Medical Xpress

Making hypersensitivity to cold a thing of the past in colorectal cancer treatment

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Putting gloves on before opening the fridge. Avoiding the refrigerated section in supermarkets. This is routine for almost all colorectal cancer patients receiving chemotherapy with oxaliplatin, which causes hypersensitivity to cold. This side effect could soon be avoided thanks to a study coordinated by Emmanuel Bourinet, senior researcher at the CNRS Institute of Functional Genomics (CNRS/ Inserm/ University of Montpellier, France). A molecule already marketed in France for the treatment of angina has been shown to restore the excitation thresholds of cold-sensitive neurons to normal levels. Results were published in the *EMBO Molecular Medicine* journal on 23 March.

Cancer of the colon is the third most common cancer in France, with nearly 40 000 estimated new cases in 2010. Chemotherapy treatment is partly based on the administration of oxaliplatin. However in 95% of patients, the drug causes increased sensitivity to cool or cold temperatures from the first infusions, resulting in tingling in the extremities. This known side effect is so uncomfortable that some patients reduce or even stop their chemotherapy. No preventative treatment is currently available.

A team of researchers from Montpellier, in collaboration with their colleagues from Clermont and Nice have shown that, as is the case in humans, administration of oxaliplatin in mice increases sensitivity to cold. Using a behavioral approach, this result was confirmed in vitro with imaging of isolated sensory neurons. A molecular study of these neurons highlighted a difference in the ion channels regulating the

electric currents carrying information(4). Neurons from animals treated with oxaliplatin have fewer inhibitory channels and more excitatory channels than those from control animals, thus explaining their higher excitation levels.

The role of these excitatory channels in hypersensitivity to cold was confirmed by the use of an inhibitory molecule, ivabradine. In vivo and in vitro, ivabradine was not only able to restore the normal excitation threshold of cold-activated neurons, but it did not affect other populations of sensory neurons, such as touch receptors. This molecule, already used in the clinic to treat angina, could be a promising preventative treatment against the acute neurotoxicity induced by oxaliplatin in colorectal cancer patients.

More information: Oxaliplatin-induced cold hypersensitivity is due to remodeling of ion channel expression in nociceptors, Juliette Descoeur, et al. *EMBO Molecular Medicine*, online publication, March 23, 2011.

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