特別講演 II

EPIDERMAL GROWTH FACTOR AND OTHER POLYPEPTIDES IN MOUSE SUBMANDIBULAR GLAND.

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The submandibular gland of the mouse contains high concentrations of different biologically active polypeptides, including the nerve growth factor (NGF), epidermal growth factor (EGF), renin, kallikreins, glucagon, amylase, peptidases. By using specific antisera, and an unlabeled antibody enzyme method, we have localized EGF, NGF, renin, and one of the major peptidases to the secretory granules of the cells of the granular convoluted tubules (GCT) in the glands of both male and female mice. The intensity of immunostaining for each antigen varied from cell-to-cell, and among the secretory granules within the same cell.

The GCTs develop under the influence of androgen hormones, and the degree of development reflects the sexual dimorphism of the gland. In addition to androgens, corticosteroids and the thyroid hormones regulate the development of the GCTs. Hypothyroidism from birth severely impaired the differentiation of the GCT cells, as reflected in the expression of the four polypeptides. Immunocytochemical stainings revealed an asynchrony in the postnatal differentiation of the GCT cells with respect to the four polypeptides studied. However, these factors appeared earlier in the glands of male than female mice.

By using sensitive radioimmunoassays, we have established that EGF is secreted in large quantities into the saliva; the secretion is mediated by alpha-adrenergic receptors. Upon stimulation of secretion a transient increase in blood EGF level occurred.

A survey of six inbred strains of mice revealed significant differences in EGF content and concentration in the submandibular glands of both sexes. A detailed analysis of two strains, RF/J and C57BL/6J, representing high and low levels of EGF, respectively, revealed that the difference in EGF levels: existed throughout the postnatal development, hence it was not due to differences in the rate of differentiation; it was not caused by differences in the level of circulating testosterone or in sensitivity towards the hormone. EGF levels were significantly different in the glands of castrated males, and castrated males in which similar steady levels of testosterone were maintained by testosterone implants. Furthermore, similar, high EGF levels were induced in the glands of female mice of both strains by the administration of 5-alpha-dihydrotestosterone. The data collectively suggest that EGF is genetically regulated and this is independent of the genetic aspects of normonal regulation.

Although the physiologic roles of salivary gland polypeptides yet have to be established, evidence is accumulating for regulatory, endocrine-like functions of the salivary glands, as suggested by eminent Japanese scientists more than 40 years ago.