

Novel approach to lose weight? Harnessing cryo-EM to understand how Retatrutide interacts with the GLP-1R

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Abstract:

The Glucagon-like peptide 1 receptor (GLP-1R) is a key target for therapeutics aimed at treating obesity and diabetes due to its role in regulating glucose homeostasis and appetite. Retatrutide, a novel drug candidate, has shown promising clinical results by acting on the GLP-1R to promote weight loss and improve metabolic health.

Here, we present the cryo-electron microscopy (cryo-EM) structure of GLP-1R in complex with the stimulatory G protein (Gs) and retatrutide, resolved to a sub-3Å resolution.

Achieving this structure involved a multi-step process from protein expression, complex purification and sample preparation for cryo-EM. This structure reveals many key molecular interactions between the GLP-1R and retatrutide, offering novel insights into its pharmacological mechanism and provides a foundation for future drug design. The poster will discuss the critical biochemical steps undertaken to reach this high-resolution structure and highlight the potential of retatrutide as a therapeutic agent for metabolic disorders.