The role of TRPA1 channels and Sigma-1 receptor in oxaliplatin-induced peripheral neuropathy

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Oxaliplatin is a platinum compound used in the treatment of different solid tumors. In a large number of patients oxaliplatin has neurotoxic effects characterized by mechanical and thermal hypersensitivity. Sigma-1 receptor (σ-1R) is a molecular chaperone broadly expressed in human tissues. It plays many physiological roles, including the modulation of different ion channels and receptors. In mice, σ-1R antagonists can reduce the symptoms of neuropathic pain in various experimental models, including oxaliplatin-induced neuropathy.

Here we investigated the modulation of TRPA1 channels by σ-1R receptor. Using a variety of biophysical and biochemical approaches, we unveiled an interaction between both proteins that ultimately affect the trafficking and expression of TRPA1 at the plasma membrane. Furthermore, in an experimental model of oxaliplatin-induced peripheral neuropathy, an antagonist of σ-1R reduced neuropathic symptoms. In vivo and in vitro experiments suggested a molecular pathway linking TRPA1 to neuropathic symptoms and mapped future strategies for clinical intervention.

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