THE ROLE OF THE CDCA3 AXIS IN EPIGENETIC SILENCING OF M-OPIOID RECEPTORS DURING CISPLATIN-INDUCED NEUROPATHIC PAIN

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Abstract - Cisplatin-induced neuropathic pain is a major dose-limiting complication of platinum-based chemotherapy, profoundly reducing patients' quality of life and constraining therapeutic efficacy. Emerging evidence indicates that epigenetic dysregulation within the dorsal root ganglia (DRG) plays a critical role in the development of chemotherapy-induced neuropathy. In this study, we identify a novel contribution of the Cdh1–CDCA7 axis to cisplatin-evoked pain hypersensitivity through epigenetic repression of the μ-opioid receptor gene. We show that cisplatin administration markedly increases CDCA7 expression in NeuN-positive DRG neurons, coinciding with the onset of mechanical allodynia in mouse models. Mechanistically, CDCA7 promotes DNA methylation at the μ-opioid receptor promoter, leading to transcriptional silencing of this analgesia-related receptor in the DRG. Importantly, siRNA-mediated knockdown of CDCA7 reverses cisplatin-induced tactile allodynia and restores both CDCA7 and μ-opioid receptor expression in the DRG. By identifying the CDCA7–DNA methylation-μ-opioid receptor pathway as a key driver of cisplatin-induced neuropathic pain, our findings provide new mechanistic insights into epigenetic regulation of pain and establish a foundation for developing targeted, mechanism-based therapeutic strategies.

Keywords - CDCA3, μ-Opioid Receptor, DRG, Cisplatin-Induced Neuropathic Pain