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HCN Channels Blockade Attenuates Chemotherapy-Induced Pain

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Introduction

Painful peripheral neuropathy is a common dose-limiting side effect caused by chemotherapy agents, such as oxaliplatin. Mechanisms underlying this devastating condition are largely unknown.

Methods

We established a rat model of chemotherapy induced pain by administering oxaliplatin at 2mg/Kg for 5 consecutive days. Mechanical hyperalgesia, a typical nociceptive pain behavior, developed after treatment with oxaliplatin. We investigated the expression of hyperpolarization-activated cyclic nucleotide-gated (HCN) channels in the dorsal root ganglia (DRG) at both gene transcripts level (real-time PCR) and protein level (immunofluorescence). In addition, we examined the functional significance of HCN upregulation after oxaliplatin treatment by using a pan HCN channels blocker-ZD 7288.

Results

DRG HCN 1 and HCN 2 were higher in oxaliplatin- treated rats than saline-treated controls, both for gene transcripts and proteins. ZD7288, when administered intrathecally, was able to alleviate, albeit not abrogate, oxaliplatin induced-pain. Interestingly, pre-treatment with ZD7288 prior to oxaliplatin administration did not prevent the development of mechanical hyperalgesia.

Learning Objectives

HCN channels are involved in chemotherapy-induced pain.

References

Oxaliplatin-induced cold hypersensitivity is due to remodelling of ion channel expression in nociceptors.

EMBO Mol Med. 2011 May;3(5):266-78.

Conclusions

Taken together, HCN1 and HCN2 channels are upregulated by oxaliplatin treatment, and that HCN blockade alleviates oxaliplatin-induced pain. Therefore, targeting HCN channels may provide a therapeutic avenue to treat chemotherapy induced-pain.