S57-3 Role of P2X ion-channels on mechanisms of chronic pain

◯Makoto TSUDA[1], Kazuhide INOUE[1]

[1]Kyushu Univ. Grad. Sch. of Pharm. Sci.

A great paradox of pain is that acute, nociceptive pain is a necessary defense mechanism that warns against existing or imminent damage to the body, whereas chronic pain can be so deleterious that individuals occasionally prefer death. One troublesome hallmark symptom of chronic pain is pain hypersensitivity to normally innocuous stimuli (tactile allodynia), which is refractory to currently available treatments. Our research has been focusing on the role of ATP-gated ion-channels (P2X) on pain signaling and has demonstrated that activating P2X4 upregulated in spinal microglia in a chronic pain model is crucial for tactile allodynia. P2X4 upregulation involves fibronectin and interferon-γ signalings. P2X4 stimulation evokes influx of Ca^{2+} and release of BDNF as a crucial factor to signal to dorsal horn neurons, changing GABA responses from inhibitory to excitatory. These findings indicate that activity of P2X4 channels in spinal microglia is crucial for causing hyperexcitability in the pain transmission network of neurons in the dorsal spinal cord. It has been shown that P2X4 protein is predominantly localized in intracellular lysosomal compartment, and, interestingly, we found that CCL2, which is also important for allodynia, increases P2X4 expression on the surface membrane of microglia. Thus, controlling P2X4 trafficking in microglia may be a new way to treat chronic pain.