# Scalable Hybrid Framework for Mapping the GPCR-Peptide Interactome: A Proactive Genome-Scale Safety Audit of GLP-1

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GLP-1 drugs address diabetes-obesity crisis that claims 12 lives per minute from associated complications, yet their uncharacterized off-targets may pose long-term health risks. Current safety protocols rely on limited wet-lab screening during drug development and post-market reporting, leaving big scalability gaps. As the 2004 Vioxx safety disaster demonstrated, proactive pharmacovigilance is essential for blockbuster therapies. With many millions of users and GLP-1 market projected to hit $268B by 2030, a genome-scale blind spot in drug safety is a critical public health challenge. To address this challenge, I developed a scalable hybrid computational framework to predict GPCR-peptide interactions. As an independent researcher using accessible web-based tools without laboratory or high-performance computing resources, I integrated AlphaFold-Multimer simulations with genome-wide biological filtering. Validated against an independent experimental benchmark (n=483), filtering improved specificity from AF-M's 42% to 85% (accuracy 79.1%), reducing structural false-positive noise. Applied to GLP-1 study, the framework audited human non-olfactory GPCRs (n=400), reducing experimental search space by 98% to identify 9 high-confidence interactions from 189 structural hits. Results validated the primary receptor while identifying 7 novel off-target leads whose biological functions suggest plausible mechanistic links to reported gastroparesis and potential long-term bone effects, warranting further experimental investigation.  My accessible, genome-scale framework proactively predicts GPCR-peptide off-targets, enabling clinical risk prioritization to improve drug safety and prevent chronic adverse events across a broader peptide-biologic landscape before population exposure.

**Awards Won:**