Summer Research Program 2026 – Projects

Project #7

Title: Role of Wnt/β-Catenin Signaling in Tirzepatide-Mediated Regulation of Adipocyte Plasticity and Metabolic Function in *in-vitro* model

Description: Adipocyte plasticity plays a critical role in metabolic homeostasis, obesity, and insulin resistance. Dysregulated adipocyte differentiation and dedifferentiation contribute to adipose tissue dysfunction, lipotoxicity, chronic inflammation, and impaired insulin sensitivity, particularly in visceral fat depots. While tirzepatide, a dual GIP/GLP-1 receptor agonist, has demonstrated strong clinical efficacy in reducing body weight and improving insulin sensitivity, the cellular and molecular mechanisms underlying its effects on adipose tissue remain incompletely understood. The Wnt/β-catenin signaling pathway is a key regulator of adipogenesis, adipocyte fate determination, and metabolic reprogramming. Aberrant activation or suppression of this canonical pathway has been linked to impaired adipocyte differentiation, altered lipid handling, and metabolic dysfunction. Understanding whether tirzepatide modulates adipocyte plasticity through Wnt/β-catenin signaling may provide critical insight into its beneficial metabolic effects.

The primary objective of this study is to determine whether tirzepatide can reverse adipocyte dedifferentiation or reprogram adipocyte metabolic function through modulation of the canonical Wnt/β-catenin signaling pathway.

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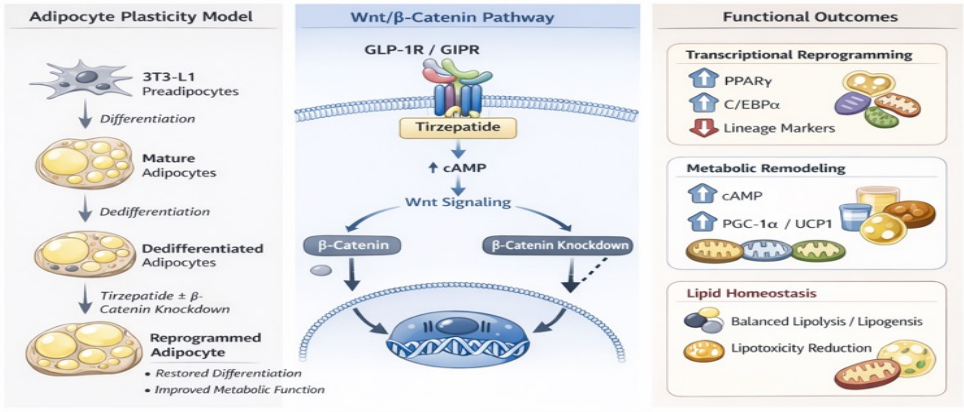

Figure 1. Experimental design and mechanistic framework of tirzepatide action on adipocyte plasticity.
3T3-L1 preadipocytes are differentiated into mature adipocytes and subsequently dedifferentiated to a preadipocyte-like state. Dedifferentiated cells are treated with tirzepatide in the presence or absence of β-catenin knockdown to assess the role of canonical Wnt/β-catenin signaling. Transcriptional, metabolic, and signaling readouts are analyzed to determine whether tirzepatide reverses adipocy te dedifferentiation and restores a metabolically healthy adipocyte phenotype.