IV. Experimental and Clinical Immunology

ULTRASTRUCTURAL CHARACTERISTICS OF THYMOCYTE MICROENVIRONMENT

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It is accepted that non-lymph cells in thymus, so-called thymocyte microenvironment are of great importance for T-lymphocyte differentiation. Epithelial cells and macrophages play a basic role in this relation (11, 12). Data concerning the distribution, structure peculiarities and mechanisms of functioning of the cells of the thymocyte microenvironment are still scanty and even in some cases contradicting (6, 9, 12, 16). We have good reasons for enlarging our investigations on the ultrastructural characteristics of non-lymph cells in mice thymus covering not only epithelial cells and macrophages but also special cells, plasmocytes, tissue basophils and granulocytes.

Material and methods

The study was carried out on 69 Swiss mice of both sexes at different ontogenetic stages (13—14 days and 18—19 days old fetuses, new-born (12-hours after birth), 7 days, 14 days, 30 days, 40 days and 45 days; 3 months, 4 months, 7 months, 18 months and 24 months old animals). Thymus material of decapitated mice was processed according to the routine method for electron microscope study (3, 15). An electron microscope JEM 7A was used for observation and electronogram taking.

Results and discussion

We observed the cells forming thymocyte microenvironment in thymus lobules of mice of any age groups studied. Some age and regional peculiarities characterize the distribution and ultrastructure of certain kinds of these cells.

Epithelial cells. Epithelial cells predominate amids non-lymph cells of thymus in close contact with lymphocytes. Epithelial cells are characterized with morphological heterogeneity (3). We reported in detail some kinds of close spatial relationships between epithelial cells and lymphocytes elsewhere (14) and data concerning the presence of morphological preconditions for direct influence of lymphocytes by epithelial cells in thymus cortex deserved a special attention.

Macrophages. Ultrastructural peculiarities of macrophages in thymus cortex and medulla are in principle identical with those described in the same organ of other mammals (1, 3, 5, 7). These cells can be found in three thymus regions scattered singly amids thymocytes and epithelial cells. The wealth of primary and various kinds of secondary lysosomes as well as parts of phagocyted lymphocytes in macrophage gives evidence for the conclusion that macrophage functional activity in mice thymus consists mainly in phagocytosis of lymphocytes.

Special cells. These cells as described by us (13) in thymus cortico-medullar transition region are mainly characteristic of the early age (15 days old mice). The productive character of their cytoplasm with characteristic rocket-like granules in it impresses deeply, indeed.

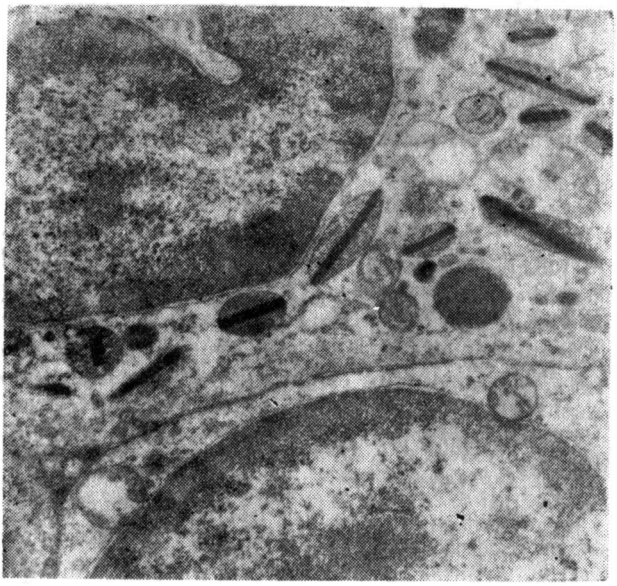

Fig. 1. Spatial proximity between eosinophilic granulocyte and thymocyte in thymic lobule inside. Electron micrograph, Magn. × 10 000

Granulocytes. Granulocytes are observed in thymus of animals of any age groups studied. They are most frequently presented in sexually mature animals (3—4 months and 2 years old mice). Eosinophils predominate (fig. 1) together with neutrophil granulocytes while basophils are rarely seen. These cells are scattered amids lymphocytes and epithelial cells in three thymus regions. They are more frequently located in the cortex. Granulocytes are in the immediate spatial proximity of lymphocytes in their neighbourhood. There are no data about the presence of specialized contacts between both cell types. We observe granules and pieces of cytoplasm near to the cellular membrane (with intact or destroyed integrity) of neighbouring single eosinophils and neutrophil granulocytes.

Tissue basophils (labrocytes). We observe tissue basophils in mice thymus of any age groups. Their permanent presence not only in connective-tissue septi but also in thymic stroma as well as their characteristic distribution mainly in the cortex allows us to consider them a component of thymocyte microenvironment. These basophils have a morphology which is typical of these cells (fig. 2). Their granules are with peculiarities which are characteristic of the species mouse (4), at a different degree of maturity, with non-equal size and content with different electron density. We observe a relatively great number of tissue basophils in the thymus of fetuses (13—14 days) and of adult (2 years) old animals. These cells are in the immediate spatial proximity of lymphocytes in any cases.

Plasmocytes. Single plasmocytes with typical morphology are seen in the thymus of any animals studied (fig. 3).

In concordance with other investigators' concepts concerning rat and guinea pig thymus (6, 9, 16) we assume that "thymocyte microenvironment" is a broader term and covers some cell types. In mice thymus elements of thymocyte microenvironment are not only epithelial cells and macrophages but also some other

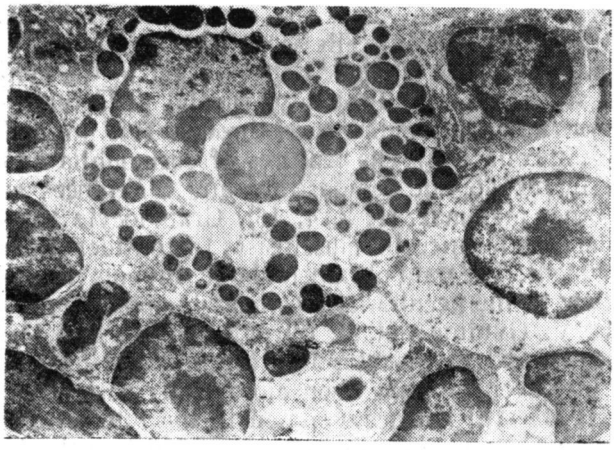

Fig. 2. Tissue basophil (labrocyte) surrounded by cortical lymphocytes. Electron micrograph, Magn. × 3000

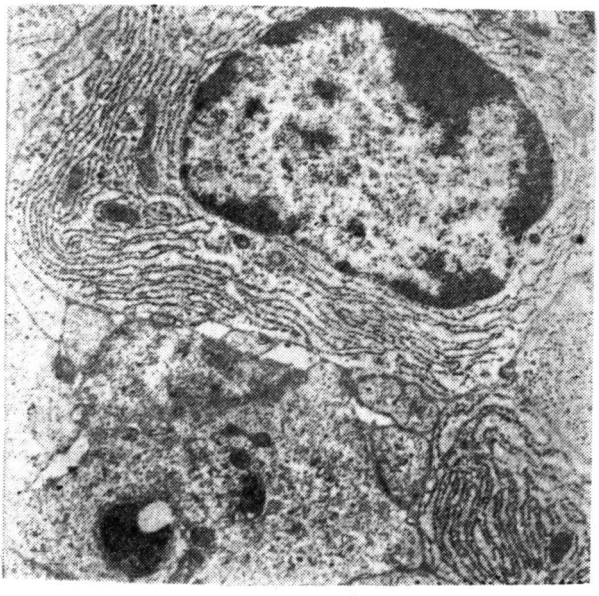

Fig. 3. Part of plasmocyte in thymic lobule cortex. Electron micrograph, Magn. × 5000

cells — special cells, labrocytes, granulocytes, and plasmocytes. The role of close spatial relationships between epithelial cells and lymphocytes in thymus cortex is emphasized by the data of other authors about the nature of TNC-phe-

nomenon (8, 9, 17). It is presumed that lympho-epithelial complexes (TNC) have a key position in the mechanisms of intrathymic T-lymphocyte differentiation (17). Concerning the interesting suggestions reported in the literature about the secretory function of macrophages and their participation in the process of regulation of lymphocyte differentiation through monokines (1, 4, 5) they require additional purposeful investigations of mice thymus. The data received by us about the morphological peculiarities of the special cells as well as some cytochemical data about them (6) confirm the concept of their participation in the synthesis of thymic humoral factors (THF) (7, 16). Probably, special cells realize their influence upon lymphocytes of the corresponding area through THF (6) and their ascertaining as antigen-receptor cells (16). The features of eosinophils and neutrophil granulocytes observed by us do not demonstrate any differences as compared with the same cells of other mammals (1, 2, 4, 16). Granulocyte localization and ultrastructural peculiarities in mice thymus insists to consider them an element of thymus microenvironment. The data obtained about thymus labrocytes present an interest with a view to the peculiarities of mast-lymphocytic rosettes observed in vitro (2) and E. V. Gyuling's et al. (2) presumption that the immediate contact between labrocytes and thymocytes is a precondition for the influence of labrocytes on thymocytes even in cases when biologically active substances containing in their granules are still not accumulated in the intercellular space. The data presented concerning plasmocytes are in concordance with the accepted view that these cells participate in thymocyte differentiation by means of immunoglobulins secreted by themselves (1).

The outlined variety of cells of thymocyte microenvironment according to origin, kind and function depends on the age and regional affiliation thus enables to consider them a complex system of multidirectional and mutually related cell interactions, indeed (6, 16, 17). These interactions are probably based mainly on the immediate cellular contact in the cortex and on humoral factor release acting within the limits of the corresponding region — predominantly in the medulla and corticomedullar thymus transition zone. The interpreted peculiarities of thymocyte microenvironment in mice thymus are important for the understanding of the complex and still not enough clarified mechanism of intrathymic T-lymphocyte differentiation (10, 16, 17).

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УЛЬТРАСТРУКТУРНАЯ ХАРАКТЕРИСТИКА ТИМОЦИТНОГО МИКРООКРУЖЕНИЯ

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РЕЗЮМЕ

С помощью стандартного метода электронномикроскопического исследования проведена характеристика нелимфатических клеток вилочковой железы конвенциональных мышей различного возраста (от фегусов 13—14 дней до двухлетних животных). В дольках железы наблюдаются эпителиальные клетки, макрофаги, специальные клетки, гранулоциты, лаброциты, плазматические клетки. Установлены возрастные и региональные особенности в распределении этих клеток среди лимфоцитов. Обсуждается роль описанных видов клеток как элементов тимоцитного микроокружения в вилочковой железе мышей, а также их роль в внутритимусной дифференциации Т-лимфоцитов.