<https://pubs.acs.org/doi/10.1021/acs.jmedchem.0c00843>

Poster presentation title:

Design and Identification of a GPR40 Full Agonist (SCO-267) Possessing a
2-Carbamoylphenyl Piperidine Moiety for the Treatment of Type 2 Diabetes Mellitus

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SCO-267 is a first-in-class full agonist of GPR40, a G protein-coupled receptor expressed in the pancreatic islets and gastrointestinal tract. SCO-267-mediated full agonism of GPR40 promotes secretions of islet and gastrointestinal hormones, including GLP-1, and is therefore expected to exert a powerful therapeutic effect in diabetes. Additionally, our research group recently reported that SCO-267 has potential as a treatment for obesity and non-alcoholic fatty liver disease (NAFLD).

In this publication, the medicinal chemistry research that led to the discovery of SCO-267 is reported. By optimization of the structure of a lead compound for strong receptor activation and improvement of its physicochemical properties—conversion of the highly planar mother skeleton to a saturated ring and introduction of a polar group into the appropriate position—we have discovered SCO-267, which has strong full agonistic activity against human GPR40 and a good profile as a drug candidate. The presentation also included potent anti-diabetic, anti-obesity, and anti-NAFLD effects of SCO-267 in the respective animal disease models.

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