

A Non-Narcotic Synergic Drug Combination for the Treatment of Severe Chronic Pain (Yissum)

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Application

Severe, high-impact chronic pain affects 20 million people in the US annually, and presents a common, difficult-to-treat clinical challenge. All the drugs currently approved for chronic treatment of severe pain are narcotics, and their main mechanism of action is activation of the mu-opioid receptor (MOR) in the CNS. Long-term narcotic use is associated with dependence and addiction, with the risk of death by overdose, and with other severe adverse effects. In the US, an estimated 2 million individuals suffer from opioid addiction associated with prescription opioids, accounting for an estimated \$78.5 billion in economic costs annually. The estimated overall annual cost of chronic pain in the US is \$560 billion in direct medical costs, lost productivity, and disability programs. Thus, there is an urgent and widespread need for safer, non-narcotic drugs that will provide strong and chronic pain relief without the adverse effects associated with narcotic use.

Our Innovation

We have identified a combination of two approved, non-narcotic drugs (Drug A and Drug B) that together are capable of activating MOR synergistically, at very low doses of either drug: Drug A at

Technology

To test the synergy between Drugs A & B, we utilized a cell-based assay system in which the human mu-opioid receptor (h-MOR) is expressed exclusively. In addition, the system includes h MOR's downstream cAMP signaling pathway, and a sensitive means to measure Gi's inhibitory effect on adenylyl cyclase activity following Gi's activation by h-MOR.

A dose-response test was performed for each drug separately, and for various combinations of Drug A and Drug B. We found that at concentrations in which Drug A and Drug B by themselves only produced negligible responses, their combination yielded robust adenylyl cyclase inhibition of more than 5 times that of the individual drugs.

Moreover, this synergic effect extended through a range close to two orders of magnitude of drug concentrations for either drug, at pharmacologically-relevant concentrations.

Opportunity

This is a novel combination of two non-opioid, clinically-approved drugs that together achieve a synergistic activation of MOR in very low doses of either drug. This combination, with a possible 505b2 route of approval, offers narcotic-strength analgesia without the dangerous adverse effects associated with chronic narcotic use.

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