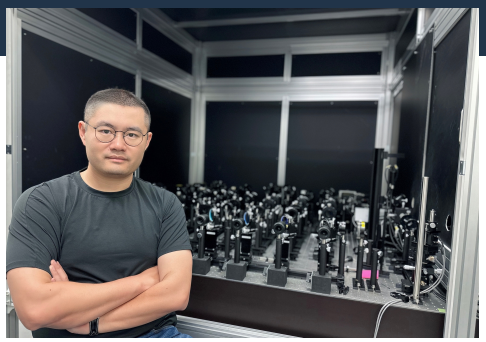

Peptide drugs for enhancing opioid analgesia and suppressing tolerance development

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What is your problem?

Opioids are essential components of clinical pain management, especially for terminal cancer and poor-risk patients. Long-term opioid therapy is, however, associated with increased risk of tolerance, dependence, and fatal overdose, with serious personal and social consequences. According to data released by National Institute on Drug Abuse that more than 2 million Americans abuse opioids, and ~90 Americans die from opioid overdose every day. Many attempts, such as opioid rotation and antagonist drugs, have been made to diversify treatments to increase efficacy and reduce undesirable side effects to opioids, but reliable solutions for better/safer long-term pain management employing opioids remain elusive.

What is your solution?

We developed a series of peptide drugs that enhance analgesia and suppress development of tolerance for the long-term opioid treatment. In principle, these short and soluble peptides modulate dimerization of opioid receptors for function, which produce a bias signal for enhancing analgesia with less side effects. In the *in vivo* tests, these peptide drugs enhanced short-term efficacy and suppressed long-term tolerance development of morphine, meanwhile, they exhibited extreme-low cytotoxicity and no binding-competition to morphine.

Initially, we proved proof-of-concept demonstration by release peptide with implanted min-pump. For the clinical use, we further modified the peptide for the blood-brain-barrier permeability and anti-degradation. Compared with existing techniques, our peptide-drugs are soluble, low toxicity and supposed to delivery to CNS with IV and nasal spray treatments, which is conducive to successful drug delivery with minor side effects.

This technology represents an important step toward more effective and safer pain management employing morphine and other opioids.

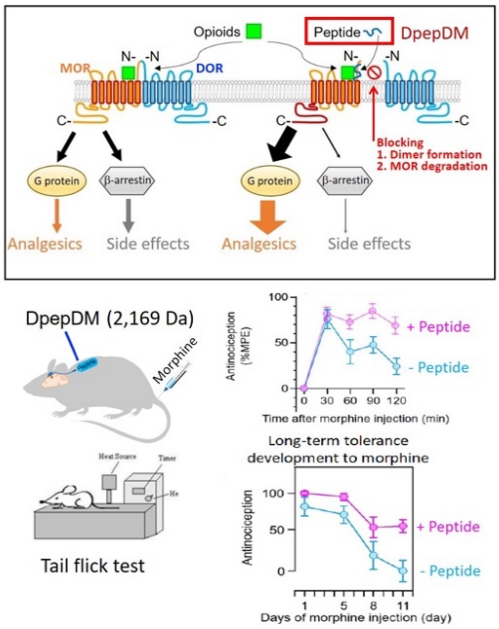

Figure 1. Soluble peptide (DpepDM) enhances efficacy and suppresses long-term tolerance of morphine in mice by modulating the heterodimerization of μ- and δ-opioid receptors in the center nervous system.

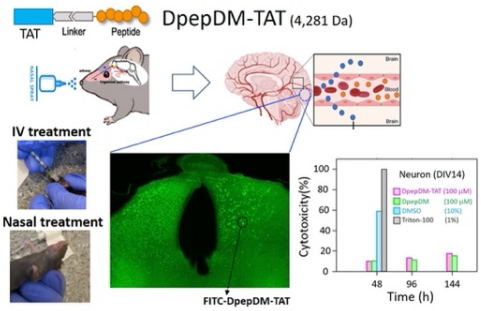

Figure 2. An optimized peptide DpepDM-TAT exhibited BBB permeability with IV or nasal spray treatment and showed extremely low cytotoxicity to hippocampal neurons at a concentration of 100uM.

Other resources

- Description of the technology

Contribution to SDGs

Keywords: Opioids, Opioid Receptor, Peptide, Tolerance, Side-effect

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