'Clear' Cells in the Normal Cervical Epithelium of the Mouse

The presence of stellate or dendritic cells in human epidermis has been well known since the original description by LANGERHANS over 100 years ago[1]. With the electron microscope these cells can be readily distinguished from the surrounding keratinocytes in stratified squamous epithelium by their lighter cytoplasm due to the paucity of ribosomes and filaments, lack of desmosomal attachments and presence of dendritic processes[2]. Similar cells usually referred to as 'clear' cells have also been reported in the normal stratified squamous epithelium of the gingiva, esophagus, nasopharynx, vulva, exocervix and vagina in man[3-10], and in the female genital tract of several mammalian species[5,6,11]. The ultrastructural features of such cells in human exocervix and vagina are identical to those of epidermal Langerhans' cells[8-10]. The clear cells of mouse cervical epithelium have been examined only with the light microscope and have shown histochemical similarities to those found in the human cervix[5]. In this communication we report the fine structure of clear cells in mouse cervical epithelium and compare them with corresponding cells of the human cervix.

Random bred 3-week-old ICR/Ha mice obtained from West Seneca Laboratories, Seneca, New York, were used in this study. The entire cervix was excised from 8 mice and each ring of tissue was further cut in the vertical plane into 4 pieces. The specimens were fixed in 3% glutaraldehyde in Sorensen's phosphate buffer at pH 7.4 for 2 h and postfixed in osmium tetroxide for 2 h. LUFT's[12] method of epon embedding was followed and sections were cut on an LKB or Reichert ultramicrotome. Thick sections were stained with toluidine blue and thin sections with uranyl acetate and lead citrate. An Hitachi HU-11E-1 electron microscope operating at 75 kV was used.

With the light microscope, the clear cells were easily identified by their lighter staining cytoplasm in thick epon sections and were found to be sparsely distributed among the basal and lower spinous layers of the epithelium. Under the electron microscope, these cells were irregular in shape and often showed dendritic processes extending into intercellular spaces between neighbouring

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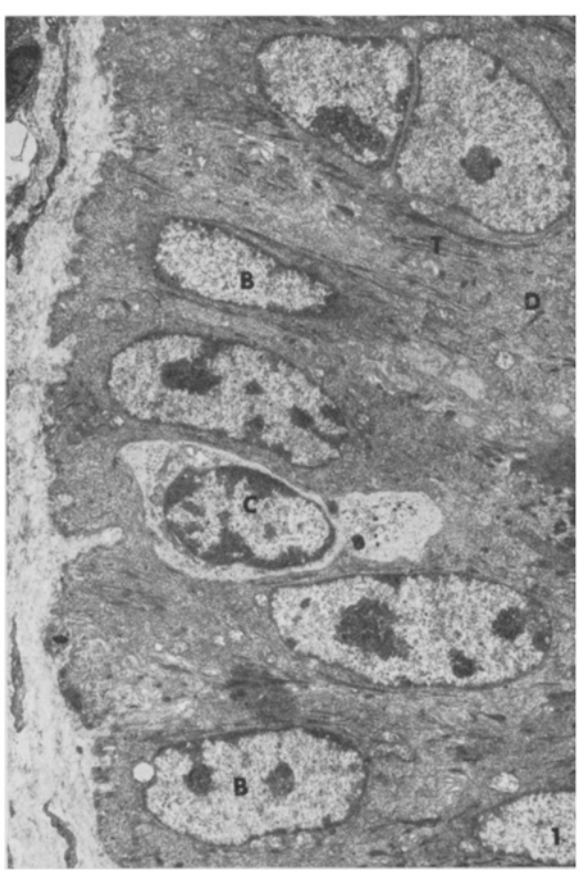

Fig. 1. Basal portion of the stratified squamous epithelium of mouse cervix. A clear cell (C) is seen among the basal cells (B), which show characteristic desmosomes (D) and tonofilaments (T). ×6,000.

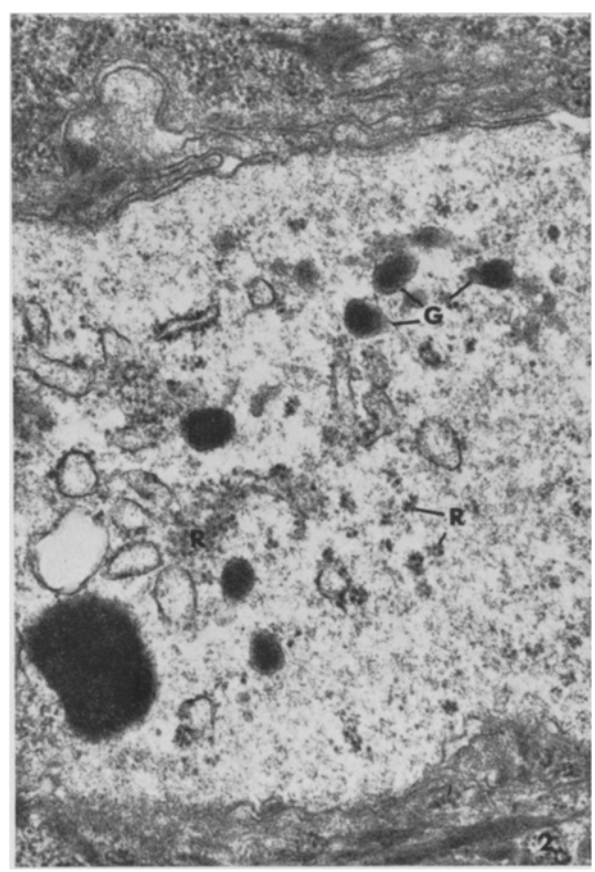

Fig. 2. A portion of the clear cell from Figure 1 showing granules (G) of variable size and density. A few small and large aggregations of ribosomes are also seen (R). ×57,500.

keratinocytes. All of the clear cells characteristically lacked desmosomes and showed a general paucity of organelles (Figure 1). The nuclei were round or oval and appeared to be smaller than those of adjacent epithelial cells. A single cleft was observed in the nucleus of a very few cells. The nuclear chromatin was usually condensed peripherally. The cytoplasm was more electron translucent and contained fewer ribosomes which were mostly aggregated in rosette-like polysomes (Figure 2). Although typical bundles of tonofilaments were absent, a few loosely arranged individual filaments with a diameter of 60–80 Å were sometimes observed. An occasional long isolated microtubule was also present in some cells. The cytoplasm contained numerous small smooth-surfaced vesicles, Golgi apparatus and a few isolated cisternae of rough-surfaced endoplasmic reticulum. A majority of the clear cells showed a variable number of dark, membrane-bound granules. These were round, oval or constricted to form an hourglass or bowling pin shape and varied from 0.07 to 0.7 μm in diameter or length. Most of the granules contained an electron-dense, homogeneous, granular core but some of the larger ones showed a heterogeneous internal appearance. The characteristic Langerhans cell granules, which have recently been recognized as cup-shaped or disc-shaped structures[13], were not seen in the clear cells of the mouse cervix. Membrane-delimited granules with a fine-grained internal substance have also been described, in addition to typical Langerhans granules, in the clear cells of normal human vagina by Hoffmeister and Rupec[10]. These authors have suggested that the granules resemble the premelanosomes present in the cytoplasm of human epidermal melanocytes. Although the precise significance of clear cells in cervical epithelium is unknown, our preliminary studies indicate and incrase in frequency of clear cells in chemically induced squamous carcinoma of the mouse cevix. A similar finding has also been reported in in situ carcinoma of the human cervix[9]. However, our studies suggest that the clear cells of mouse cervix might represent a different morphological type of cells than the Langerhans cells of human specimens[14].

Résumé. Un examen au microscope électronique des cellules «claires» de l'épithelium cervical de la souris a révélé qu'il leur manque les granules caractéristiques de Langerhans décrites dans les cellules correspondantes de l'exocol humain.

M. G. Joneja and H. E. Scoggan

Department of Anatomy, Queen's University, Kingston (Ontario, Canada), 12 April 1972.

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Seizing Mechanism and Fate of Intranuclear Mitochondria

During a fine-structural study of a transplantable tumor originated from an adrenal cortical carcinoma of the Syrian golden hamster, induced by s.c. injections of urethane given during the suckling period[1], mitochondria and small vesicles were observed in the nuclei of tumor cells. These structures were found in many of the cells at early interphase, which showed dilated perinuclear space and the chromatin tended yet to be disposed throughout the nuclei, in larger numbers (Figure 2). In other resting cells these structures were found in smaller number. No nuclear envelope surrounding these mitochondria and vesicles was discernible. Many of these structures could be definitely identified as mitochondria, in that they showed a double limiting membrane and internal cristae. Sometimes swollen and altered mitochondria, which were surrounded only by a single thicker membrane and contained what seemed to represent remnants of cristae, were encountered. Some of them showed a severe decrease in the density in the matrix areas associated with the appearance of fine filamentous components simulating the mitochondrial DNA[2] and aggregates of electron-dense material (Figure 3). No intranuclear mitochondria were detected in cells at prophase. The small vesicles were probably derived from the endoplasmic reticulum which are very rich in the cytoplasm in this tumor cell line.

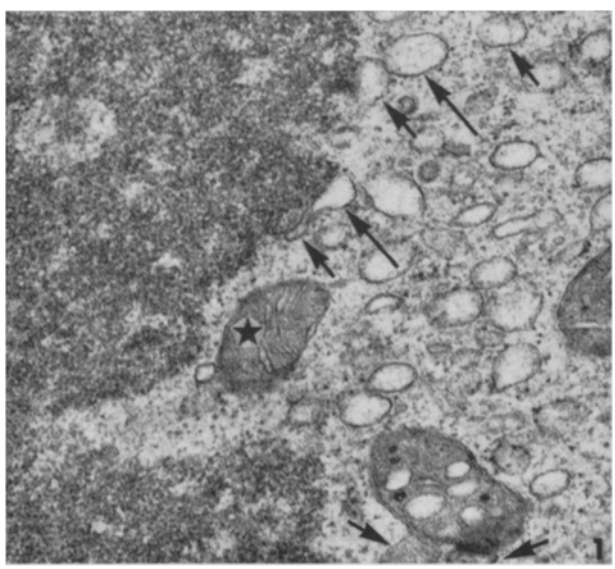

Fig. 1. Portion of a cell, at ana-telophase, of a transplantable adrenal cortical carcinoma of the Syrian golden hamster. Vesicles are gathering near a coalescent chromosomal mass and surrounding a mitochondria (asterisk). Some of them are adhered to both of the structures (arrows) and fusing each other (long arrows). ×45,400.

The abscence of a nuclear envelope surrounding the mitochondria and vesicles indicates that they are not 'nuclear pseudo-inclusion'[3]. Several possibilities can be suggested to explain their location within the nuclei. It has been assumed[4–7] that passage through enlarged nuclear pores, incorporation within a pinched-off invagin-

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