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Design of novel receptor selective bioavailable peptide and peptidomimetic ligands for G protein coupled receptors involved in major degenerative diseases

G-protein Coupled Receptors (GPCRs) are targets for 30% of current drugs, but there are many unmet needs because these receptors and their ligands are intimately involved in many of our degenerative diseases. It has been difficult to obtain drugs that are effective and without side effects because there often are multiple subtypes of receptors and the endogenous hormones and neurotransmitters are non-selective. The 5 melanocortin receptors (MCRs) and the 3 opiate receptors (ORs) are important examples that are involved in many degenerative diseases, both central and peripheral. There is only 1 drug on the market for the MCRs, and the drugs on the market for the ORs are toxic and currently a great concern because of the drug overdose epidemic, which is costing billions and thousands of lives. To address this problem, we have developed a multimodal approach, using a combination of novel peptide and peptidomimetic scaffolds that address drug design in 3-dimensional space, with novel cyclic templates, computer assisted ligand/receptor interactions, orthosteric and allosteric agonist and antagonist activities, receptor selectivity and bioavailability for both the blood brain barrier and oral/transdermal availability. As time permits, we will illustrate this approach with design of melanotropin ligands that are highly selective agonists or antagonists for only 1 of the melanocortin receptors involved in pigmentary disorders, cancer, feeding and sexual disorders and neurodegeneration. For the opiate receptors, multivalent ligands that target opiate receptors and other receptors involved in pain pathways all in single ligands which do not have the toxicities of current opiates.

Biography

Victor J Hruby has received his PhD from Cornell University and has completed his Postdoctoral studies with Noble Laureate Vincent du Vigneaud. Currently, he is a Regents Professor at the University of Arizona, with major research interests in peptide hormones and neurotransmitters and their GPCR receptors, and their relationships to health and disease. He has over 1300 publications, chapters and reviews and over 25 patents. He has received numerous awards for his research, has been an editor and associate editor and on the Editorial Boards of several journals. He has served on several NIH Study Sections and been a consultant for many drug companies.

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