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Harnessing endogenous opioids for pain relief: Lessons learned from endomorphin 2

Opioids are the most commonly used and most effective drugs for pain relief. However, tolerance develops to the analgesic effects of opioids, which are also addictive, leading to abuse. Recent research provides insights into utilizing endogenous opioids as an alternative to prescription narcotics. The magnitude of pain relief elicited by the spinal application of an opioid found endogenously, endomorphin 2 (EM2), a highly selective mu-opioid receptor (MOR) agonist, varies across the rat estrous cycle – high in proestrus (when circulating estrogens are elevated) but minimal in diestrus (when circulating estrogens are low). This ebb and flow of spinal EM2 analgesia results from variable levels of spinal glutamate and dynorphin activity, as well as pliable interactions within an oligomer containing estrogen receptor α (ERα), MOR, kappa-opioid receptor, aromatase (aka estrogen synthase) and $mGluR_1$/$mGluR_{2/3}$. During diestrus, ERα activated by spinally synthesized estrogens, acts with $mGluR_1$ to suppress spinal EM2 analgesia. In proestrus there is a disengagement of suppressive aromatase/ERα signaling. This is paralleled by both the differential signaling by $mGluR_1$ (when it is activated by glutamate instead of ERα), and elevated spinal dynorphin-activated kappa-opioid receptors. These aggregate changes in diestrus vs. proestrus function as a switch, preventing or promoting spinal EM2 antinociception. The finding that the analgesic effectiveness (in female rats) of spinally applied EM2 depends on functional interactions among multiple identified oligomerized components provides novel targets for developing pharmacotherapies that harness endogenous EM2, and potentially other endogenous opioids, for pain relief. This would likely reduce the need for prescription opioids, lessening the current epidemic of prescription opioid abuse ravaging society.

Biography

Alan Gintzler has completed his PhD from New York University School of Medicine, USA. He is Distinguished Professor and Director of Research, Department of Obstetrics and Gynecology, State University of New York, Downstate Medical Center, USA. He has over 100 publications that have been cited over 4,000 times and his publication H-index is 38. He has been serving as an Editorial Board Member of many reputed journals.

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