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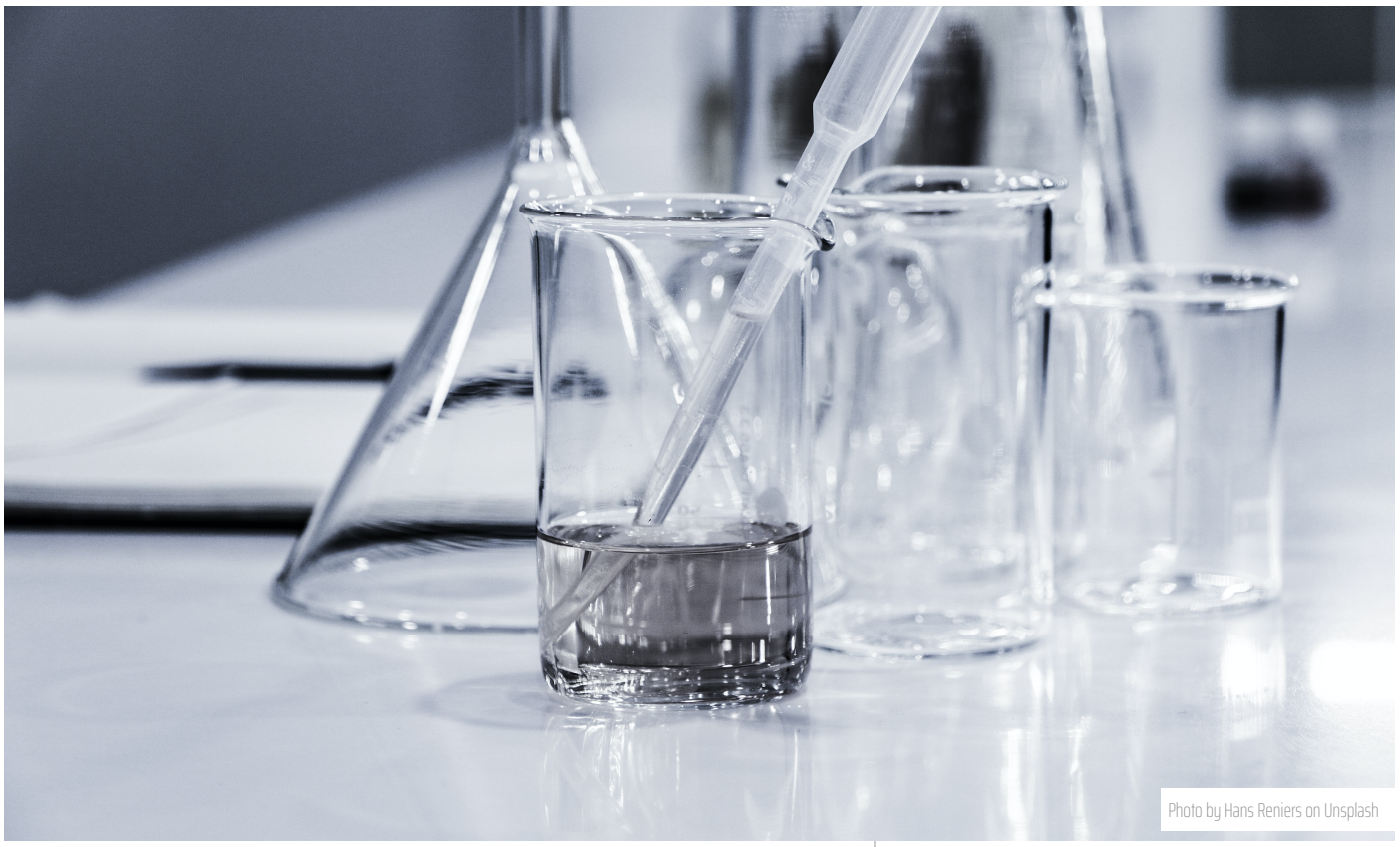

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OPIOID DRUGS

Targeting Alternative Opioid Receptor Reduces Drug Side Effects

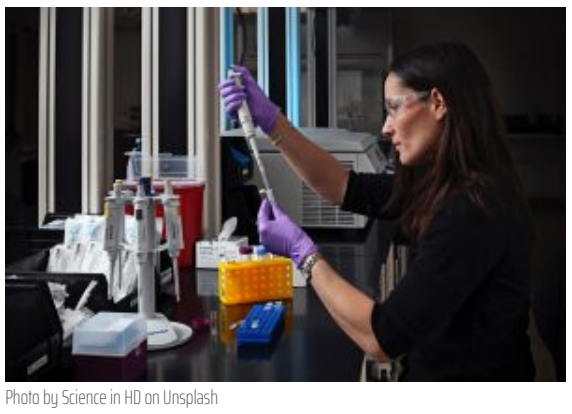
SARA E. TELLER — June 30, 2020

Scientists discover that targeting the delta opioid receptor provides safer pain relief.

A new study published in *Proceedings of the National Academy of Sciences (PNAS)* indicates, "Delta opioid receptors have a built-in mechanism for pain relief and can be precisely targeted with drug-delivering nanoparticles, making them a promising target for treating chronic inflammatory pain with fewer side effects." Researchers used cells from humans and mice with inflammatory bowel disease, which can cause chronic pain, in order to facilitate the study.

The body's opioid receptors relieve pain when they are activated by opioids and the majority of these medications act on the mu opioid receptor. However, for purposes of the current study, researchers focused on the delta opioid receptor, which also inhibits pain when activated with fewer side effects, including life-threatening airway complications and overdose. If pain could be managed by targeting this alternative receptor, it would act as a safer alternative.

"Using biopsies from the colons of people and mice with ulcerative colitis, an inflammatory bowel disease," the researchers discovered that "the delta opioid receptor provides a built-in mechanism to relieve inflammatory pain. The inflammatory cells from the colon release their own opioids, which activate the delta opioid receptor and block the activity of neurons in the gut that transmit painful signals."



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"We've shown that the delta opioid receptor has a built-in mechanism of pain control and inhibits pain by signaling within an endosome. With this new knowledge, we thought the receptor would be a promising target for the treatment of chronic inflammatory pain," said senior author Nigel Bunnett, Ph.D., professor and chair of the Department of Molecular Pathobiology at New York University (NYU) College of Dentistry.

The team encapsulated the painkiller DADLE, which binds to the delta opioid receptor, inside nanoparticles. They then coated the nanoparticles with the same painkiller.

“Incorporating drugs into nanoparticles can enhance the stability and delivery of drugs, improving their effectiveness and often requiring smaller doses – and smaller, more targeted doses lower the risk of drugs causing unwanted side effects,” said Bunnett. “Our findings demonstrate that not only are delta opioid receptors in endosomes a built-in mechanism for pain control, but also a viable therapeutic target for relief from chronic inflammatory pain.”

They noted finding that “the delta opioid receptor doesn’t just signal at the plasma membrane, as previously thought,” but also signals from a compartment within the cell called the endosome.

“Nanoparticles activated DOPr at the plasma membrane, were preferentially endocytosed by DOPr-expressing cells, and were delivered to DOPr-positive early endosomes,” the authors revealed, adding, “Nanoparticles caused a long-lasting activation of DOPr in endosomes, which provided sustained inhibition of nociceptor excitability and relief from inflammatory pain. The realization that GPCRs can signal from endosomes to mediate pain has revealed endosomal GPCRs as a viable therapeutic target.”

In conclusion, the researchers found, “Our results demonstrate the feasibility of using nanoparticles to target nociceptors with consequent reductions in dose. Nanoparticles might allow the simultaneous delivery to endosomes of agonists or antagonists of several endosomal GPCRs involved in pain. Since multiple GPCRs control pain transmission, the ability to target multiple receptors in pain-transmitting neurons for prolonged periods might provide effective and long-lasting antinociception.”

Sources:

Delta opioid receptor identified as promising therapeutic target for inflammatory pain relief

Inflammatory Pain Relief That Targets Delta Opioid Receptor May Have Fewer Side Effects

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About Sara E. Teller

Sara is a credited freelance writer, editor, contributor, and essayist, as well as a novelist and poet with nearly twenty years of experience. A seasoned publishing professional, she's worked for newspapers, magazines and book publishers in content digitization, editorial, acquisitions and intellectual property. Sara has been an invited speaker at a Careers in Publishing & Authorship event at Michigan State University and a Reading and Writing Instructor at Sylvan Learning Center. She has an MBA degree with a concentration in Marketing and is currently pursuing an MA in Clinical Mental Health Counseling, concentrating in Substance Abuse and Addictions. She has maintained a 4.2/4.0 GPA, and is a member of Chi Sigma Iota and a 2020 recipient of the Donald D. Davis scholarship, recognizing social responsibility. Sara is also certified in children's book writing, HTML coding and social media marketing. Her fifth book, *PTSD: Healing from the Inside Out*, was released in September 2019 and is available on Amazon. You can find her others books there, too, including *Narcissistic Abuse: A Survival Guide*, released in December 2017. For more information and to subscribe to her weekly newsletter, please visit [sarateller.com.](sarateller.com)

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