Mechanisms underlying the development of chronic pain

Chronic pain is a common, complicated, distressing problem affecting approximately 20% of the human population worldwide. Pain-related diseases are the top 10 leading causes of disability and disease burden globally and are increasing yearly. The revised definition of Pain is an **unpleasant sensory** and **emotional experience** associated with, or resembling that associated with, actual or potential tissue damage (Pain, 2020). Different stimuli, such as acid, heat, noxious cold, pressure, and chemicals, are detected by sensory nerve endings on our skin, muscle, and internal organs. The nociceptive signals are transmitted to the dorsal horn of the spinal cord and then to different brain regions, including the amygdala, thalamus, and cortex, to form the pain sensation. Amygdala nuclei play important roles in emotional responses, fear, depression, anxiety and pain modulation. In this talk, I will talk about our finding that that PKCδ+ and SOM^{+} neurons in the central nucleus of the amygdala differentially regulate the pain- and anxiety-like behaviors in mice, respectively.

We have shown previously that the anterior nucleus of paraventricular thalamus (PVA) neurons play an essential role in the development of chronic mechanical hyperalgesia in neuropathic and inflammatory pain models. Activation of PVA neurons using pharmacological or optogenetic tools was sufficient to induce chronic pain in naïve mice without peripheral injury. Conversely, inhibition of PVA neuronal activity attenuates chronic pain. Our data suggest that targeting PVA neurons at the proper time alleviates the pre-existing mechanical hyperalgesia persistently in mice. We recently discovered that the PVA nucleus is involved in both **sensory** and **emotional** aspects of pain. I will present our recent data showing that different efferent innervations from PVA regulate sensory and emotional aspects of pain.