6-Azaindole GNF2133 as DYRK1A Inhibitor for Promoting β-Cell Proliferationv

Yahu A Liu

GNF/Novartis Institutes for BioMedical Research, San Diego, CA 92121, USA

Abstract

Either type I or type II diabetes results from insufficient pancreatic β-cell mass or function. Dual specificity tyrosine-regulated kinase 1A (DYRK1A) plays a key role in pancreatic β-cell proliferation. Hence, inhibition of DYRK1A to regenerate functional insulin-producing β-cells could be an approach toward diabetes intervention. Through medicinal chemistry optimization of an initial hit, we identified DYRK1A inhibitor 6-azaindole GNF2133 which demonstrated significant dose-dependent glucose disposal capacity and insulin secretion in response to GPAIS challenge in RIP-DTA mice. The work offers a potential to treat diabetes with oral therapies by restoring β-cell mass, insulin content and glycemic control. **Either type I or type II diabetes results from insufficient pancreatic β-cell mass or function. Dual specificity tyrosine-regulated kinase 1A (DYRK1A) plays a key role in pancreatic β-cell proliferation. Hence, inhibition of DYRK1A to regenerate functional insulin-producing β-cells could be an approach toward diabetes intervention. Through medicinal chemistry optimization of an initial hit, we identified DYRK1A inhibitor 6-azaindole GNF2133 which demonstrated significant dose-dependent glucose disposal capacity and insulin secretion in response to GPAIS challenge in RIP-DTA mice. The work offers a potential to treat diabetes with oral therapies by restoring β-cell mass, insulin content and glycemic control.**

Biography:

Yahu A. Liu is Senior Outsourcing Manager and a Principal Scientist (II) at GNF/Novartis Institutes for BioMedical Research, and also serves as a Vice Chairman of the Board of Directors in Sino-American Biotechnology and Pharmaceutical Professional Association (SABPA). Yahu has 25+ years of experience in drug discovery and development. He previously worked in medicinal chemistry teams at ChemBridge, Vertex, and Pfizer. Prior to coming to the states, he had worked as an associate director in the Chinese Institute of Standards and Technology, CTO of Huarui Fine Chemical Co. Ltd. and a Certificate Engineer (Process Chemistry) at WH Chemical Co. (Beijing, China). In drug discovery research, Yahu has contributed to four drug/drug candidates. His main contribution to organic chemistry includes his discovery of three rearrangement reactions and syntheses of two natural products. He has been a co-editor of one book, a member of the editorial boards of two biochemistry journals, an issue editor of two journals, a co-organizer of 40+ conferences/ symposiums, and a co-author of ~160 publications, patents and conference presentations. He received SABPA Distinguished Service Award in 2017, SABPA Outstanding Service and Leadership Award in 2016, SABPA Outstanding Leadership Award in 2011, SABPA Achievement Award in 2008 and SBTSC Scientific and Technical Achievement award twice.

Yahu received his Ph.D. degree from Case Western Reserve University in the laboratory of the late Prof. Lawrence M. Sayre (Chemistry/Pathology/Environmental Health). He earned a degree of Master of Engineering from Beijing Institute of Light Industry and obtained his early chemical education at Shanxi Teacher's College (China).

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