Pancreatic Centroacinar Cells

The Regulator of Both Exocrine and Endocrine Function

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Summary

The relationship between pancreatic centroacinar cells (CAC), the acinar cells, and the endocrine cells was examined in fetuses and newborn Syrian hamsters histologically, immunohistochemically, and electron microscopically. Pancreatic anlage, composed of undifferentiated cells and a few α cells, were found at day 12, δ cells at day 13, acinar cells at day 14, and β cells at day 15 of the gestation. Intermediate cells (hybrid cells with both zymogen and endocrine granules) were also found after day 14. In the late-gestational period and after birth, two types of acini could be distinguished: one was composed exclusively of acinar cells and the second of acinar and CAC. In the latter type, some CAC covered the surface, lateral, and basal portion of the acinar cells, which showed a relative reduction of zymogens and increased autophagic vacuoles, a finding that indicated that CAC control the zymogen release from the acinar cells. Two types of CAC were encountered: dark cells with cytoplasmic processes located on the surface of acinar cells and larger light cells located between the acinar cells. The transitional forms between the light CAC and endocrine cells were found frequently at day 15 and a day after birth. During the endocrine cell differentiation, the committed cells lost their connection to the lumen by the force of the cytoplasmic processes of the dark CAC, which then overlaid the differentiated endocrine cells. From these findings, it can be concluded that CAC control both the pancreatic exocrine secretion and endocrine cell function.

Key Words: Pancreas; centroacinar cells; function; differentiation; endocrine cells; acinar cells.

Introduction

The complex relationship between pancreatic acinar cells and centroacinar cells (CAC) and their functional interaction have received little attention.

Although, according to several investigators, CAC are pluripotent cells capable of differentiation into islet cells (1–8) and perhaps also acinar cells (9), no evidence has been presented.

The potency of CAC for proliferation has been shown in birds, rodents, and humans in many pancreatic diseases and during pancreatic regeneration (10–20). The author has observed that during the early stages of pancreatic carcinogenesis in Syrian hamsters, the CAC proliferate and form long cytoplasmic processes, which extend along the luminal
and basolateral surface of acinar cells and cause acinar cell degeneration (14–17). The proliferated CAC then replace the affected acinar cells and culminate in the development of tubular (ductular) structures with subsequent malignant changes (14,17). A similar observation was made in Guinea fowl (20).

The results of these studies suggested that during the neoplastic process, some CAC differentiate into endocrine cells, which were found during the entire neoplastic process intermingled with malignant ductular cells (18,19,21), as is the case in humans (22,23). However, in the tissues that were examined, there was no transitional stages between the CAC and endocrine cells. It was also unclear whether the observed interaction between the CAC and acinar cells and between the CAC and islet cells reflected a neoplastic process or an exaggerated natural event.

Because the neoplastic process of many tissues mimics the embryonic development (24), the author examined the pancreas of a Syrian hamster during fetal development. The process of differentiation is dynamic and, in a mature organism, difficult if not impossible to visualize. During tissue development and differentiation, such a dynamic process can be constructed by putting together the fragments of changes that take place between the beginning and the end of the differentiation process. The chance of depicting intermediary changes certainly depends on the frequency and duration of the process. Rapidly developing tissue, particularly in an animal such as the Syrian hamster, which has a short gestation period (15 d), provides an ideal condition for such studies. In this study, a relationship between centroacinar, acinar, and endocrine cells during the fetal and postnatal life of hamsters was examined. Details of the developing hamster pancreas will be presented elsewhere.

**Material and Methods**

**Histology and Immunohistochemistry**

Fetuses (five each) from days 8, 10, 11, 12, 13, 14, and 15 of the gestation and 1 day after birth were fixed in *toto* in Bouin’s solution overnight, washed in 70% alcohol, processed for histology according to conventional methods, and cut in the head-tail direction in 20-step sections (0.1 mm apart), going vertically through the abdominal organs. The slides, containing the digestive tissue of the fetuses, were stained with hematoxylin and eosin. For demonstration of α, β, and δ cells, the respective antibodies (MAXXUM/Omnitag, Lipshaw, Detroit, MI) were used by the avidin-biotin method (Vector Lab, Burlingame, CA), as reported (23).

**Electron Microscopy**

From the same dam, the pancreatic tissue from five fetuses at the gestational days 14 and 15 and 1 day after birth was taken under a dissecting microscope, immediately fixed in 2.5% glutaraldehyde in 0.13M balanced phosphate-buffered 1.3% recycled osmium tetroxide at 4°C, and dehydrated through a gradient series of ethanol and propylene-oxide prior to embedding in BEEM capsule with Epon 812. During dehydration, the samples were stained with 2% uranyl-acetate at 80% ethanol step. Ultrathin sections were stained on the grid with 2% uranyl acetate and 0.4% lead citrate, and were examined by a Siemens Elmiskop 101.

**Results**

**Histological and Immunohistochemical Findings**

Histologically, the primitive pancreatic tissue could be identified at day 11 as a small group of undifferentiated cells that extended from the outer wall of the upper gut. At this stage, single cells that were immunoreactive with antiguacagon, but not with antinsulin or antisomatostatin were identified between the undifferentiated cells. At day 12, the number of tubules had increased. They formed elongated and branched tubules with scattered isolated cells immunoreactive with antiglucagon and antisomatostatin, but not with the antiinsulin antibody (Fig. 1). The beginning of glandular formation and acinar cell differentiation was noticeable.

At day 14, acinar cells were formed. They lined part of the tubular structures and were intermingled