UG CBCS Semester-IV (MJC-7: Endocrinology)

Islets of Langerhans

The mammalian pancreas is a mixed gland of exocrine and endocrine components that play essential roles in digestion and metabolism, respectively. The digestive role of the pancreas is accomplished by the exocrine portion that produces digestive enzymes and secretes an alkaline pancreatic fluid. The endocrine portion of the pancreas secretes hormones that regulate carbohydrate, lipid, and protein metabolism. The endocrine pancreas or the islets of Langerhans consists of small masses or islands of endocrine cells scattered among the acinar tissue (Figure 12-20). The pancreatic islets secrete at least four regulators: insulin, glucagon, SST, and an additional peptide known as PP. Insulin is primarily a hypoglycemic agent that lowers blood glucose, whereas glucagon is a hyperglycemic hormone. Glucagon and insulin may produce opposing effects on lipid metabolism as well, with glucagon promoting lipolysis. The major role of pancreatic SST may be as a paracrine agent released by neural stimulation that inhibits local release of the other pancreatic peptides. The role for PP is not well established, but its increase in the circulation following ingestion of a meal suggests a role in postabsorptive metabolism.

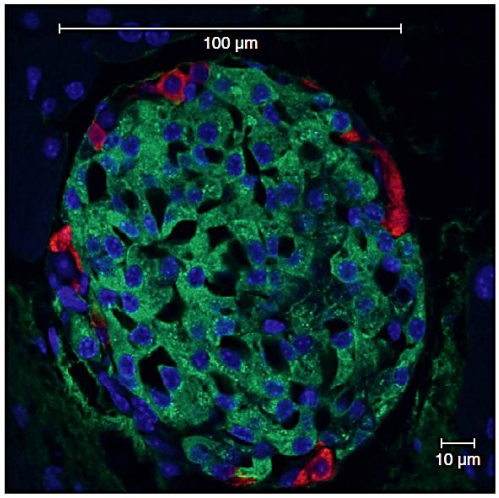

FIGURE 12-20 **Pancreatic islet of Langerhans.** This islet from the mouse pancreas exhibits insulin-producing B cells in green and glucagon-producing D cells in red. *(Photograph by Christin Süß, Jakob Suckale, and Michele Solimena, Solimena Lab, University of Technology, Dresden, Germany.)*

Development of the Mammalian Endocrine Pancreas

The exocrine tissue in the developing pancreas can be identified by the formation of small ductules. These ductules coalesce into larger ducts until they form a large pancreatic duct connecting the exocrine pancreas with the lumen of the small intestine. Small buds develop from the ductules and become the islets of Langerhans. In addition, some of the endocrine cells may be scattered singly or in groups of only a few cells throughout various regions of the pancreas. Immunoreactivity of the various peptides occurs in humans at about 8 to 10 weeks of development, marking the first synthesis of pancreatic hormones. Although the islets originate as outgrowths from the pancreatic ductules, the actual embryonic origin for the endocrine cells is not clear. It has been suggested that they arise from mesoderm or from neural crest cells of neuroectodermal origin or from endoderm of the gastrointestinal tract. However, experiments have shown that the islet cells are not derived from neural crest, at least in birds, and it is probable that mammalian islet cells are not derived from either neural crest or other neuroectoderm. Until the origin of its secretory cells is confirmed, the endocrine pancreas can be considered to be of endodermal origin. Several functional schemes have been proposed for the origins of the endocrine pancreatic cells that are divorced from their possible germ layer origins. These endocrine cells may represent modified gastrointestinal mucosal cells that initially synthesized “inducers.” In the fetal guinea pig pancreas, immunoreactive glucagon, PP, insulin, and SST can be demonstrated in cells of the pancreatic tubules about 10 to 15 days before they appear in the islets, supporting the notion that they are derived from exocrine enzyme secreting cells. These modified mucosal cells presumably lost their contact with the gut mucosa and specialized as centers for internal secretion.

Cellular Types in Pancreatic Islets

At least five different cellular types have been identified in the mammalian endocrine pancreas: B, A, D, PP, and amphophils. Although first identified by their staining characteristics, they now are identified by their immunoreactivity to antibodies prepared against the specific pancreatic peptides. Immunocytochemistry reveals that several peptides may be localized in one cell type, and the pattern of colocalization may differs markedly in different animals.

1. B Cells

The first cellular type identified in the pancreatic islets was the B cell (= β-cell in an alternative scheme for naming pancreatic cellular types) that stains with aldehyde fuchsin (AF+) and pseudoisocyanin (PIC+). The latter staining procedure applied following an oxidation step has been claimed to be specific for insulin granules, but it stains other intracellular structures in non-pancreatic tissues that do not contain insulin (for example, some neurosecretory granules). Immunocytochemical techniques have verified that insulin is produced and stored in the B cell as granules of about 300 nm in diameter.

2. A Cells

Cells of the pancreatic islets that are acidophilic and argyrophilic (affinity for silver- staining techniques) are called A cells (= α or α_2 cells). They do not stain with AF or PIC procedures. The A cell is the source of the second major pancreatic hormone, glucagon, which is shown by immunocytochemistry to be stored in secretory granules of about 235 nm diameter. In some species, the secretory granules of A cells may contain other peptides in addition to glucagon. The round secretory granules in the cytoplasm of the A cells are morphologically distinct from the angular insulin granules of the B cells, making these cells easy to distinguish with the aid of the transmission electron microscope.

3. PP Cells

PP has been localized by immunocytochemical techniques in 125-nm granules of cells found at the periphery of the endocrine islets as well as in cells scattered throughout the exocrine pancreas. These PP cells are distinct cytologically and immunologically from other cell types. The distribution of PP-secreting cells (= F cells) on the periphery of the islets varies greatly among different species, and it is difficult to generalize for all mammals.

4. D Cells

Immunoreactive SST is localized in the cytoplasmic granules of D cells (also called α_1 cells or d cells). Although D cells contain cytoplasmic granules similar in size to those of A cells, they are cytochemically distinguished from A cells by applying the toluidine blue staining procedure and from both A cells and B cells by their staining with PIC following methylation but not following oxidation. Granule size (230 nm) is very similar to that of A cells.

5. Amphophilic Cells

Amphophils have been demonstrated in the islets of many mammalian species as well as in sharks, teleosts, amphibians, and reptiles, but no conclusions have been generated regarding their functional roles. They may represent either ungranulated and/or differentiating or granule-depleted degenerating forms of any of the four cellular types described above.

References

- Norris DO & James AC (2013). Vertebrate Endocrinology (5th edition). Academic Press, USA. http://dx.doi.org/10.1016/B978-0-12-394815-1.00001-X.