



HOKKAIDO UNIVERSITY

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INFORMATION

Hokkaido University conferred the degree of Doctor of Philosophy (Ph.D) in Veterinary Medicine on September 24, 2004 to 1 recipient and December 24, 2004 to 3 recipients.

The titles of theses and other information are as follows :

The cellular distribution of *src*-suppressed C kinase substrate (SSeCKS) in the mouse:
in situ hybridization and immunohistochemical study

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SSeCKS (*src*-suppressed C kinase substrate) is an important C kinase substrate which regulates cell shaping, movement and differentiation via cytoskeletal reorganization. The present study aimed to reveal the distinct cellular and subcellular localization of SSeCKS with respect to functional significance. First, I investigated the detailed localization of SSeCKS in the liver and lymph node in order to elucidate its roles in the scavenging function. SSeCKS immunoreactivity in the liver and lymph node of mice was below a detectable level under normal conditions. After lipopolysaccharide (LPS) stimulation, intense immunoreactivity for SSeCKS became noticeable in sinusoidal endothelial cells of the liver and medullary reticular cells of the lymph node. Ultrastructurally, SSeCKS immunoreactivity was localized predominantly along the cytoplasmic membrane of both cell types. These SSeCKS-expressing cells under normal conditions incorporated a small amount of injected foreign particles (carbon particles and 20 nm-latex microspheres). In LPS-stimulated conditions, the uptake of particles increased both in terms of amount and extent of uptaking sites. The subcellular localization of SSeCKS in endothelial

cells correlated with some pinocytotic pits and vacuoles. These findings suggest that the SSeCKS-expressing cells vigorously take up exogenous substances in response to invasion of pathogens as central members of the reticulo-endothelial system (RES).

Next, I revealed the precise distribution and localization of SSeCKS in the peripheral nervous system and sensory organs of mice. In the peripheral nervous system, SSeCKS was expressed intensely both in sensory and autonomic ganglia, but differently in cellular distribution. Only small- and medium-sized neurons in sensory ganglia expressed SSeCKS mRNA and protein. Intense expression was also distributed in Schwann cells and some satellite cells which frequently enveloped SSeCKS-negative ganglion cells. In autonomic ganglia (celiac and pelvic ganglia, and intestinal myenteric plexus), SSeCKS immunoreactivity was restricted to the satellite cells and Schwann cells, whereas no immunoreactivity was detected in any neuronal somata. No significant immunoreactivity for SSeCKS was found in most sensory organs, including the retina, organ of Corti, taste buds, and olfactory mucosa. Only the vomeronasal organ in both postnatal and adult mice

exhibited intense and selective signals for SSeCKS in the sensory epithelium, where the supporting cells were selectively labeled. The expression in the vomeronasal organ was strengthened by the consistent localization of SSeCKS from Schwann cells along the vomeronasal nerve to the terminal organ, the accessory olfactory bulb.

It is concluded that the expression patterns of SSeCKS have dual aspects, namely induced expression in the RES and constitutive expression in some selected cells. In the

former, SSeCKS is involved in the elimination of exogenous particles and waste products from the blood and lymph circulation. As for the latter cell group, the present study added glia-like cells in the peripheral nervous system and the vomeronasal organ to the list of SSeCKS-expressing cells. The finding of expression patterns outside the RES, though still fragmentary, suggests another role of SSeCKS in the regulation and homeostasis of the peripheral nervous system and sensory organs.

Original papers of this thesis appeared in *Arch. Histol. Cytol.*, 67 : 135-147 (2004) and *Biomed. Res.*, 25 : 155-164 (2004).

In vitro production of mouse embryos using oocytes derived from *in vivo*
and *in vitro* grown follicles

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Original papers of this thesis appeared in *Jpn. J. Vet. Res.*, 52 : 77-84 (2004) and *J. Reprod. Dev.*, 50 : 579-586 (2004).

Production of calves by nuclear transfer in cattle using embryonic and somatic cells

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Original papers of this thesis appeared in *Theriogenology*, 54 : 675-684 (2000), *Cloning Stem Cells*, 5 : 43-49 (2003) and *Anim. Sci. J.*, 74 : 363-368 (2003).

Establishment of a murine bipotent chondroprogenitor cell line (CL-1)
and elucidation of the chondrogenic mechanisms of a novel
cartilage-regenerative compound (AG-041R)

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Original papers of this thesis appeared in *Osteoarthr. Cartil.*, 12(1): 25-37 (2004) and *Eur. J. Pharmacol.*, 418(3): 225-230 (2001).