

ORAL PRESENTATION

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# Imaging orofacial pain in mice

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From Seventh Scientific Meeting of The TMJ Association, Genetic, Epigenetic, and Mechanistic Studies of Temporomandibular Disorders and Overlapping Pain Conditions  
Bethesda, MD, USA. 7-9 September 2014

Nociceptors in the dorsal root ganglia (DRG) and trigeminal ganglion (TG) play an essential role in initiating pain by detecting painful stimuli through their peripheral axons and sending signals to the spinal cord via their central axons [1]. Pathological conditions such as inflammation and nerve injury can sensitize nociceptors, causing heightened pain sensitivity and often leading to chronic pain conditions like TMJ disorders. Despite its importance in understanding the mechanism of nociceptor sensitization, monitoring neuronal activity of nociceptors in tissue explants or in live animals is still technically challenging due to the interference of the surrounding tissues. Recently, we have developed a novel approach to directly monitor neuronal activity and hyperactivity after injury and revealed the contribution of central terminal sensitization of primary nociceptive neurons to molecular mechanisms underlying the maintenance of trigeminal neuropathic pain. We generated *Pirt-GCaMP3* mice in which GCaMP3, a genetic-encoded  $Ca^{2+}$ -sensitive indicator [2], is specifically expressed in >95% of all DRG and TG neurons under the *Pirt* promoter [3]. Because of the specific expression of the  $Ca^{2+}$  sensor (i.e., only in DRG and TG and not in skin cells or spinal cord neurons), we detected robust neuronal hyperexcitability in TG explants and TG's axons in the skin explants and trigeminal brainstem slices of animals with nerve injury compared with naïve or sham-treated mice. In addition, we are developing techniques to image DRG neuronal activity in live mice in response to various sensory stimuli applied to sensory peripheral receptive fields. The advantages of the functional imaging using *Pirt-GCaMP3* mice include simple tissue preparation and imaging procedures, intact sensory somatotopic organization, and simultaneously monitoring a large population of neurons and nerves. Previous and

ongoing studies using this technique have revealed new mechanisms underlying chronic pain conditions including orofacial pain.

## Disclosures

Dr. Caterina is an inventor on a patent on the use of products related to TRPV1, which is licensed through UCSF and Merck, and may be entitled to royalties related to these products. He is on the Scientific Advisory Board for Hydra Biosciences, which develops products related to TRP channels. These conflicts are being managed by the Johns Hopkins Office on Policy Coordination.

## Acknowledgements

We thank Dr. Loren Looger at Howard Hughes Medical Institute, Janelia Farm for providing us GCaMP3 cDNA and Yixun Geng for technical assistance. We thank Chip Hawkins and Holly Wellington of Transgenic Mouse Core at Johns Hopkins University School of Medicine for assistance with *Pirt-GCaMP3* mouse generation. This work was supported by National Institutes of Health Grants (R01DE022750 and R01GM087369 to X.D.; R01DE018573 to F.W.), Johns Hopkins University Brain Science Institute grant, and T32 (T32NS070201 to Y.S.K.) Johns Hopkins University Pain Fellowship.

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Published: 15 December 2014

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doi:10.1186/1744-8069-10-S1-O2

**Cite this article as:** Kim *et al*: Imaging orofacial pain in mice. *Molecular Pain* 2014 **10**(Suppl 1):O2.

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