Drug Discovery & Development

Activating Appendages To Induce Polypharmacology In Peptide Hormone Analogues, Including Dual GLP-1R / GIP Agonism

View U.S. Patent Application Publication No. US-2025-0026782 in PDF format.

WARF: P230413US02

Inventors: Samuel Gellman, Kyle Brown, Rylie Morris

The Invention

UW-Madison researchers have developed a synthetic peptide through a single amino acid substitution and chemical conjugation of an aromatic molecule at the site of mutation that turns a peptide that binds one of the class B GPCRs into a dual agonist. The peptides the researchers designed bind and activate both the glucagon-like peptide-1 receptor and glucose-dependent insulintropic polypeptide receptor. This is the mechanism of activity for the recently approved obesity drug Mounjaro.

GLP-1 and GIP each contain 29 or more amino acid residues, but their sequences differ. GLP-1 does not activate the GIPR, and GIP does not activate the GLP-1R. The inventors discovered that a single change (mutation to a Lys followed by conjugation of an aromatic molecule) in the sequence of GLP-1 can “turn on” agonist activity at the GIPR. In addition, they discovered that a single change in the sequence of GIP can “turn on” agonist activity at the GLP-1R. They do observe a slight loss in affinity to the receptors for the mutant peptides as compared to the native sequence. They have *in vitro* data showing that the mutant peptide can bind and activate the two GPCRs.

Additional Information

For More Information About the Inventors

- Samuel Gellman

Tech Fields

- Drug Discovery & Development : Drug production & design
- Therapeutics & Vaccines : Biologics
- Therapeutics & Vaccines : Metabolic disorders

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847