

VIRUS-LIKE PARTICLES IN THYMUS EPITHELIAL CELLS OF CONVENTIONAL MICE

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The functional interrelations between the thymus epithelial cells (TEC) are the object of constant investigations during the recent years. Certain interest create out some data about the presence of leucoviruses in epithelial cells of healthy mice whose thymuses show no pathological disorders from the normal structure (4, 5, 7, 13). The rarity of such findings and the new aspects of unknown parts and mechanisms of the functional activity of the epithelial cells were the reason for our present study.

Materials and methods

Thymus specimens of 24 conventional mice Swiss in different stages of their postnatal development (7, 14 and 40 days, 3 and 4 months) were under our investigation. A fixation in 5% glutaraldehyde (0.1 mol. phosph. buffer with pH 7.4 for 2 hours at 4° C) and 1% osmium tetroxide (0.1 mol. phosph. buffer with pH 7.4 for 1½ hour at 4° C), dehydration in ascendant alcohols and incorporation in Durcupan ACM, was performed. Semithin cuts were stained and ultrathin cuts were double contrasted after Reynolds E. (1963). Electron microscope JEM-7A was used in the study. Histological preparations from the thymus of some experimental animals were prepared and fixated after Bouin — Hollande (12).

Results and discussion

Characteristic spherical formations with a diameter 80—105 nm were detected in single TEC of two of the investigated animals. The latter consisted of a centrally located mass with high electron density, surrounded by electrondense ring. A concentric envelope with a morphology of elementary membranes is peripherally located; it shows a characteristic 3-layer structure (2 peripheral electrondense layers and included between them bright layer). The envelope-membrane and the underplaced electrondense ring are separated by an optically bright stripe.

Our previous studies analysed several characteristic types of TEC for any of the three regions of the mouse thymus (2, 9). The spherical formations from the present investigation were detected in only 2 types of TEC located in the cortico-medullar zone and the medulla itself.

The first type of TEC is characterized by a nucleus with a finely dispersed chromatin, reticular nucleolus and wider perinuclear space. Numerous polysomes and free ribosomes with well developed granular endoplasmatic reticulum whose cisterns fill almost the whole cytoplasm, sometimes with a content of moderate electron density, are established in the cytoplasm.

The studied spherical formations are detected in these epithelial cells only in groups intracellularly (several in number) or separately. Part of them are located free in the cytoplasm without a contact to any of the well-known cell organelles, while others are found in the volume of the cisterns of the granular endoplasmic reticulum or attached to its membranes. Single spherical formations are observed in the perinuclear space. However, not all spherical formations show the depicted submicroscopic structure. The electron-dense mass of some of them is not well outlined or it is incompletely surrounded by the membrane envelope.

The second type of TEC is characterized with the presence of eccentric nucleus and numerous cytoplasmic vacuoles. The latter are surrounded by an elementary membrane and possess individual microvillae directed towards the lumen inside. Some of them are absolutely empty optically, others — with a homogeneous or small-flocculated, with moderate electron density mass. They are located just near to the Golgi-vesicles. These TEC possess well-developed Golgi-complex, relatively developed granulated endoplasmic reticulum, free ribosomes, mitochondria, single dense corpuscles and thick intermediary cytofillaments (8—9 nm) which are organized in bundles and when cut transversally they are attributed to the tubular type. Greater part of the spherical formations are concentrated inside the lumen of the characteristic vacuoles, certain part of them are located separately in the cytoplasm. Sometimes the peripheral membrane of the spherical formations is in a constant contact to the surrounding vacuole membrane or it is connected to the latter by means of an electron-dense "foot".

Spherical formations with a similar submicroscopic characteristics were not established in lymphoidal cells neighbouring the studied TEC or in the intercellular space.

The ultrastructural characteristics of the investigated spherical formations coincides with the well-known (by bibliographical data) oncogenic RNA-viruses (leucoviruses, oncornaviruses, retroviruses, Rausviruses), specially those defined as C-type leucoviruses (1, 4, 5, 6, 7, 13). Excluding the possibility that the cited formations were ordinary thymus structures (collagen fibrilles, microvillae, small cytoplasmic vesicles, nuclear pores), as well as substances synthesized in the cell, we could undoubtedly identify them as C-type leucoviruses. But having in mind the initial stage of our study we suggest the term "virus-like particles".

Greater part of the investigated spherical formations shows a morphological characteristics of mature virus-like particles, but there are others, whose structure corresponds to the early phases of their morphogenesis. Based on our data we can presume that the outlining membrane of the vacuoles, characteristic for the second type TEC, participates in the surrounding of the centrally accumulated virus-like particles. It is hardly to analyse the degree of participation of the rest cytoplasmic membranes in the final differentiation of these particles.

It is interesting that we detected the cited particles in only two of several types of TEC. The present, as well as our previous studies, prove that it is a question of cells with a productive type, participating in the synthesis (eventually in the secretion) of certain substances. Differing from data of some other authors (4, 7) our investigations establish such particles only intracellularly and not in neighbouring lymphoid cells or intercellularly.

Deviations from the ordinary ultrastructural characteristics of TEC with virus-like particles were not detected. It is very possible that there exist an equilibrium between the virus-like particles and epithelial cells, known as a latent (chronic) viral infection (1). Our results confirm the opinion of Bikovskii A. F. et al. (1975) that the prolonged (latent) carrying of viruses is a characteristic feature of leucoviruses.

Various hypothesis are worked out tending to indicate the precise biological importance of the leucoviruses found in some epithelial cells of normal thymus from healthy mice:

1. Virus-like particles (including leucoviruses) can be found in TEC of healthy (even sterile) mice without any their pathological influence or affection over the normal functions of the thymus (4, 5).

2. C-type leucoviruses are necessary for the normal thymus functions. Mandel T. (1968) reports that the cortical epithelial cells provide a control upon the thymus lymphopoiesis. E. de Harven (1964) presumes that there should be a possible relation between the presence of these viruses and the process of synthesis of thymus factors by epithelial cells. It is very probably too, that C-type leucoviruses play certain role in the process of differentiation of TEC (7).

3. The presence of the cited viruses is related to the development of some tumour (non-leucaemic) diseases in mice, such as spontaneous adenocarcinoma of glandulae mammae, thymic lymphoma, etc. (3, 4, 5, 13).

4. TEC play an important role for the pathogenesis of mice lympholeucosis (4, 13).

Our results are not satisfactory statistically in order to confirm some of the aforementioned hypothesis, but undoubtedly prove the necessity of further profound investigations which will add an important information for the functional relations between TEC.

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**ВИРУСОПОДОБНЫЕ ЧАСТИЦЫ В ЭПИТЕЛЬНЫХ КЛЕТКАХ
ВИЛОЧКОВОЙ ЖЕЛЕЗЫ КОНВЕНЦИОНАЛЬНЫХ МЫШЕЙ**

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Р Е З Ю М Е

Изучены цитоморфологические особенности эпителиальных клеток вилочковой железы инфантильных и половозрелых конвенциональных мышей породы Swiss. Вирусоподобные частицы, идентичные по своей структуре С-типу лейковирусов, наблюдались в двух видах эпителиальных клеток кортико-медуллярного перехода костного мозга и медуллы вилочковой железы. Электронно-микроскопические данные обсуждаются с точки зрения возможного биологического значения вирусоподобных частиц и функциональной активности эпителиальных клеток вилочковой железы.