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YOU ARE INVITED TO ATTEND THE

DEFENSE OF THE DOCTORAL

DISSERTATION

"The roles of sensory STIM1 in pain"

by

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Thursday, July 8, 2021
1 P.M.
Zoom Meeting:
https://rutgers.zoom.us/j/91639922166?pwd=YXRHekZsSk55b0pIT2RLZ3NXZnBWUT09

Meeting ID: 916 3992 2166
Password: 822046

ABSTRACT

Stromal interaction molecule 1 (STIM1) is an endoplasmic reticulum (ER) calcium (Ca^{2+}) sensor that can sense a Ca^{2+} drop in the ER and react to extracellular stimuli. STIM1 is expressed in the peripheral nervous system (PNS) and mediates store-operated Ca^{2+} entry (SOCE). However, its functional significance in the PNS remains unclear. Here we show that deletion of STIM1 in sensory neurons (SN-STIM1 knockout) significantly reduces noxious mechanical-, cold-, allyl isothiocyanate (AITC, a TRPA1 activator)-, capsaicin (Cap, a TRPV1 activator) and bradykinin (BK, an inflammatory mediator)-induced nociception. Activation of STIM1 by thapsigargin (TG, an ER Ca^{2+}-ATPase inhibitor) evokes nociceptive behavior and induces pain hypersensitivity, which is attenuated in SN-STIM1 knockout (KO) mice and L3/4 DRGs STIM1 knockdown mice. In addition, SN-STIM1 KO mice develop less thermal hypersensitivity under a chronic inflammatory condition induced by complete Freund adjuvant (CFA). Bradykinin-induced Ca^{2+} release from the ER is sufficient to activate STIM1. BK-induced SOCE and an increase in neuronal excitability are significantly reduced in STIM1 KO neurons. Activation of TRPV1 triggers ER Ca^{2+} release, resulting in STIM1 translocation and SOCE, indicating a novel coupling between STIM1 and TRPV1. Mechanistic studies reveal that activation of STIM1 decreases potassium (K^{+}) currents and increases neuronal excitability.

Taken together, our studies demonstrate that STIM1 plays an important role in sensing peripheral painful stimuli and modulating pain sensitivity, suggesting that STIM1 may represent a potential target for the treatment of painful conditions. Our findings also provide new insight into TRPV1-mediated nociception.