Nature-inspired peptide hormones as next generation GPCR drug scaffolds

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Peptides are central mediators of intercellular communication and exert many of their biological effects through G protein-coupled receptors (GPCRs), the largest and most pharmacologically tractable receptor family. Despite their high potency and selectivity, the therapeutic development of peptide ligands has been limited by poor metabolic stability and an incomplete understanding of receptor-specific signalling mechanisms. In this seminar, I will present peptide-based strategies for GPCR drug discovery that integrate natural peptide mining, pharmacology-guided screening, as well as rational and computational design, while also leveraging peptides as molecular tools to dissect GPCR signalling. By exploiting diverse natural scaffolds, we generate peptide ligands with enhanced stability, improved receptor selectivity, and finely tuned signalling profiles. Selected examples targeting the κ-opioid receptor, oxytocin/vasopressin receptors, and the cannabinoid 2 receptor illustrate how stabilized peptides enable detailed exploration of molecular signalling properties and how functional specificity and improved drug-like characteristics can be achieved, highlighting the potential of peptides as next-generation therapeutic candidates.

Christian W. Gruber is Research Group Leader and Associate Professor at the Medical University of Vienna. He studied Biochemistry at the University of Tübingen and obtained his PhD in Molecular Biosciences from The University of Queensland. His research focuses on the discovery, structural optimization, and pharmacological characterization of nature-derived peptides from plants and invertebrates, with a particular emphasis on GPCR ligands and peptide drug development. He currently leads a large international consortium ‘Biodiversity2Drugs’ with a strong focus on GPCR-targeted peptide discovery and pharmacology. He is also co-chair of the European Peptide Symposium 2026 to be held in Vienna.
Further Information: www.gruber-lab.com & www.eps2026.com