



Therapeutic compound for chronic inflammatory pain without dependence or tolerance (20140357, Dr. Philip Portoghese)

An analgesic compound without side effects that relieves chronic pain associated with arthritis, sickle cell disease, chemotherapy, AIDs and inflammation.

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Opioid based therapy without dependence or tolerance

Opioids like morphine have been used extensively for the treatment of chronic pain, including pain that is the result of diseases like cancer, AIDS and sickle cell disease. The analgesic effect from activation of the mu opioid receptor (MOR) is unfortunately accompanied by undesirable side-effects including tolerance and dependence. Furthermore, the administration of morphine and other opioids has been shown to actually enhance HIV infection in patients. To overcome these limitations, researchers at the University of Minnesota developed a two-part molecule, MCC22, that activates MOR to deliver analgesic effects while antagonizing CCR5 to suppress opioid-induced side effects.

Technology ID

20140357

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Choosing the right target

Although mu opioids reduce pain, chronic use promotes increased pain sensitivity through the release of pro-inflammatory chemokines, including CCL5. This chemokine binds CCR5 (which colocalizes with MOR in glia and neurons) and the CCL5/CCR5 complex plays a major role in neuroinflammation. CCR5 is also the main co-receptors utilized by HIV-1 viruses to enter cells and accelerate AIDS progression. Through activating MOR and blocking CCR5, MCC22 is a potent

analgesic that mitigates the pain sensitivity and neuroinflammation commonly associated with opioids. Furthermore, MCC22 inhibits immune cell migration into the central nervous system, which is a critical step in HIV-mediated neuropathogenesis that leads to NeuroAIDS. MCC22 shows promise as a treatment of both inflammatory and neuropathic pain conditions where conventional analgesics have reduced efficacy.

Phase of Development

In vivo animal studies. MCC22 exhibits potent analgesic properties and no observed tolerance in mice. Shown to be effective for reducing pain in a mouse model of sickle cell disease, chemotherapy-induced pain and arthritis.

Key Benefits & Differentiators

- **Highly potent analgesic:** MCC22 is significantly more potent with a longer effective duration than morphine in a mouse models for inflammatory pain, arthritis, chemotherapy-induced pain and sickle cell disease
- **Does not induce tolerance or dependence:** No tolerance or dependence has been observed following repeated dosing in multiple mouse models (tested up to 115 days). Furthermore, MCC22 does not show rewarding properties in mice as compared to morphine.
- **Does not impair motor function:** Mice showed no alteration in motor function following administration of MCC22.
- **Potential to slow progression of HIV and neuroAIDS:** Blocks the main co-receptor (CCR5) used by HIV to enter cells and inhibits deleterious immune cell migration into the CNS.

Applications

- Relief from chronic pain caused by AIDS, chemotherapy, sickle cell disease, arthritis and other inflammatory diseases
- Pain relief with reduced progression of HIV infections and neuroAIDS
- Analgesia without dependence or tolerance

Researchers

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Publications

[*Inhibition of inflammatory and neuropathic pain by targeting a mu opioid receptor/chemokine receptor5 heteromer \(MOR-CCR5\)*](#)

Journal of Medicinal Chemistry, 2015 Nov 12; 58(21): 8647–8657.

[*Bivalent ligand MCC22 potently attenuates nociception in a murine model of sickle cell disease*](#)

Pain, 2018 Jul;159(7):1382-1391

[*A bivalent compound targeting CCR5 and the mu opioid receptor treats inflammatory arthritis pain in mice without inducing pharmacologic tolerance*](#)

Arthritis Research & Therapy, 2018 Jul 27;20(1):154

[*The bivalent ligand MCC22 potently attenuates hyperalgesia in a mouse model of cisplatin-evoked neuropathic pain without tolerance or reward*](#)

Neuropharmacology, 2019 Nov 1;158:107598

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