The Association of Endoplasmic Reticulum and Mitochondria in Placental Cells[1] (36273)

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Endoplasmic reticulum, of both the smooth and rough variety, has often been observed in close association with mitochondria (1–3). Indeed, so closely and regularly are these two organelles associated that various investigators have speculated as to the functional significance of their relationships (1, 2, 4). In investigating the fine structure of the placentas of several species, a variant configuration was noted in the yolk sac epithelium of carnivores and in the cytotrophoblastic cells of Langhans in the human chorion. These unusual variants are the subject of this report.

Materials and Methods. Specimens were obtained from anesthetized pregnant dogs and cats by hysterotomy. The human specimens were obtained by curretage, hysterotomy, or hysterectomy. All specimens were fixed immediately in cold Dalton's fluid or in glutaraldehyde, followed by osmication, dehydration, and embedding in Araldite (Durcupan). Thin sections were cut with a diamond knife on a Porter-Blum MT-1 microtome. They were stained with lead citrate (5) and examined in an RCA EMU-3H electron microscope. Photographs were made at initial magnifications of 2000 to 10,000 and subsequently enlarged as desired.

Observations. In the yolk sac epithelium of the cat (Fig. 1) and dog (Fig. 2), and in the cells of Langhans in human chorionic villi (Fig. 3), profiles of endoplasmic reticulum are customarily approximated to or wrapped around mitochondria. The distance between the outer membrane of the mitochondrion and the inner membrane of the concave cisternal profile is frequently rather constant. Upon occasion, two or more nearby mitochondria have been seen sharing a single cisternal profile; in such cases the endoplasmic reticulum may assume an S- or C-shape with the mitochondria cupped in its arms (Fig. 3).

More remarkable even than this close association is the relationship between the granules characterizing the rough endoplasmic reticulum and the mitochondria. A preponderance of these granules are located in the regions between the two membranes, the one of the mitochondrion and the other of the endoplasmic reticulum. Conversely, the membrane on the side of the profile opposite the mitochondrion normally is of the smooth variety, lacking granules. This relationship is evident in the profiles of cisternae dilated with moderately dense, amorphous material (Fig. 2), and is equally characteristic of profiles with little or no contained material (Fig. 1).

A similar appearance was observed in the cells of Langhans of human chorionic villi. Characteristically, the ribosomal granules associated with rough endoplasmic reticulum are located on the side of the membrane apposed to mitochondrial surfaces, and are absent or scant on the surfaces opposite mitochondria (Fig. 3). As was the case in the carnivore yolk sacs, this disposition is evident regardless of the degree to which the endoplasmic reticulum is dilated by material contained within its lumen.

Discussion. So characteristic is the appearance of the mitochondria-endoplasmic reticulum complex in the cells of Langhans that it

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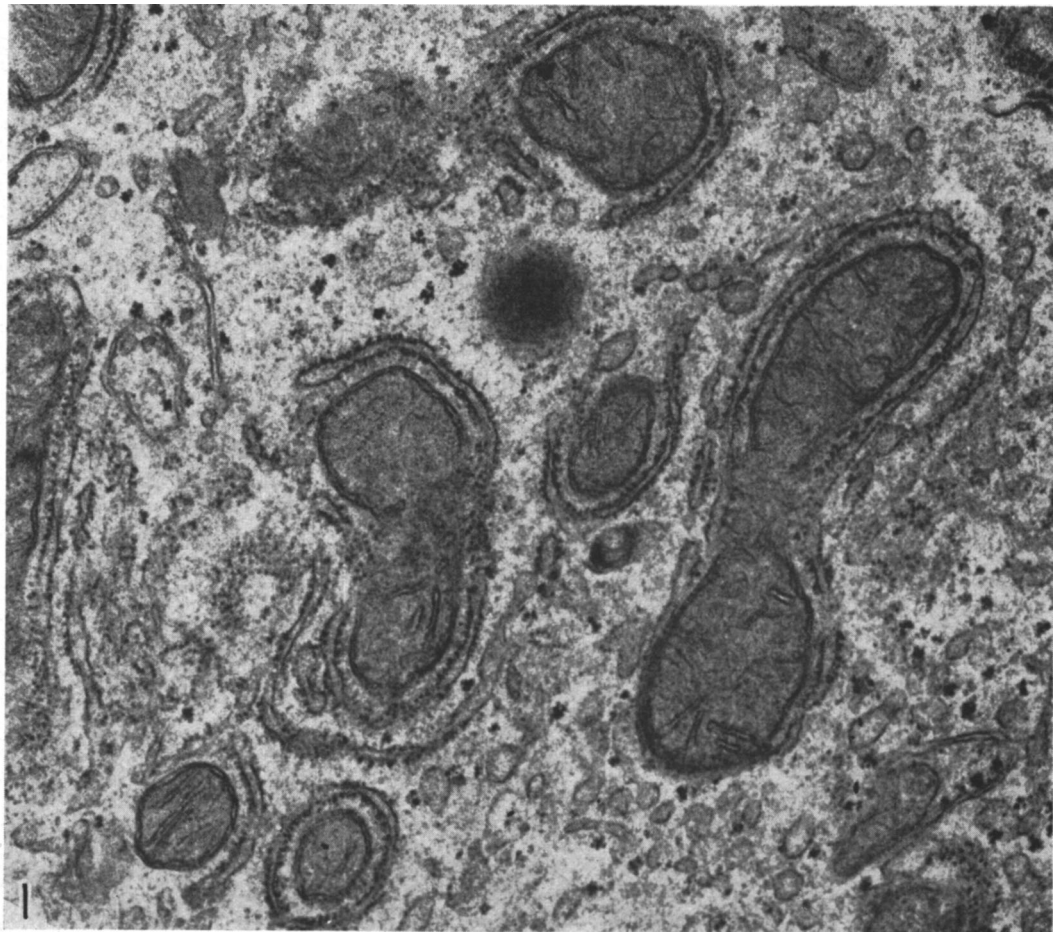

FIG. 1. Electron micrograph of mitochondria with closely associated endoplasmic reticulum from the yolk sac of a cat: Ribosomes are more frequent on the membranes facing the mitochondrion than on the opposite side. Dalton's fixation; ×25,000.

can be used as one indicator of the origin of the syncytium. Several cytological similarities relate the Langhans cells to the basal syncytiotrophoblast (3, 4) among which we must now include the unusual and characteristic complex of the mitochondria and endoplasmic reticulum described here.

Close association between mitochondria and endoplasmic reticulum is a well-known phenomenon. However, the ribosomes of the granular endoplasmic reticulum ordinarily have been seen on both sides of the cisternae (2) or concentrated on the side opposite to the mitochondria (3, 4, 7). Only in the guinea pig yolk sac has a similar situation been encountered (1). Indeed, in experiments causing proliferation of membraneous endoplasmic reticulum, a smooth variety lacking ribosomes is the rule (8, 10) and this situation occurs in cells involved in steroid synthesis (9) or degradation (10).

The discovery that mitochondria contain both DNA and RNA and that these nucleic acids are specifically different from those of the nucleus and cytoplasm has led to many questions concerning the biogenesis of mitochondria and to the formation of their components. Many of these components are thought to be formed by the endoplasmic reticulum (11). The close association of mitochondria and endoplasmic reticulum could be explained, therefore, by the rapid forma-

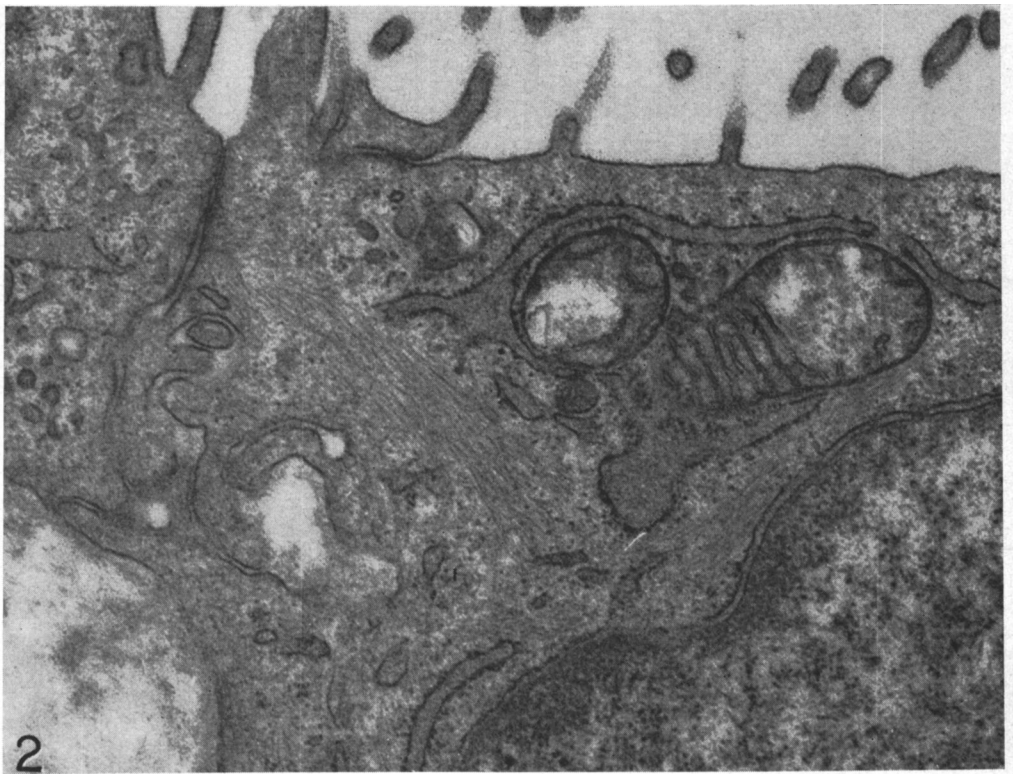

FIG. 2. Mitochondria with associated, dilated endoplasmic reticulum from the yolk sac of a dog: As in the cat, a preponderance of ribosomal granules faces the mitochondrion. Dalton's fixation; ×25,000.

FIG. 3. Endoplasmic reticulum wrapped around a cluster of mitochondria in a cytotrophoblastic cell of Langhans in a human chorionic villus: glutaraldehyde fixation; ×20,000.

tion of new mitochondria in a fetal, rapidly growing tissue. However, this explanation does not account for the characteristic location of the ribosomes described here, nor does it fit well with the fact that the yolk sac is a slowly proliferating organ as compared with the trophoblast, yet both show the same characteristic pattern.

Close morphological linkage between the sites of energy release and protein synthesis suggest that the fetal organism requires some substance at a very rapid rate, or needing a great energy source. The placenta synthesizes several protein hormones of which chorionic gonadotropin is noteworthy. It produces numerous enzymes, especially proteases and esterases (6). Lastly, it is a likely source for the components of fetal serum, especially during early weeks of gestation during which hemopoiesis and vasculogenesis are occurring in the placenta. These synthetic processes, directed toward the formation of fetal products, seem a more likely concern of the mitochondria-endoplasmic reticulum association described here than that they are involved with maternally directed activities. The predominantly basal location of these complexes, *i.e.*, toward the fetal circulation, lends some slight weight to this speculation.

Summary. A characteristic complex of mitochondria and endoplasmic reticulum occurs in the yolk sac epithelium of carnivores and guinea pigs, and in the cytotrophoblastic cells of Langhans in the human placenta. In this complex, ribosomes are located predominantly on the cisternal membrane facing the mitochondrion. The significance of this complex is discussed briefly with respect both to protein synthesis and to fetal physiology.

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