MORPHOLOGY AND PATHOMORPHOLOGY

Age-Related Changes of Thymalin Content in Human Epidermis

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Immunomorphological analysis revealed the presence of thymalin in human epidermis and in fetal reticuloepithelium. These structures are developed from the common embryonic primordium ectoderm. In embryos and adult humans thymalin is present only in young epidermal cells, which undergo age-related involution. By the age of 70 years, the layer of thymalin-containing cells looks thinned and discontinuous. The content of thymalin, a thymic factor, decreases with age.

Key Words: thymalin; human skin; postnatal ontogenesis

Recent studies provided new data on the participation of the skin in the function of the immune system containingf a special set of immunocompetent cells. As early as 1968, the histogenetic and functional similarity between skin epithelium and thymus was established in mammals [10]. Close coupling of genes responsible for the formation of hairs and those controlling the development of thymus was established in nude mice [7]. The skin has antigen-presenting Langerhans cells characterized as the dendritic macrophages [4]. According to some authors, basal skin keratinocytes contain thymopoietin- and thymalin-like hormones [8,9]. Keratinocytes induce synthesis of terminal deoxynucleotidyl transferase in T-lymphocytes during combined culturing, which normally present in the thymus at the early stages of T-lymphocyte maturation.

We previously detected thymalin in youngest keratinocytes of human fetal epidermis [6] and concluded that the skin possesses components of the T-cell immune system. We found no data on postnatal distribution of thymalin-containing keratinocytes and on

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changes in their weight in parallel with thymus involution.

In this paper we detected thymalin in reticular epithelium of fetal thymus (Fig. 1) and showed that endocrine function of the thymus develops earlier than its lymphopoietic function (*i. e.* weeks 7-8) [6]. It is also established that thymalin is present in the epithelium developed from ectoderm, which gives rise to the epidermis and thymic reticuloepithelium.

Our aim was to detect thymalin-positive cells (TPC) in human epidermis during postnatal period and to describe the dynamics of thymalin content in the skin and some of skin derivatives (hair) during age-related involution of the thymus.

MATERIALS AND METHODS

The skin of human embryo aged 23 weeks and adult humans at the age of 40 and 70 years was studied. The embryos were obtained after premature birth. The skin of adult humans was obtained at mortuary No. 1 in Moscow.

Cryostat sections (4-6 μ) of frozen skin were dried in air, fixed in cold acetone, and washed for 15 min

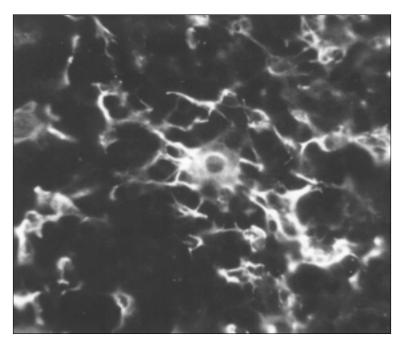


Fig. 1. Thymus of a 23-week-old human embryo with thymalin-positive cells. Here and in Figs. 2 and 3: indirect Kuns staining, $\times 800$.

in cold buffered saline of isotonic NaCl. The sections were incubated with rabbit antithymalin antiserum and then with FITC-labeled donkey anti-rabbit immunoglobulin antiserum [3]. Thymic hormone thymalin was determined (polypeptides with molecular weight of

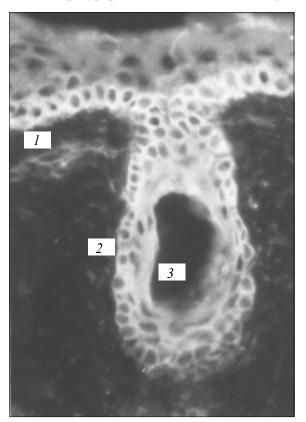


Fig. 2. Epidermis and developing hair of a 23-week-old human embryo. Thymalin in young cells. 1) epidermis; 2) section across hair primordium (hub); 3) hair primordium.

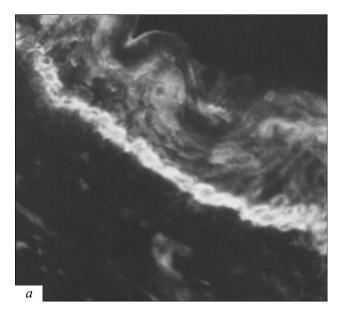
1000-6000 Da). Thymalin is characterized in details [1,2] and is used in clinical practice as an immunomodulator. The sections were incubated in a humid chamber at room temperature and examined under a LYuMAM-P3 fluorescent microscope. Control sections were treated with intact serum.

RESULTS

Examination of embryonic skin showed that all young keratinocytes contain thymalin before the appearance of the corneal layer in fetal epidermis (Fig. 2). Thymalin gradually disappears with the appearance of keratin and cornification and only basal cells of the epithelium still contain this hormone. The same regularity was observed during hair development: young thymalin-containing cells are located within the hair bulb. Thymalin disappears from the cornified cells of the hair shaft, which is formed in the upper levels of hair primordium.

In adults the thickness of skin epithelium increases. TPC are present and concentrated only in the basal layers of skin epithelium. These cells form a continuous layer of young thymalin-containing structures (Fig. 3, *a*).

In this layer, the weight of cells does not decrease during aging. By 70 years TPC layer does not disappear, but is reduced to a single row of thymalin-containing cells. In some places this row is interrupted, and in other places TPC are arranged in small clusters (Fig. 3, b). At this time, thymus involution is not completed: during the age-related involution thymus parenchyma is replaced by adipose tissue with clusters of glandular tissue.



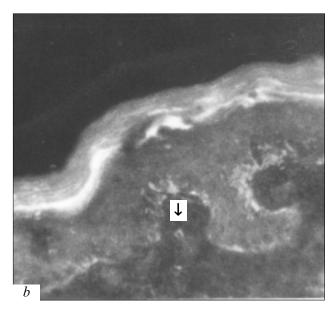


Fig. 3. Epidermis of a 40- (a) and 70-age-old subjects (b). a) Basal layer of thymalin-positive cells; b) clusters of thymalin-positive cells in the basal layer (arrow).

REFERENCES

- 1. V. G. Morozov and V. Kh. Khavinson, in: *Immunobiology of Thymic Hormones* [in Russian], Kiev (1989), pp. 125-142.
- 2. V. G. Morozov, V. Kh. Khavinson, and V. V. Malinin, *Peptide Thymomimetics* [in Russian], St. Petersburg (2000).
- 3. I. V. Moskvicheva, G. A. Ryzhak, V. G. Morozov, et al., Mikrobiologiya, No. 3, 74-78 (1985).
- 4. M. V. Pashchenko and B. V. Pinegin, *Immunologiya*, No. 4, 7-16 (2001).
- 5. V. S. Smirnov and V. G. Morozov, *Ibid.*, No. 4, 53-55 (1991).
- Z. S. Khlystova, I. I. Kalinina, S. P. Shmeleva, et al., Byull. Eksp. Biol. Med., 130, No. 10, 453-456 (2000).
- 7. R. L. Edel'son and D. M. Fink, V Mire Nauki, 8, 16-24 (1985).
- 8. A. C. Chu, J. A. K. Paterson, G. Goldstein, et al., Invest. Dermatol., 81, 194-197 (1983).
- K. Kato, S. Jkeyama, M. Takaoki, et al., Cell, 24, No. 3, 885 (1981).
- 10. T. Mandell, Exp. Biol. Med. Sci., 46, 775 (1968).