# The Silencing of GIGYF Promotes the Involvement of Mglur5 in the Development of Neuropathic Pain in Dorsal Horn

**Siao-Tong Nie**
Institute of Biomedical Sciences, MacKay Medical College, New Taipei City, Taiwan

**An-Chi Chen**
Department of Physiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

**Mei-Ci Chen**
Department of Physiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

**Ming-Chun Hsieh**
Department of Medicine, Mackay Medical College, New Taipei, Taiwan

**Hsien-Yu Peng***
Institute of Biomedical Sciences, MacKay Medical College, New Taipei City, Taiwan
Department of Medicine, Mackay Medical College, New Taipei, Taiwan

## Abstract:

The treatment of pain is regarded as one of the most prominent issues in current medical development. Focusing on critical pain signaling pathways and potential mRNA targets is seen as a promising strategy for advancing pain therapeutics. GRB10-interacting GYF protein (GIGYF) is known to be a key regulator in translation, closely associated with translational repression and mRNA degradation. GIGYF has been demonstrated to have a strong connection with neuropathic pain and neural plasticity in the brain. More importantly, GIGYF can regulate the expression of key pain mediators, such as MMP-9 and TNF-α, through translational repression. However, the molecular mechanisms by which GIGYF-dependent translational repression regulates neural plasticity and drives the progression of neuropathic pain remain unclear. On the other hand, metabotropic glutamate receptors (mGluRs) play a critical role in excitatory neurotransmission, synaptic plasticity, and central sensitization. The gene encoding mGluR5, Grm5, has been identified as an effective analgesic target, and our previous studies have demonstrated that mGluR5 plays an essential role in spinal plasticity and the development of neuropathic pain. Recently, we showed that nerve injury leads to a reduction in a transcriptional and translational repressor within the promoter region of mGluR5, resulting in increased translation and expression of mGluR5 in the dorsal horn of the spinal cord. Interestingly, research has revealed that enhanced mGluR5-dependent plasticity in the hippocampus is associated with GIGYF mutations. Therefore, we further explore whether inhibiting GIGYF expression in the dorsal horn of the spinal cord could promote mGluR5 translation and contribute to the progression of neuropathic pain.

## Keywords:

GIGYF, metabotropic glutamate receptors, spinal cord, nerve injury-induced neuropathy.