Tue 07. June 2022
Time: 12:00 h

Institute of Biochemistry and Molecular Medicine (IBMM)
Seminar Room
Gertrud-Woker-Str. 5,
3012 Bern

Everybody is welcome

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Rajesh Khanna is Professor at the Department of Molecular Pathobiology, College of Dentistry, New York University (USA)

This lecture is hosted by Prof. Hugues Abriel (IBMM).

NCCR TransCure Lecture in Physiology
by Rajesh Khanna

Navigating a new path to Nav1.7 for pain

The voltage-gated sodium Nav1.7 channel, critical for sensing pain, has been actively targeted by drug developers; however, there are currently no effective and safe therapies targeting Nav1.7. Here, we tested whether a different approach, indirect Nav1.7 regulation, could have antinociceptive effects in preclinical models. We found that preventing addition of small ubiquitin-like modifier (SUMO) on the Nav1.7-interacting cytosolic collapsin re-sponse mediator protein 2 (CRMP2) blocked Nav1.7 functions and had antinociceptive effects in rodents. In silico targeting of the SUMOylation site in CRMP2 (Lys374) identified >200 hits, of which compound 194 exhibited selective in vitro and *ex vivo* Nav1.7 engagement. Orally administered 194 was not only antinociceptive in preclinical models of acute and chronic pain but also demonstrated synergy alongside other analgesics—without eliciting addiction, rewarding properties, or neurotoxicity. Analgesia conferred by 194 was opioid receptor dependent. Our results demonstrate that 194 is a first-in-class protein-protein inhibitor that capitalizes on CRMP2-NaV1.7 regulation to deliver safe analgesia in rodents.

NCCR TransCure Excellence in Membrane Transport Research

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