Epigenetic regulations of purinergic P2X receptors under various pain conditions

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More than 20% of adults worldwide suffer from different types of chronic pain, which are frequently associated with several comorbidities and adverse impact on patients' quality of life. Several approved analgesic drugs are currently available, but they are often hampered by severe side effects and/or insufficient efficacy. One of the most likely possibilities is to develop novel drugs from outcomes of studying the epigenetic mechanisms of chronic pain. A growing body of evidence has emerged in the field of pain epigenetics; however, it is still very much in its infancy. Epigenetic mechanisms include regulations of DNA methylation, post-translational histone modification, chromatin remodeling and non-coding RNAs. One of the most popular and key epigenetic mechanisms in regulation of gene expression is cytosine methylation. In the past decade, our group has been focused on the functions of DNA methylation under different chronic pain conditions. Our data strongly suggest that imbalance of DNA demethylation homeostasis contributes to the development of chronic pain hypersensitivity. In particular, we demonstrated that purinergic P2X receptors, which are significantly demethylated, played an important role in chronic pain processing pathways. In addition, we have evidence to support an idea that DNA methylation is pain- and/or tissue/cell-type specific. These findings might shed light into the mechanisms of chronic pain and the development of novel pain drugs. Obviously, there are many challenging research issues that need to be well addressed to fill in the gaps in our knowledge related to the potential for drugging the pain epigenome.

Key words: Chronic pain, Purinergic receptors, Epigenetic regulation, DNA methylation and demethylation Homeostasis

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