学位論文抄録

Akhirin is involved in the neural stem cell regulation in the mouse spinal cord
（Akhirin はマウス脊髄の神経幹細胞制御に関与する）

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ABSTRACT

Background and Purpose: Though the central nervous system is considered a comparatively static tissue with limited cell turnover, cells with stem-cell properties have been isolated from most neural tissues. The spinal cord ependymal cells show neural stem cell potential *in vitro* and *in vivo* in an injured spinal cord. However, very little is known regarding the ependymal niche in the mouse spinal cord. We previously reported that a secreted factor, chick *Akhirin* (C-*AKH*), is expressed in the ciliary marginal zone of the eye, where it works as a heterophilic cell-adhesion molecule. Here, we describe a new crucial function for mouse *Akhirin* (M-*AKH*) in regulating the proliferation and differentiation of progenitors in the mouse spinal cord.

Methods: *In situ* hybridization, and immunostaining were performed to check *AKH* expression pattern at different developmental stages. BrdU labeling to determine whether Akhirin is involved in an important role for prolifereation of a mouse spinal cord. Immunostaining using different stem/ proliferation/ progenitor markers to check the distribution between wild type and *AKH-/-* littermate mice. To conclude AKH function in vitro, we performed neuroshere culture. Finally, we checked the expression pattern of AKH in an injured spinal cord and compared to adjacent control section.

Results: During embryonic spinal cord development, M-*AKH* is transiently expressed in the central canal ependymal cells, which possess latent neural stem cell properties. Targeted inactivation of the *AKH* gene in mice causes a reduction in the size of the spinal cord and decreases BrdU incorporation in the spinal cord. Remarkably, the expression patterns of ependymal niche molecules in *AKH* knockout (*AKH-/-*) mice are different from those of *AKH*+/+, both *in vitro* and *in vivo* Furthermore, we provide evidence that *AKH* expression in the central canal is rapidly up-regulated in the injured spinal cord.

Conclusion: Our results indicate the possibility that Akhirin control the cell proliferation and differentiation in the neural tube. Our findings suggest that AKH is involved in a role in neural stem cell regulation in the mouse spinal cord.