Peptides from the Pituitary Gland and Cortex Stimulate Differentiation of Polypotent Embryonic Tissue

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We studied the effects of synthetic peptides from the pituitary gland and brain cortex on differentiation of polypotent ectodermal tissue of the early gastrula of *Xenopus laevis*. It was shown that the pituitary gland peptide stimulates differentiation of polypotent tissue into epidermis and nerve tissue, while brain cortex peptide induces the development of mesenchyma and epidermis. Differentiation of polypotent tissue under the effect of the peptide is a mechanism of their geroprotective effect and suggests that they are promising as preparations for the treatment of neurodegenerative diseases.

Key Words: *pituitary gland peptide; brain cortex peptide; polypotent cells; differentiation*

Tissue differentiation is an important mechanism supporting homeostasis during the embryonic period and throughout the ontogeny [1,3,8,9]. The pool of polypotent cells verified practically in all tissue of the body is an additional resource decelerating the involution processes in the organism [1,3]. Moreover, reduced differentiation capacity of polypotent cells is a manifestation of aging [2,4].

Synthetic pituitary gland peptide exhibits a pronounced geroprotetive effect on the whole body and on tissues, cells, and genetic apparatus of the cell. It was found that pituitary gland peptide increases the mean lifespan in mice by 25-30%, reduces (by 2-7 times) the probability of carcinogenesis in animals, suppresses the expression of breast cancer gene, enhances activity of telomerase, and increases the length of telomeres by 2.4 times, which reflects overcoming of Hayflick cell division limit [4,5]. Activation of reparative processes, memory improvement, and accelerated development of brain functions after stress exposure were observed under the effect of this peptide [5].

In light of this, analysis of the effect of pituitary gland and brain cortex peptides on differentiation of polypotent cells is an important step in the study of the mechanism of their protective effect.

Here we studied the effects of synthetic pituitary gland and cortical peptides on differentiation of polypotent ectodermal tissue of the early gastrula of *Xenopus laevis*.

MATERIALS AND METHODS

We used synthetic peptides of the pituitary gland (H-Ala-Glu-Asp-Gly-OH, epithalon) and brain cortex (H-Ala-Glu-Asp-Pro-OH, cortagen) created at St. Petersburg Institute of Bioregulation and Gerontology, North-Western Division of the Russian Academy of Medical Sciences [4,6,7]. Fragments of fission cavity of *Xenopus laevis* early gastrulas were placed in a solution containing synthetic peptides of the pituitary gland and brain cortex in concentrations of 2, 10, 20, 50, 100, and 200 ng/ml for 60 min. Then cultured fragments were transferred to sterile Niu–Twitty solution containing antibiotics and cultured for 4-5 days. Control fragments were incubated in Niu–Twitty solution containing antibiotics instead of incubation with peptides. For each peptide concentration, 30 cultures were examined, 20 intact cultures served as the control. For evaluation of peptide effects on differentiation of polypotent tissue, the explants were fixed in Bouin

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fixative. Deparaffinized 5-μ sections were stained with azocarmine after Mallori.

RESULTS

On day 5 of incubation, only atypical epidermis developed in all control cultures of polypotent embryonic tissue of *Xenopus laevis*.

Addition of epithalon and cortagen in concentrations of 2, 10, 20, 50, 100, and 200 ng/ml to the culture of polypotent embryonic tissue induced the development of epidermis, mesenchyma, and nervous tissue. Induction of this of that type of differentiated tissue in the polypotent tissue culture depended on the structure of the studied peptide and its concentration.

Cortagen in a concentration of 10 ng/ml induced differentiation of 80% cells in the studied culture towards epidermis and mesenchyma. Cortagen in doses of 2, 20, and 100 ng/ml produced less pronounced effect (30-48%) and in concentrations of 50 and 200 ng/ml had no effect on differentiation of polypotent cells (Fig. 1).

In contrast to cortagen, pituitary gland peptide epithalon did not induce mesenchymal differentiation of polypotent cells. At the same time, epithalon stimulated differentiation of polypotent cells into nervous tissue and epidermis. Epithalon in doses 10, 50, and 100 ng/ml produced similar effect and stimulated differentiation of about 14% polypotent cells into epithelial and nervous tissues. However, epithalon in doses of 2, 20, and 200 ng/ml had no effect on differentiation of polypotent ectodermal tissue of *Xenopus laevis* early gastrula (Fig. 2).

Our experiments showed that peptides from the pituitary gland (epithalon) and brain cortex (cortagen) induce differentiation of polypotent ectodermal tissue of *Xenopus laevis* early gastrula into epidermis, nervous tissue, and mesenchyma. Epithalon stimulated the development of the nervous tissue and epidermis, while cortagen induced differentiation of the epidermis and mesenchyma. The effects of both peptides were dose-dependent.

Thus, the capacity of synthetic peptides of the pituitary gland and brain cortex to stimulate differentiation of polypotent tissue can underlay their tissue-specific geroprotective effect.

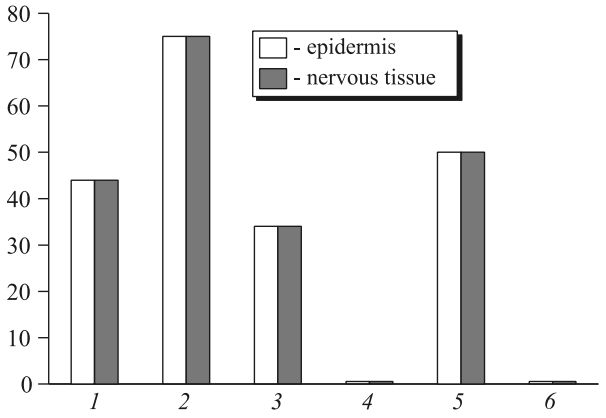

Fig. 1. Tissues developing from polypotent ectoderma of *Xenopus laevis* early gastrula under the effect of cortagen peptide in different concentrations. Here and in Fig. 2: *1*) 2 ng/ml, 2) 10 ng/ml, *3*) 20 ng/ml, *4*) 50 ng/ml, *5*) 100 ng/ml, *6*) 200 ng/ml. Ordinate: % of induced tissue.

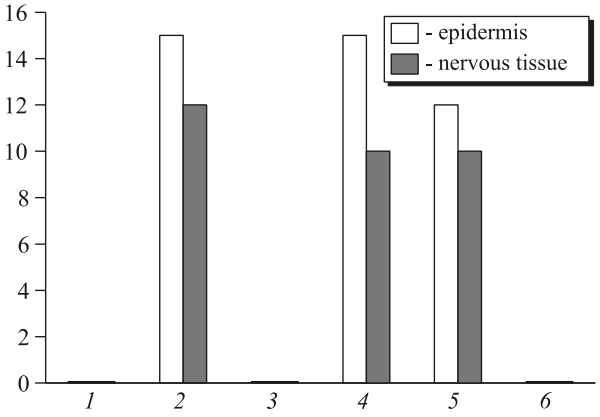

Fig. 2. Tissues developing from polypotent ectoderma of *Xenopus laevis* early gastrula under the effect of epithalon peptide in different concentrations.

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