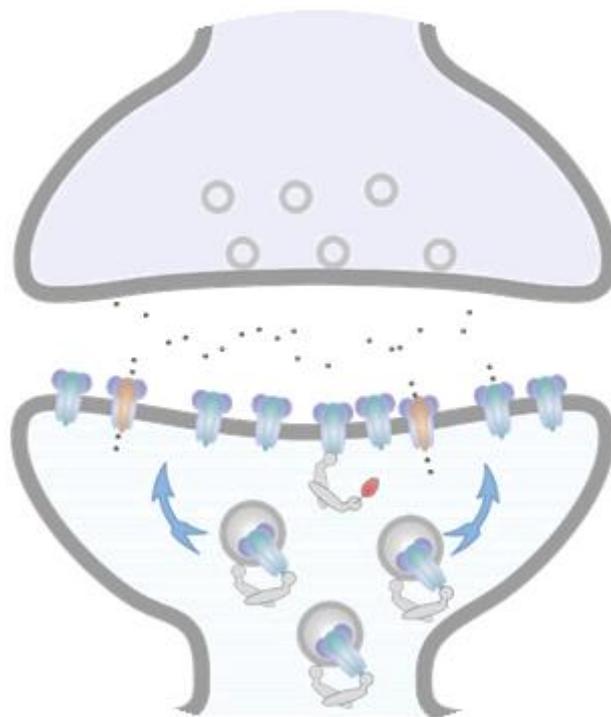


Targeting the cause of neuropathic pain

TPD5: a peptide analogue with a novel mechanism of action and the potential to vastly improve patients' quality of life



Background

Neuropathic pain is a chronic condition, which affects up to 10% of people. It is a malfunction of the nervous system resulting from nerve damage (for example, a spinal cord injury, or damage caused by cancer or diabetes). In this condition, instead of alarming a person to tissue injury, the nervous system itself causes the pain.

Patients experience excruciating pain, painful sensitivity to touch or numbness, and the condition is often associated with anxiety, depression, poor sleep and high use of prescription drugs.

There is no treatment specifically for neuropathic pain. Symptoms can be relieved with antidepressants, antiepileptics or opiates like morphine. But, the efficacy of those medicines is moderate – many patients do not at all benefit from them – and side-effects, including opiate addiction, are common and often severe.

So, there is a huge unmet need for targeted treatments.

The invention

A key feature of neuropathic pain is overexpression of AMPA receptors in neurons in the spinal cord, which receive signals from the damaged nerve. Because of the many AMPA receptors, too many pain signals are sent to the brain. The medicines used in neuropathic pain often work by blocking this transmission and therefore also affect normal nerve function.

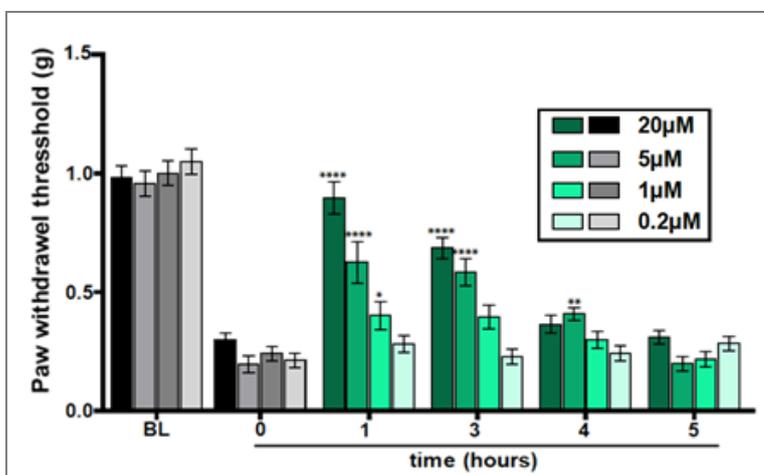
TPD5 inhibits a protein called PICK1, which controls the overexpression of AMPA receptors. That way, AMPA receptor expression is normalised in affected neurons, without affecting normal AMPA receptor function elsewhere.

Key selling points

- Novel, targeted mechanism
- High binding affinity
- Not addictive

Development status

The inventors have evidence of TPD5's efficacy in a mouse model of neuropathic pain. They have received an Exploratory Pre-Seed grant from the Novo Nordisk Foundation and are negotiating a Pre-Seed programme to complete experiments addressing key features like target engagement and specificity, route of administration, pharmacokinetics, toxicology *in vitro*, and effect on acute, chronic or spontaneous pain.



The effect in mice of TPD5 on sensitivity to touch: At baseline (BL), before surgical introduction of hypersensitivity, the normal paw withdrawal threshold was measured. After surgery and immediately before dosing with TPD5 (time 0), their paw withdrawal threshold was about quartered. TPD5 restored the threshold in a time and dose-dependent manner (times 1–5 h).

Intellectual property rights

A priority application was filed in October 2018.