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学 位 論 文 要 旨

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論 文 名 ラット唾液腺におけるプロサポシンとその受容体の雌雄差

学位論文要旨

Saliva, a watery substance in the mouth, is secreted from the salivary glands by double autonomic sympathetic and parasympathetic innervation. Dysregulation of salivary secretion causes various oral diseases like xerostomia. The salivary glands produce various neurotrophins that are thought to regulate salivary function during normal and pathological conditions. Prosaposin (PSAP), a saposin precursor, is a potent neurotrophin found in several tissues and various biological fluids. Although PSAP is a clinically significant and potent neurotrophin with a postulated role regulating salivary function, little is known about its localisation and distribution in salivary glands. Accordingly, this study examined whether PSAP and its receptors, G protein-coupled receptor 37 (GPR37) and GPR37L1, are expressed in the major salivary glands of rats. As the functions of salivary glands vary based on age and sex, this study also examined whether sex and age affect expression of PSAP and its receptors in salivary glands. To clarify this, we used male and female Wistar rats at different ages from young adult to postmenopausal (2, 6, 18 and 27 months old). Histopathological analysis revealed the prominent changes in the size, shape, and type of cells in both sexes of older aged rats. However, the number of cell types in the major salivary glands of male and female rats did not differ at any age examined in this study.

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Immunohistochemical analysis provide evidence that the immunoreactivity of PSAP and its GPR37 and GPR37L1 receptors is detectable in the major salivary glands of rats, suggesting that the PSAP originating from the salivary glands might be functioning in an autocrine fashion. The immunohistochemical analysis also revealed that the expression of PSAP and its receptors were varied considerably based on the type of gland, acinar cells, age, and sex. In fact, PSAP, GPR37, and GPR37L1 were predominantly expressed in granular convoluted tubule cells of the submandibular gland, and the intensity of their immunoreactivity was higher in young adult female rats than age-matched male rats, which was more prominent at menopause. On the other hand, weak PSAP, GPR37, and GPR37L1 immunoreactivity was observed mainly in basal layer of mucous cells of the sublingual gland. Triple label immunofluorescence analysis revealed that PSAP, GPR37, and GPR37L1 were co-localised in the basal layer of acinar cells in the major salivary glands, although immunoreactivities varies between male and female rats. Therefore, it is possible that sex-related differences of PSAP in salivary glands might play a role in the changes in saliva biochemistry causing oral discomfort, particularly in cases where sex and age are affected unequally, such as xerostomia. In conclusion, we found sex- and age-dependent differences in the expression of PSAP and its GPR37 and GPR37L1 receptors in the major salivary glands of rats. The identification of PSAP and its receptors is the first step toward further studies to identify the specific roles of this potent neurotrophic factor in the regulation of salivary functions in normal and pathological conditions.

キーワード (3~5)	Prosaposin, Salivary glands, Aging, Sex, Rat
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