"A Bivalent Ligand Approach to Study the Interaction of the mu Opioid Receptor and the Chemokine Receptor CCR5 in Neurological Disorders" VCU # 12-001

Applications

- Further research into the dimerization of MOR and CCR5 receptors
- Potential development of new treatments for opioid addicted patients with HIV

Advantages

- Bivalent ligand containing Naltrexone and Maraviroc pharmacophores
- Binds both MOR and CCR5 receptors
- Ligand binding does not affect function of MOR or CCR5
- Developed synthesis reaction with moderate to good yields

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Market Need

Drug abuse has major implications on the prevention and treatment of human immunodeficiency virus (HIV). Use of the opiod morphine has been observed to accelerate the onset of HIV infection through the up-regulation of chemokine receptor CCR5, used by the HIV virus to infect host cells. Recent studies have shown the mu opiod receptor (MOR), which is bound by morphine, forms a putative MOR/CCR5 heterodimer. This could revolutionize treatment options for opiod addicted HIV patients. Current treatments involve simultaneous opiod substitution therapy and HIV antiretroviral agents, but this treatment regime has been observed to have an adverse drug-drug interaction. Further characterization of the MOR/CCR5 heterodimer should be performed to explore the possibilities of the simultaneous treatment of opiod dependence and HIV infection.

Technology Summary

This is a novel bivalent ligand that binds both the MOR and CCR5 receptors. Through a unique 16 step reaction, a compound is synthesized such that two distinct pharmacophores, Naltrexone and Maraviroc, are joined by a 21 atom linkage. Both Naltrexone and Maraviroc interact with MOR and CCR5, respectively, while retaining their original antagonistic properties. This bivalent ligand can serve as a pharmacological probe to study the function of MOR/CCR5 dimers and their involvement in opiate addiction and HIV infection.

Technology Status

U.S. Patent Pending: 14/377,205

Ligand and synthesis reaction have been developed with moderate to good yields. Further experiments are being performed to increase each pharmacophore's binding affinity to its respective receptor. Further details are available in *Org. & Biomol. Chem.* 2012 Advanced Publication.

This technology is available for licensing to industry for further development and commercialization.