



Novel Opioid Analgesics with Reduced Tolerance

Summary

UMB 425 is a novel opioid with bi-functional activity that combines a delta-opioid antagonist and a mu-opioid agonist in a single compound with antinociceptive effects comparable to morphine. With reduced tolerance liabilities, UMB 425 provides a novel therapeutic approach in the treatment of patients who suffer from chronic pain with reduced risk for the development of tolerance and addiction.

Key Investigator

Andrew Coop
Alexander MacKerell
Rae R. Matsumoto

Field

Pain Therapeutic

Technology

Small Molecule
Pain

Advantages

Novel compound

Status

Available for licensing
Available for sponsored
research

Patent Status

US Patent 9,422,302 issued
8/23/2016, AU 2014225685,
CA 2,911,681, EU 14 759
505.2 filed 8/28/2015

UMB Docket Reference

AC-2013-055

External Reference

[Bioorg Med Chem. 2012 Jul
15;20\(14\): 4556-63.](#)

[J Phys Chem B. 2011 Jun
9;115\(22\): 7487-96.](#)

[Curr Top Med Chem.
2011;11\(9\): 1157-64.](#)

Market

Opioids such as codeine, morphine and oxycodone have long been used to treat moderate to severe pain. Opioid effects are mediated through activity on the delta- and mu- opioid receptors found in the Central Nervous System. Although invaluable in alleviating pain, opioids have the potential for tolerance, wherein the body becomes less responsive to their effects. Tolerance occurs when opioids exert a synergistic analgesic effect that activates both delta- and mu-opioid receptors. Tolerance leads to increased dose requirements to keep the patient in a pain free state. However, increasing doses result in undesired effects such as respiratory depression, tolerance, physical/psychological dependence, constipation, sedation, nausea/vomiting and dizziness. Current therapeutic approaches circumvent tolerance by co-administering a delta-opioid antagonist with a mu-opioid agonist.

Technology

Researchers at UMB have developed a novel opioid analgesic compound (named UMB 425) that combines the activities of both a delta-opioid antagonist and a mu-opioid agonist in a single compound. UMB 425 reduces the development of tolerance to analgesia with substantially fewer side effects than current opioids (such as morphine or oxycodone). In vivo studies performed where Swiss Webster mice (male) were treated with UMB 425 demonstrated a significant reduction in pain sensitivity in the hot plate and tail-flick assays over morphine during a six day tolerance paradigm. UMB 425 has nanomolar affinity and efficacy for mu-opioid receptors similar to morphine and moderate affinity for delta-opioid receptors for which it exhibits antagonistic effects. The bi-functional activity of UMB 425 has the potential to be an effective treatment for patients who suffer from chronic pain with reduced risk for the development of tolerance and addiction. UMB 425 minimizes tolerance development with no corresponding increase in dosage required, obviating most undesirable side effects associated with opioid use.

Technology Status

UMB 425 is a novel opioid compound.

1. In vivo studies performed where Swiss Webster mice (male) were treated with UMB 425 demonstrated a significant reduction in pain sensitivity in the hot plate and tail-flick assays over morphine during a six day tolerance paradigm.
2. UMB 425 has nanomolar affinity and efficacy for mu-opioid receptors similar to morphine and moderate affinity for delta-opioid receptors for which it exhibits antagonistic effects