

Development of animal models of herpetic pain and postherpetic neuralgia and elucidation of the mechanisms of the onset and inhibition of allodynia

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Herpes zoster characterized by clustered vesicles and severe pain is caused by the reactivation of varicella-zoster virus in the sensory ganglion in human subjects. In some herpes zoster patients, pain persists long after healing of the skin lesions, which is postherpetic neuralgia (PHN). Patients with PHN report various types of pain. In addition, a large proportion describes “allodynia”, which is a painful sensation elicited by normally innocuous light mechanical stimulation. Once established, PHN is particularly difficult to treat, and is often resistant to conventional analgesics. The mechanisms that underlie the induction and maintenance of herpetic pain and PHN still remain unclear. In the present study, we attempted to establish the animal models of herpetic pain and PHN.

(1) Development of mouse models of herpetic pain and PHN

Because of species specificity of varicella-zoster virus, there are no animal models that correspond to human herpes zoster and herpetic pain. We have found that percutaneous inoculation of herpes simplex virus type-1 (HSV-1) to hindpaw of mice induced herpes zoster-like skin lesions and aversive responses to innocuous tactile stimuli (allodynia). We also found that some of mice with acute herpetic pain show allodynia long after the lesions are completely healed, suggesting the development of PHN.

(2) The mechanisms of allodynia

We found that COX-2 – PGE₂ – EP3 receptor pathway in the dorsal root ganglia is involved in the development of herpetic allodynia. We also found that herpetic and postherpetic allodynia is mediated by nitric oxide in the spinal cord and that NOS2 and NOS1 are responsible for herpetic and postherpetic allodynia, respectively.

(3) The risk factor of PHN

It is suggested that severity of the acute herpetic pain is a risk factor of PHN. Using these mouse models, we demonstrated that the inhibition of acute herpetic pain results in the decrease of the incidence of PHN. Therefore, it is suggested that the relief of acute herpetic pain is important for the complete prevention of PHN.