S58-5 New mechanisms of intractable chronic pain revealed by studies on ATP receptors

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Extracellular nucleotides play an important role to cell-to-cell communication through P2 purinoceptors even though ATP is recognized primarily to be the source of free energy and nucleotides are key molecules in cells. P2 receptors are divided into two families, ionotropic (P2X) and metabotropic receptors (P2Y). P2X receptors (7 types; P2X1 - P2X7) contain intrinsic pores that open by binding of ATP. P2Y (8 types; P2Y1, 2, 4, 6, 11, 12, 13 and 14) are activated by nucleotides and couple to intracellular second-messenger systems through heteromeric G-proteins. Our laboratory has been investigating the role of P2X/Y receptors in pain signaling. In particular, we have demonstrated that P2X4, P2X7 and P2Y12 are essential for the development and maintenance of intractable chronic pain caused by nerve damage (called neuropathic pain). More importantly, our findings in studies of these P2 receptors also provides an exciting insight into pain mechanisms indicating that spinal microglia are crucial cells for causing hyperexcitability in the pain transmission network of neurons in the dorsal spinal cord after nerve damage. In this talk, I will present recent advances in our understanding of the mechanisms producing neuropathic pain, focusing on the roles of P2X/Y receptors, and also discuss a new drug discovery target for chronic pain.