Nonaddictive drug compound could replace opioids for chronic pain sufferers

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A new nonaddictive drug compound discovered by Purdue University researchers could lead to the treatment of chronic pain without the need to rely on opioids, just as a bipartisan package of bills moves through the U.S. House and Senate to battle the nation's opioid epidemic.

A compound developed by a research team led by Val Watts, professor of medicinal chemistry and molecular pharmacology and associate dean for research in Purdue's College of Pharmacy, shows unparalleled selectivity in inhibiting the adenylyl cyclase 1 (AC1), making it a potential target for treating pain and reducing the dependency on opioids for pain management.

"This compound shows promise in inhibiting one class of AC1, which could decrease physical symptoms of opioid addiction withdrawal, and that could help reduce psychological dependence," Watts said.

Last year, the U.S. Department of Health and Human Services declared a public health emergency regarding the spike in opioid overdoses. In 2016, 116 people died each day from opioid-related drug overdoses. According to the Centers for Disease Control and Prevention, overdose deaths involving prescription opioids have quadrupled since 1999. From 1999 to 2015, more than 183,000 people have died in the United States from overdoses related to prescription opioids. Watch a video from the CDC about opioids here.

Opioids are a class of drugs that include the illicit drug heroin as well as prescription pain relievers oxycodone, hydrocodone, codeine, morphine, fentanyl and others. They interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain.

New legislation designed to address the opioid epidemic is expected to land to President Donald Trump's desk this month. The legislation includes bills that would make it easier to stop illegal drugs at the border, speed up research for new nonaddictive prescription painkillers and make treatment more readily available for those who are addicted.

The Watts group is the first to identify a compound that is selective for

AC1 only. Findings from the study by Watts' group are published in *Science Signaling*. This group has recently identified additional novel modulators of adenylyl cyclase 1 activity.

Adenylyl cyclases like AC1 are enzymes that organize the production of cyclic adenosine monophosphate, an important biological messenger in numerous organisms including the communication of pain in the body.

"With the AC1 technology, there's a chance to treat chronic pain directly or through reducing the side effects of the opioids," said team member Richard van Rijn, assistant professor of medicinal chemistry and molecular pharmacology in Purdue's College of Pharmacy.

More information: Tarsis F. Brust et al. Identification of a selective small-molecule inhibitor of type 1 adenylyl cyclase activity with analgesic properties, *Science Signaling* (2017). DOI: 10.1126/scisignal.aah5381

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