Technology Offer: P1408247

A novel class of kappa opioid receptor (KOR) ligands

The invention describes a novel class of kappa opioid receptor (KOR) ligands which can be used for the therapy of a variety of human disorders

Background

The opioid receptor family consists of three structurally homologous but functionally distinct receptors, the mu opioid (MOR), delta opioid (DOR), and kappa opioid receptor (KOR). Intense interest in the pharmacology of the KOR receptor over the past years has revealed its important role in pathways related to pain, affective disorders, drug addiction, and psychiatric disorders. The KOR is well-known to contribute in mediation of pain, and pain remains a valuable indication for KOR agonists, as activation of KOR produces analgesia, while it is not involved in the unwanted side effects such as respiratory depression, inhibition of gastrointestinal motility, dependence, or abuse liability, like the MOR. Nowadays, the KOR is emerging as an essential target for the treatment of a variety of other human disorders. The KOR represents a central player in the regulation of both reward and mood. Drugs directed at the KOR as antagonists or partial agonists have potential utility as antidepressants and anxiolytics. Additionally, KOR agonists are gaining attention as potential anti-addiction medications, and for the treatment of inflammatory and itching skin diseases.

Technology

A series of KOR ligands has been synthesized, analytically characterized and pharmacologically evaluated in vitro in opioid receptor binding and functional assays, and in vivo for analgesic activity. Several compounds exhibited high affinity and selectivity for the KOR in comparison to MOR and DOR, while they were high efficacy agonists, partial agonists or antagonists. Some of the ligands showed high antinociceptive potency in a mouse model of visceral pain (abdominal stretching) after subcutaneous administration. They were more potent as antinociceptive agents than the prototypical KOR agonist U50,488. The new KOR compounds did not induce sedation and impairment of motor dysfunction at the analgesic dose and multiples of it.

Benefits

- The new class of KOR ligands is synthetically readily accessible and cost-effective to prepare.
- The KOR agonists show high efficacy in an animal model of visceral pain, while the partial agonists were also active but with lower potency.
- No signs of sedation and motor impairment are detected.

Potential Application

Novel drugs interacting with the KOR for the treatment of:

- Pain
- Psychiatric disorders: dysphoria, depression, bipolar disorders, mood disorders, anxiety spectrum disorders (stress, phobias, panic)
- Psychotic disorders: schizophrenia
- Neurological disorders
- Neurodegenerative diseases: Alzheimer´s disease, Parkinson´s disease
- Addiction: drug and behavioral addiction
- Eating disorders: obesity, overweight
- Epilepsy
- Inflammatory diseases: Crohn´s disease, ulcerative colitis, irritable bowel syndrome
- Itching: pruritus
- Water retention: oliguria, edemas

Patent status

US-Application: priority date March 30, 2015
Owner: University of Innsbruck

Development status

- KOR as specific molecular target identified and validated in vitro
- Proof of principle - Efficacy in an animal model of visceral pain
- Safe toxicity profile, first results are promising

Cooperation options

License agreement

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