学 位 論 文 の 要 旨

所　　属	三重大学大学院医学系研究科 生命医科学専攻　神経感覚医学講座	氏　　名	芝　　真 人

主論文の題名

Imatinib Mesylate Prevents Cerebral Vasospasm After Subarachnoid Hemorrhage via Inhibiting Tenascin-C Expression in Rats

主論文の要旨

Platelet-derived growth factor (PDGF) has been implicated in the pathogenesis of cerebral vasospasm after subarachnoid hemorrhage (SAH), but the mechanism remains unknown. The purpose of this study was to assess whether imatinib mesylate (imatinib), an inhibitor of the tyrosine kinases of PDGF receptors (PDGFRs), prevents cerebral vasospasm after SAH in rats, and to elucidate if tenascin-C (TNC), a matricellular protein, is involved in the mechanism. Imatinib was administered intraperitoneally to rats undergoing SAH by endovascular perforation, and the effects were evaluated by neurobehavioral tests and India-ink angiography 24-72 hours post-SAH. Western blotting and immunohistochemistry were performed 24 hours post-SAH. Recombinant TNC was administered intracisternally to imatinib-treated SAH rats, and the effects were evaluated by neurobehavioral tests, India-ink angiography and immunohistochemistry 24 hours post-SAH. Both dosages of imatinib significantly prevented post-SAH neurological impairments and vasospasm 24-72 hours. SAH caused PDGFR-β upregulation, PDGFR activation, mitogen-activated protein kinases activation, and TNC upregulation in the spastic cerebral arteries, all of which were significantly suppressed by imatinib treatment. Recombinant TNC reversed the anti-vasospastic effects and protein expression changes by imatinib. This study suggests that imatinib prevents cerebral vasospasm at least partly via inhibiting the upregulation of TNC.

（注）２，０００字以内にまとめて記入すること。