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Poster session

Analgesic effects of a novel monoclonal antibody against Nav1.7 sodium channel

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[Background] Neuropathic pain is a complex and chronic disease caused by injury or dysfunction in peripheral and central nervous system. Current analgesics are often inadequate due to the lack of efficacy and dose-limiting side effects. The voltage-gated sodium channel Nav1.7 is preferentially expressed in peripheral sensory neurons, and humans that lack this channel are completely insensitive to pain. In this viewpoint, Nav1.7 inhibitors could be promising analgesics for a broad range of pain conditions. However the search of Nav1.7-specific inhibitor has not been successfully progressed because small molecules are limited to have high selectivity in high sequence similarity among Nav channel subtypes. Here, we present a monoclonal antibody which binds Nav1.7-specific extracellular domain and reduces pain behaviors.

[Method] Mice were immunized with the Nav1.7 extracellular peptide-KLH conjugate. Monoclonal antibodies were established by hybridoma technology. Prepared antibodies were evaluated by binding affinity to immunogen peptide and Nav1.7 expressed on cell membrane and rat DRG tissue. Inhibition activity of the antibody on Nav1.7 sodium channel was measured by manual patch clamp. To evaluate analgesic effects, the antibody was injected intraplantarly or intravenously in partial sciatic nerve ligation (pSNL) model rats.

[Results] Prepared monoclonal antibodies had high affinity to immunogen peptide with selectivity among Nav channel subtypes and had ability to bind Nav1.7 expressed on cell membrane and rat DRG tissue. The antibody functionally inhibited Nav1.7 sodium channels expressed in cells. Next, intraplantar injection of the antibody reduced pain behavior in pSNL model rats. Furthermore, intravenous injection of the antibody also showed the analgesic effect which was correlated to the antibody concentration in the plasma. Lastly, repeated intravenous injection of the antibody showed enhanced and prolonged analgesic effects after the last injection.

[Conclusion] These results suggest that our novel antibody against Nav1.7 sodium channel would be a promising analgesic.