

High Secretory Activity in the Pancreatic B Cells of a Diabetic Strain of the Japanese Mouse

In a series of previous morphological and biochemical studies¹⁻⁴, we have shown that a strain of the Japanese native mouse named KK is genetically diabetic. This was confirmed by other workers in subsequent investigations on the mouse strain⁵⁻⁷, and it has now received international acceptance among diabetologists⁸. Previously, in an attempt to find morphological changes in various organs associated with diabetic syndromes in the mice, their pancreatic islets were examined by light microscopy using chromium hematoxylin phloxin and other stains^{1,3,4,9}. Subsequently, the insulin content of their pancreas and serum was measured⁷. According to these studies, the insular tissues of the diabetic mice undergo hypertrophy and hyperplasia, and the insular B cells are large in size and degranulated. The insulin content of the pancreas and serum is significantly higher than that of control mouse strains. Thus, in the pancreas of

The Golgi apparatus is likewise extensive and consists of numerous vesicles, vacuoles and both flattened and dilated saccules (Figure 2). In the territory of this organelle, figures suggestive of formation of dense secretory granules are more frequent (Figure 2) than in the B cells of control animals (Figure 1). In the B cells of diabetic mice, however, formed secretory granules are obviously less in number (Figure 2), as compared with the cells of control mice (Figure 1). These ultrastructural characteristics in the cytoplasm are regarded as implying that insulin synthesis and release are elevated in the pancreatic B cells of the diabetic mice. In view of a recent report¹¹ that hypernormal insulin-like activity (ILA) levels are noted in human prediabetics, juvenile-onset diabetics and maturity-onset untreated diabetics, the present results are meaningful for elucidation of the etiology of diabetes mellitus.

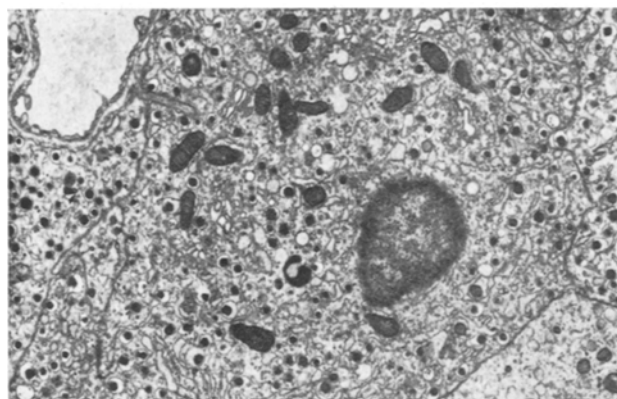


Fig. 1. Pancreatic B cells of a control (C57BL/6J) mouse. In the cytoplasm dense secretory granules are abundant. $\times 6000$.

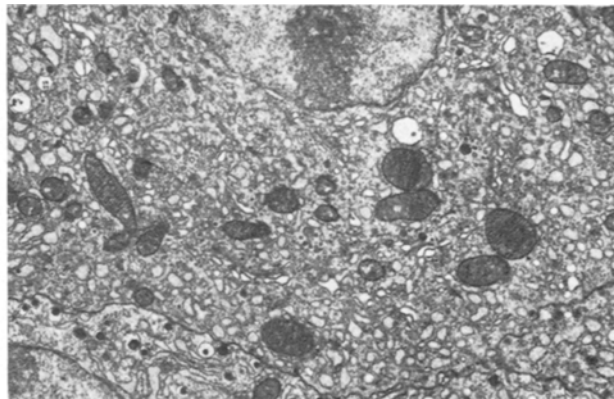


Fig. 2. Pancreatic B cells of a diabetic (KK) mouse. In the cytoplasm abundant free ribosomes, large mitochondria, numerous dilated cisternae of granular endoplasmic reticulum and extensive forms of the Golgi apparatus are seen, while dense secretory granules are scanty. $\times 6000$.

the diabetic animals, hypersecretion of insulin is likely. It is the object of the present work to observe the pancreatic islets of the diabetic (KK) and normal (C57BL/6J) mice by electron microscopy and to confirm a high activity of secretion in the pancreatic B cells of the diabetic mouse strain.

A total of 5 diabetic (KK) and 5 control (C57BL/6J) male mice, ranging in age from 7–10 months, were used. At the sacrifice of the animals their urine was tested for glucosuria by Tes-tape (Lilly), and all the diabetic mice had intense glucosuria. Tissue pieces of the pancreas were removed from the donor animals, fixed in chilled 2% bichromate phosphate buffered osmium tetroxide (modification of Dalton's fixative¹⁰), dehydrated and embedded in Epon 812. Thin sections were subjected to a double staining with methanolic uranyl acetate and aqueous lead citrate and were examined electron microscopically.

In the pancreatic islets of the diabetic mice, B cells are provided with cell organelles better developed than those in the same cell type of control animals (Figures 1 and 2). In the cytoplasm of B cells of diabetic animals, free ribosomes are markedly abundant and large mitochondria contain copious cristae (Figure 2). In the cytoplasm the cisternae of granular endoplasmic reticulum are extremely numerous and are dilated with their lumen filled with materials of relatively low electron density (Figure 2).

Zusammenfassung. Elektronenmikroskopische Untersuchung von B-Zellen der Pankreas eines diabetischen Stammes japanischer Mäuse erbrachte den Hinweis gesteigerter Insulin-Synthese, bzw. gesteigerten Insulin-Ausflusses.

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