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ROS-dependent modulation of Rab7 contributes to chronic pain processing

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Introduction: Chronic pain in response to tissue damage (inflammatory pain) or nerve injury (neuropathic pain) is a major clinical health problem, affecting up to 30% of adults worldwide. Currently available treatments are only partially susceptible and are accompanied with therapy limiting side effects. Thus it is important to elucidate molecular mechanisms of pain signaling in detail to obtain new insights in potential future therapies.

Objectives: Chronic pain is accompanied by production of reactive oxygen species (ROS) in various cells that are important for nociceptive processing. Recent data indicate that ROS can trigger specific redox-dependent signaling processes, but the molecular targets of ROS signaling in the nociceptive system remain largely elusive. **Materials & methods:** Here, we performed a proteome screen for pain-dependent redox regulation using an OxICAT approach, thereby identifying the small GTPase Rab7 as a redox-modified target during chronic pain in mice. We further performed immunofluorescence staining and analyzed chronic pain behavior in Rab7-deficient mice.
Results: Prevention of Rab7 oxidation by replacement of the redox-sensing thiols modulates its GTPase activity. Knockout mice lacking Rab7 in sensory neurons showed normal responses to noxious thermal and mechanical stimuli, however their pain behavior during inflammatory pain and in response to ROS donors was altered. **Conclusion:** The data suggest that redox-dependent changes in Rab7 activity in the dorsal horn modulate pain sensitivity.