The pancreas is an organ that actually consists of two glands: one exocrine and one endocrine gland. The glandular epithelium is a specialized epithelial tissue which produces and excretes substances to control our bodily functions. The exocrine gland secretes its fluids via ducts (into the intestinal lumen), while the endocrine gland secretes its substances via the extracellular space into the vascular- and the lymphatic system. The two parts of the pancreas differ both in structure and function. The following article should give you an overview of the histological features of the two glandular parts.

A Macroscopic View of the Pancreas

The lobe-like structure of the pancreas can already be seen by the bare eye. This is due to the capsula fibrosa that is forming connective tissue septa containing vessels and nerves that divide the parenchyma.

The Exocrine Pancreas

**Task:** The exocrine pancreas produces 1.5 – 2 liters of fluid which contains enzymes that help to break down carbohydrates and fats, proteolytic proenzymes (preliminary stages of enzymes) and bicarbonate.

**Enzymes produced by the exocrine pancreas:**

- Trypsinogen and chymotrypsinogen
- Procarboxypeptidase
- Proelastase
- Lipase
- Cholesterinesterase enzyme
- α-amylase
- Ribonuclease and deoxyribonuclease

**Enzymes for:**

<table>
<thead>
<tr>
<th>Carbohydrates</th>
<th>Fats</th>
<th>Proteins</th>
<th>Nucleotides</th>
<th>Ions and water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase</td>
<td></td>
<td></td>
<td></td>
<td>HCO₃⁻</td>
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<tr>
<td>• Lipase</td>
<td>• Lipase</td>
<td>• Trypsinogen</td>
<td>• Ribonuclease</td>
<td></td>
</tr>
<tr>
<td>• Pro-phospholipase A2</td>
<td>• Cholesterol esterase</td>
<td>• Chymotrypsinogen</td>
<td>• Deoxyribonuclease</td>
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</tr>
<tr>
<td>• Pro-elastase</td>
<td>• Pro-carboxypeptidase</td>
<td>• Pro-elastase</td>
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</table>

Bicarbonate is responsible for the alkaline pH-value of the pancreatic fluid, which is about 8 and therefore able to neutralize the acid content of the stomach in the duodenum. The pancreatic fluid is secreted via the ductus pancreaticus into the lumen of the duodenum. The duodenal cuticular layer and the Brunner’s glands secrete the enzyme enterokinase that transforms trypsinogen into trypsin. Trypsin transforms all the other pancreatic proenzymes into their active form.

99 % of the pancreas consists of exocrine glandular tissue, a serous, merocrine, composed acinar gland. What does that mean?

- The exocrine pancreas secretes a serous fluid: These fluids contain proteins and are thin in their viscosity.
- The way of secreting is **merocrine**: the secretion happens via exocytosis — that keeps the cell intact.
- It is a **composed gland**: the excretory ducts branch out.
- It is an **acinar gland**: the acini — where secretion happens — are spherical.
with a small lumen.

As mentioned above the lobe-like structure of the pancreas can be seen macroscopically. These **lobes** consist of hundreds of serous acini. Every acinus contains about 70 pyramid-shaped gland cells located on a basal lamina with big, round and basal-lying nuclei.

The basal part of the exocrine cells shows a strong basophilic part which is the rough endoplasmic reticulum. The apical part of these cells is strong acidophilic and contains the proenzymes that are wrapped in **zymogenic granules**. These are emitted via the apical cell-pole, which is mounted with microvilli for this reason.

**Intercalated ducts** — cells of cubic to flat epithelium — are connecting several acini with the excretory ducts by sliding into the acini and thus creating the microscopic image of **centroacinar** cells. There are no striated ducts as you can find them in the excretory ducts of the parotid gland.

**Excretory ducts** can be found inside every lobule (=intralobular) and be recognized on their simple cylindrical epithelium. They connect inside the septa to extra tubular excretory ducts with a stratified epithelium containing goblet cells and **enterochromaffin** cells.

The ducts inside the septa unite again to bigger ducts before leading to the one big excretory duct of the pancreas — the **pancreatic duct**. Together with the common bile duct, it leads to the major duodenal papilla, a small mucosal elevation in the duodenum. In the duodenal lumen, the pancreatic fluid and its enzymes are activated.

**The cystic fibrosis transmembrane conductance regulator CFTR**

On the basolateral side of the acinar cells potassium, sodium and chloride are transported into the cells by using ATP. A transporter for chloride on the apical side — or **cystic fibrosis transmembrane conductance regulator** — is pumping the chloride from the stroma inside the cellular lumen which causes sodium and water to follow. The intercalated ducts take the chloride in exchange for bicarbonate.

![Cystic fibrosis transmembrane regulator](Image by Lecturio)

Patients with cystic fibrosis (mucoviscidosis) have a mutated gene that codes CFTR. Less
chloride and water are transported into the glandular lumen, the secretion becomes viscous, hence is backed up and leads to inflammation. In the intercalated ducts, the lack of chloride leads to a lower exchange with bicarbonate which is essential to neutralize the thymus in the duodenal lumen and to activate the pancreatic enzymes. The consequences are digestive disorders that are typical for cystic fibrosis.

The Endocrine Pancreas

**Task:** There are several types of endocrine cells and each of them is producing a special hormone that particularly regulates the carbohydrate metabolism.

Inside the pancreatic lobules between the acini are the insular clusters of endocrine cells – also called islets of Langerhans. The pancreas of an adult contains about 1 million of these islets, especially in cauda and corpus pancreatis.

All these cell clusters together are building one functional unit. Every endocrine gland, also the islets of Langerhans – lose connection to the epithelium during the fetal period and thus are not emitting their secretion via excretory ducts. The secretion happens on the basal side first into the stroma and finally via the vascular- and lymphatic-system to the place where it is needed.

The endocrine pancreas — histochemical differentiation of cells

The endocrine pancreas consists of 4 different types of cells each producing different hormones:

- **Beta cells** producing insulin to lower the blood sugar
- **Alpha cells** producing glucagon to increase blood sugar level
- **Delta cells** (that can be found in the entire gastrointestinal tract) producing somatostatin, inhibiting secretory processes.
- **PP cells** producing pancreatic polypeptide – its function is not entirely clear yet
- Isolated serotonin-producing **EC-cells** can be found in the pancreas.
Beta cells are forming the largest part (70%) of the islets of Langerhans and they are more likely located in the islets’ center. Their hormone – the peptide hormone insulin – is stored in secretory-granules (β-granules) and released via exocytosis as soon as the glucose level in the extracellular space exceeds a particular value. Once released, the insulin ensures that more glucose transporters are integrated inside the cell membrane especially of muscle- and fat cells and thus more glucose is moved from the blood into the cells. The blood sugar level gets lower. Insulin deficiency leads to diabetes mellitus.

Alpha cells form about 20% of the endocrine pancreas and are mainly located in the islets’ periphery. They produce the hormone glucagon which causes the liver to convert on the one hand the stored glycogen and on the other hand amino acids into glucose. This mechanism allows a rapid increase of the blood sugar level.

The endocrine pancreas as it is seen under the microscope

The endocrine islets, that are distributed between the exocrine pancreatic tissue and have a spherical to ovoid or strung-out form. The thread-like arrangement of the epithelial cells and the dense meshwork of capillaries are apparent. The glandular cells are chromophobic, that means they can not be dyed very good, that is why they can be recognized by their light color when dyed with hematoxylin-eosin. Special dyes help to make the various types of cells visible because the secretory granules appear in different colors.

The endocrine pancreas — neural control

The endocrine pancreas has adrenergic and cholinergic synapses. Neurites of the sympathetic nerve stimulate the release of glucagon. The secretion of insulin is activated by the vagus nerve and inhibited by the sympathetic nervous system.

Hepatobiliary — Secretion Constituents

Biliary secretion contains:

- Three bile salts: Cholesterol, Lecithin, and Bilirubin
- Ions

Concentration (5—20 %) of these constituents occurs in the gallbladder.

Structure and Functions
Mucoviscidosis = cystic fibrosis

Mucoviscidosis is a hereditary disease that affects especially the pancreas, lungs and sweat glands. Mutations of the gene which codes the transmembrane protein **CFTR (Cystic Fibrosis Transmembrane Conductance Regulator)** protein cause this chronic disease.

CFTR is the apical transporter for chloride ions. Its missing induces disturbances in the exchange of electrolytes and liquids of the glandular cells. The produced secretion is not serous anymore but mucous, which causes the secretion to back up and thus leads to chronic inflammations. The parenchyma of the pancreas is replaced by fibrotic fibres and can not fulfill its task anymore. That causes symptoms like dyspepsia and failure to thrive. The lungs react with chronic bronchitis and the sweat glands excrete a higher amount of salt. This is why a simple examination of the sweat can serve as a diagnostic method just as well as a stool sample.
The acute pancreatitis

Acute pancreatitis is a life-threatening condition that can occur when the acini are damaged and release their enzymes. Already being activated, the enzymes cause massive damage and a “self-digestion” of the pancreatic parenchyma, up to necrotizing processes. If the enzymes enter the blood, other organs might be affected and in that consequence, it can lead to life-threatening shock symptoms. Severe cases are treated by intensive care medicine.

![Image: "Acute exudative pancreatitis in computed tomography with extensive liquid streets around the pancreas" by Hellerhoff. License: CC BY-SA 3.0]

Causes of acute pancreatitis may be:

- Obstruction of the bile ducts or the pancreatic duct by stones or tumorous processes
- Chronic alcohol abuse
- Viral infections, e.g. epidemic parotitis (mumps)
- Collagenosis, e.g. systemic lupus erythematosus

Diabetes mellitus

Diabetes mellitus literally translated as „honeyed flow“. The name refers to one symptom of this disease — in consequence of the high blood sugar level the amount of glucose in the urine increases which leads to polyuria.

**Diabetes mellitus type 1**

**Note:** The pancreas produces no more insulin!
The Beta-cells are destroyed because of an immune-mediated reaction that causes a **complete insulin deficiency**. Because of this, the body is not able to secrete any amount of insulin and thus life-long exogenous insulin must be administered subcutaneously or intravenously. The patients are also at increased risks of diabetic complications such as hypoglycemia and ketoacidosis as the exogenous insulin does not accurately mimic the body's physiological functions.

**Diabetes mellitus type 2**

*Note: the produced insulin has no effect!*

Diabetes type 2 arises due to an insulin resistance of receptors which results in a **relative insulin deficiency**. Genetic dispositions as well as changes in the metabolic system, e.g. Syndrome X, may be the trigger for this disease, but scientists still do researches for the actual causes of insulin resistance.

In former times diabetes type 2 was also called "diabetes of old people", which is not common anymore. As also very young people suffer nowadays more and more of adiposity and Syndrome X, diabetes type 2 occurs at all ages. It is possible to be almost cured with the right treatment. Especially weight loss, regular physical activity and a change of diet are showing good result.

To go deeper into this subject you can read another article about the pancreas.

**Review Questions**

The correct answers are below the references.

1. **Which statement about the exocrine pancreas is right?**

   A. The exocrine pancreas is a serous, tubuloalveolar gland.
   B. The cells are secreting the fluids together with a part of the plasmalemma (cell membrane) and the cytoplasm.
   C. The glandular cells have only one excretory duct, but several acini are leading to it.
   D. The typical microscopic appearance of the exocrine pancreas is a branch-like
system of excretory ducts with striated ducts and intercalated ducts.
E. The histological image shows centroacinar cells as parts of the intercalated ducts.

2. Which statement about the islets of Langerhans is wrong?

A. The islets of Langerhans consist of about 1 million cell-clusters that are spread like islands between the exocrine parts of the pancreas.
B. Beta-cells are producing the peptide hormone insulin, which decreases the blood sugar level.
C. Somatostatin can be found in the Delta-cells of the entire gastrointestinal tract and it is inhibiting the secretion of pancreatic fluid.
D. About 70% of the islets’ cells contain the peptide hormone insulin inside their β-granules.
E. Glucagon activates the synthesis of glycogen.

3. Which statement about diabetes mellitus is right?

A. Diabetes type 2 is characterized by absolute insulin deficiency.
B. Diabetes type 2 occurs only in old people.
C. Diabetes type 1 can be cured completely with the right treatment.
D. Diabetes mellitus means “honeyed flow” and refers to this name to polyuria as one symptom of the disease.
E. The insulin receptors are becoming resistant against insulin at diabetes type 1.

References


**Correct answers:** 1E, 2E, 3D

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