THE EPITHELIAL RETICULAR CELL OF THE THYMUS

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These cells are also called the EPITHELIOCYTES. Some are named as THYMIC NURSE cells, because they play a role in the maturation of the lymphocytes, making them responsible for cell mediated immunity.

Embryologically, their origin is from the endodermal cells of the third pharyngeal pouch. Their epithelial origin is confirmed by the presence of basement membrane and the desmosomes with tonofibrils. The cells later become flat and spindle shaped.

These cells are seen in the following area: (1) outside the capsule (2) just deep to the capsule in the subcapsular zone (3) within the trabeculae forming septae (4) as a sheath, covering the blood vessels within the gland, and probably play a role in the formation of the partial blood-thymic barrier (5) in the cortico medullary zone, (6) lastly, they form a lattice like structure both in the cortex and medulla (Figure 1).

Fig. 1: Thymus gland showing lobular architecture. Hasall's corpuscles as seen in medulla (TPA stain X 20)

The lymphocytes lie in this network of epithelial reticular cells. Since there is crowding of the lymphocytes in the cortex, the reticular cells are not clearly visible in the cortex. But in the medulla, there are only a few lymphocytes and hence epithelial cells are clearly seen and they form the Hassall's corpuscles.

As it is a part of the blood thymic barrier, these cells prevent the antigens present in the blood from reaching the T lymphocytes. The epitheliocytes also promote proliferation of T cells and T cell differentiation.

According to recent studies, several differences are noted in their structure(1) . Hence they are classified into five types.

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Type I - Line the inner aspect of the capsule, the septa and the blood vessels. These form the blood – thymic barrier.

Type - II and Type - III are seen outside the cortex and inner parts of the cortex. These are the network on which the lymphocytes are placed and hence are not seen clearly.

Type IV – are cells in the deeper part of the cortex – in the Cortico-medullary junction and the medulla (Figure 2).

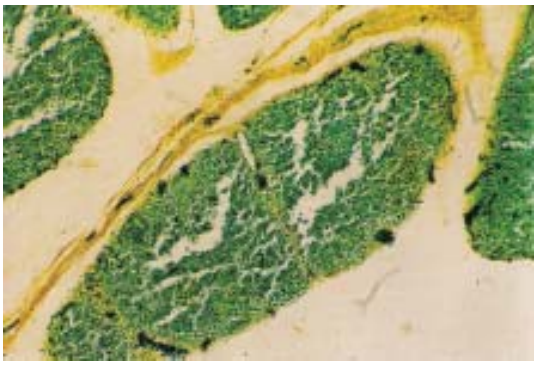

Fig. 2: Epithelioreticular cells highlighted by amidoblock dye in the subcapsular region, in the septae and corticomedullayr junction (TPA stain X 20)

Type V – are cells in and around the Hassell's corpuscles. They probably destroy T cells reacting with self antigens by phagocytosis. That is why some authors(2) call the Hassall's corpuscles as the 'graveyard' for the incompetent lymphocytes. These cells predominate in the medulla during early gestational period in human foetal thymus. Hassell's corpuscles first appears during the 17th week of gestation and increases in size subsequently.

The thymic micro-environment is mainly created by these epitheliocytes. Ultrastructural evidence suggest that these cells provide the three dimensional framework for the thymic cells. By their contact with the lymphocytes and probable secretion of certain hormones they induce INTRATHYMIC LYMPHOCYTIC DIFFERENTIATION and influence the events associated with the maturation of T cells.

The identity of these cells has been established by their consistent ultrastructural features such as 1) presence of tonofilaments and desmosomes, (2) basal lamina associated with cell membrane. These cells have long cytoplasmic process which connect with adjacent cells. These connections are shown in electron and light microscopic studies using special staining method called TPA (Tannic acid - phosphomolybdic acid - Amido black) technique developed by Clermont & Leblond to show epithelial cells in tissues other than thymus. These cells form a three dimensional frame work of thymic parenchyma. These reticular cells are distinguished from the reticular cells

of mesodermal origin in the spleen and lymph nodes. Their epithelial origin is proved by presence of keratin in Hassall's corpuscle and by the presence of tonofilaments and desmosomes. Hence these cells are also called "EPITHELIOCYTES"

Several workers have described ultrastructural differences between the cortical and medullary epithelial reticular cells. It is not clear whether the cells of the same origin are seen differently according to their functions in varied situations (1, 3).

Under the Electron Microscope, two main types are described – PALE EPITHELIAL RETICULAR CELL (PER) and DARK EPITHELIAL RETICULAR CELL (DER) according to their electron density, created by the increased density of cytoplasmic ground substance(3,4). The pale epithelial cell shows the heterochromatin along the inner nuclear membrane as a thin rim rarely clumped (Figure 3).

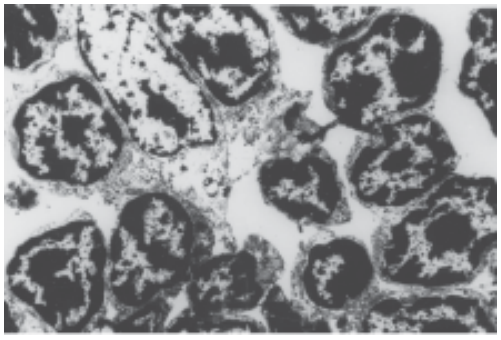

Fig. 3: Ultrastructural appearance of a pale epithelioreticular cell seen on electron microscopy.

Nuclei are distinct and there is space distribution of ribosomes. Some pale cells form the Hassell's corpuscles. The dark cells are associated with collagen fibres (figure 4). The long cytoplasmic processes extend from the cell body to encompass the bundle of collagen fibres. The collagen fibers are definitely extracellular in position.

Both pale and dark epithelial reticular cells have in common rough endoplasmic reticulum, moderately developed golgi bodies, membrane bound vesicles, electron dense granules and lysosome like bodies.

A few of these cells show vacuoles and small cystic inclusion in their cytoplasm. These vacuoles may contain

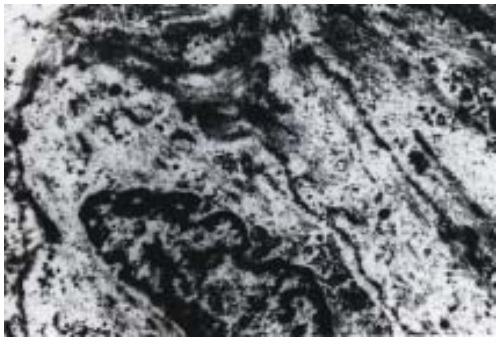

Fig. 4 : A dark epithelioreticular cell with desmosomal junction seen on electron microscopy.

degenerating material which may be lymphocytes reacting with self antigens and hence getting destroyed by some factors released from these epithelial reticular cells. Hence, the epithelial reticular cells are called THYMIC NURSE CELLS(5).

These are epithelial cells, which show evidence of hormonal secretion(3). At least eight hormones have been isolated since 1966, but the details of the synthesis, production and its transportation are not clear.

Still, thymus is considered as a PRIMARY LYMPHOID ORGAN, along with the bone marrow.

The proliferation of T lymphocytes and their conversion into cells capable of reacting with antigens are events dependant on the hormones produced by these epithelio-reticular cells. The hormone affects LYMPHPOIESIS in the peripheral lymphoid organs. If thymus is removed during neonatal period, the peripheral lymphoid organs do not develop in the normal way.

Recent studies have identified some of these hormones originating from epitheliocytes:

a. THYMULIN - enhances function of T cells
b. THYMOPOIETIN stimulates production of cytotoxic T cells
c. THYMOSIN alpha I – stimulates lymphocyte and also antibody production.
d. THYMOSIN Beta – 4
e. Thymic humoral factor controls the multiplication of helper and suppressor T cells.

Apart from actions on the lymphocytes, hormones or any other substance formed in the thymus probably also influence the adenohypophysis gland and ovaries. In turn, the activities of thymus is influenced by the hormones from these organs.

REFERENCES:

1. Singh I.B Text book on Human Histology 2005
2. Blau J.C, Hassall's Corpuscles – Site of thymocyte death, Br.J.Exp.Path. 1973; 53: 634
3. Kendall & Singh The Thymus Gland 1981 (AC.PRESS)
4. Clark.S.L E/M studies on thymus. Am.J.Anat.1963; 112:1-33.
5. Clermont Y. Epithelial Ret.cell in Rat thymus. Anat Rec. 1965 ;151-337