



NIH-Funded Research Team Engineers New Drug Targeting Pain Sensation Pathway

Study of CB1 receptor has implications for chronic pain treatment.

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A research team funded by the National Institutes of Health (NIH) has developed a medication that shows promise in treating acute and chronic pain. The drug, known as VIP36, targets the body's cannabinoid receptor type 1 (CB1). It was found to be effective in three different animal models for pain and does not appear to cause the harmful side effects that have frustrated other efforts to target CB1.

These results enhance understanding of how to design safer and more effective drugs targeting cannabinoid receptors and are an important step towards developing novel, non-addictive treatments for pain. [The study was [published in Nature](#) on March 5, 2025.]

CB1 receptors can be found throughout the body and are particularly dense in the brain's pain circuitry. They have long been considered a potential target for non-opioid-based pain treatment; however, previous attempts to target this pathway have been met with two challenges.

First, repeated exposure to a drug leads to tolerance that limits its efficacy. Second, the dose required to reduce pain in the periphery tends to be high enough for the drug to make its way into the central nervous system. In humans, this can cause unwanted changes in mood, cognition, or emotional state.

To overcome these issues, researchers leveraged computer modeling of the CB1 receptor to design molecules that better interact with CB1, much like a key fitting into a lock. The newly designed drug, VIP36, is more "peripherally restricted" compared to previous drugs, meaning that much less of it leaks into the central nervous system where it can cause unwanted side effects. VIP36 also interacts with CB1 differently than treatments tested previously and in a way that reduces tolerance.

CB1 is part of a wide-ranging class of receptors known as G-protein-coupled receptors, which are involved in countless functions throughout the body including smell, vision, mood regulation, immune system responses, autonomic nervous system responses such as blood pressure and

heart rate, and growth and metastasis of some tumors. In addition to their implications in pain care, the findings of this study could also help spur the design of other drugs that target similar receptors involved in other conditions.

This research was funded by NIH's [Helping to End Addiction Long-term® Initiative](#), or NIH HEAL Initiative, an NIH-wide effort that seeks to speed scientific solutions to the overdose epidemic, including opioid and stimulant use disorders, and the crisis of chronic pain.

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