MD Program
UNIVERSITY OF TORONTO

Histology

The Liver, Gall Bladder, and Pancreas

eMODULE TUTORIAL

CLICK TO BEGIN

H15 Accessory Digestive Organs

All images are from Junqueira's Basic Histology, 14th ed., © 2016 by Mescher, denoted by "J", a recommended resource, unless otherwise noted.

Recommended online resources:

Western University Virtual Slide Box

University of Michigan Virtual Microscopy

University of Minnesota Histology Guide

University of Leeds Histology Guide

University of Illinois Cell and Tissue Biology

When you have learned the material presented here, you will be able to describe the:

- histological structure of the liver lobule
- flow of blood and bile through the liver lobule
- the different ways of describing the structure-function relationship of the liver
- the structure of the biliary tree and gallbladder
- histological structure of the pancreas, including both its exocrine and endocrine components

The liver is primarily in the upper right quadrant of the peritoneal cavity. It is the largest visceral organ at 1.5 kg in mass. It serves a number of purposes:

1. metabolic: the cells of the liver, ***hepatocytes***, regulate circulating levels of nutrients, other cells store fat-soluble vitamins and remove metabolic wastes and toxins from blood
2. hematological: it is a blood reservoir, receiving ~25% of cardiac output; it functions in the phagocytosis of circulating debris and the synthesis of plasma proteins
3. digestive: hepatocytes function in the synthesis and secretion of bile
   - bile contains water, ions, bilirubin & bile salts
   - bile salts **emulsify** fats, thereby increasing the surface area exposed to lipases in the digestive tract and facilitating their digestion.
   - bile is stored in the gall bladder and secreted, as needed, via a duct system into the duodenum

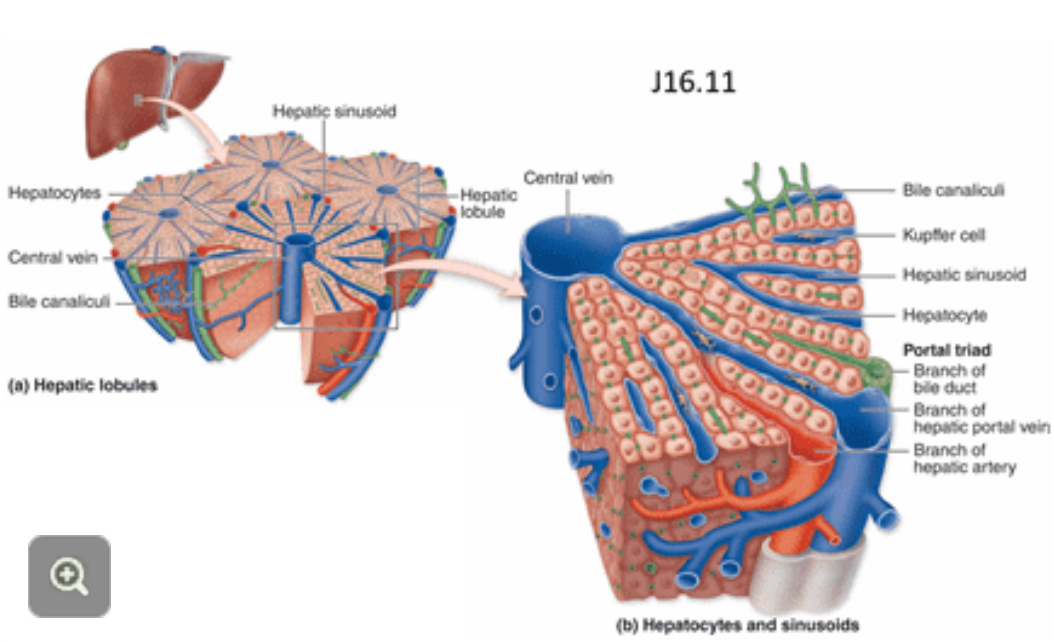
The Porta Hepatis

You will recall from the gross anatomy lab that at the porta hepatis, the liver receives blood from two sources, the **hepatic artery proper**, a branch of the celiac trunk which is surrounded by an extension of the celiac plexus of autonomic nerves, and the **hepatic portal vein**, which drains venous blood from the digestive tract to the liver. Also at the porta hepatis, bile drains from the liver toward the duodenum via the **hepatic duct system** and lymph nodes in the porta drain toward the celiac nodes.

You will further recall that the hepatic veins drain blood from the liver into the IVC.

Fine reticular fibre CT septa divide the liver into its basic functional units, called **liver lobules**.

Lobules are roughly hexagonal subunits with a **portal area** at each of its six corners. A portal area includes **a branch of each of the hepatic artery proper, hepatic portal vein and bile duct** . There are often nerves and a lymphatic associated with the portal area, as well. At its centre is a **central vein**, which is a tributary of a hepatic vein.



Hepatic sinusoids connect the **afferent blood** in the portal area with the **efferent blood** in the central vein.

The blood flow of the liver can therefore be described as consisting of **three components**:

1. **pre-hepatic** (inflow) via the **hepatic portal vein** (70-80%) and the **hepatic artery proper** (20-30%)
2. **intrahepatic**, including the **vascular components of the portal triad**, i.e. the branches of the hepatic portal vein and hepatic artery proper, the **sinusoids**, and the **central vein**
3. **post-hepatic** (outflow) via the **hepatic vein**, which drains into the **IVC**

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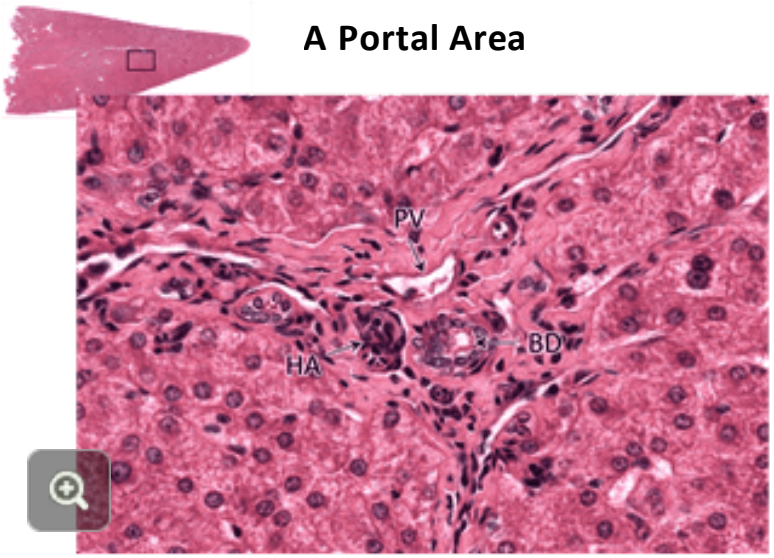
A Portal Area



PV – **Portal venule**, a branch of hepatic portal vein
BD – **Bile ductule**, simple cuboidal epithelium
HA – **Hepatic arteriole**, a branch of the hepatic artery proper

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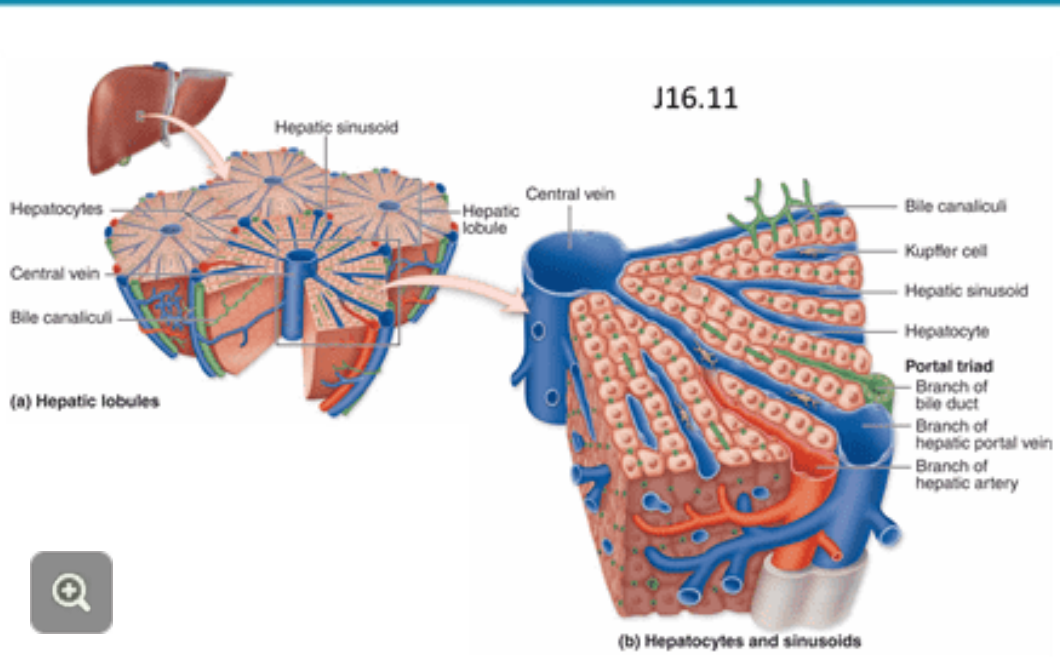
Hepatic **sinusoids** are lined by **endothelium with large fenestrae** and a **discontinuous basement membrane**. Between the hepatic sinusoids are anastomosing plates of **hepatocytes**, one to two cells thick, that radiate outward from the central vein. The microscopic **perisinusoidal space of Disse**, which separates the endothelial cells from the hepatocytes, contains extravasated plasma. **Microvilli** on the surface of the hepatocytes extend into the perisinusoidal space, increasing the cell surface area exposed to plasma.



Phagocytic **Kupffer cells (K)**, derived from the **monocyte-macrophage lineage**, patrol the hepatic sinusoids. They are antigen-presenting cells which engulf pathogens, toxins and cellular debris, such as aged RBCs.

Hepatic **stellate (Ito) cells** are located in the perisinusoidal space. They function to accumulate vitamin A and other **fat-soluble vitamins** in lipid droplets. In response to liver damage, they become **myofibroblasts** and produce components of the extracellular matrix.

As blood percolates through the hepatic sinusoids from the portal area to the central vein, it is processed by hepatocytes, Kupffer cells and stellate cells. From the central vein, it flows into the hepatic vein, then IVC.

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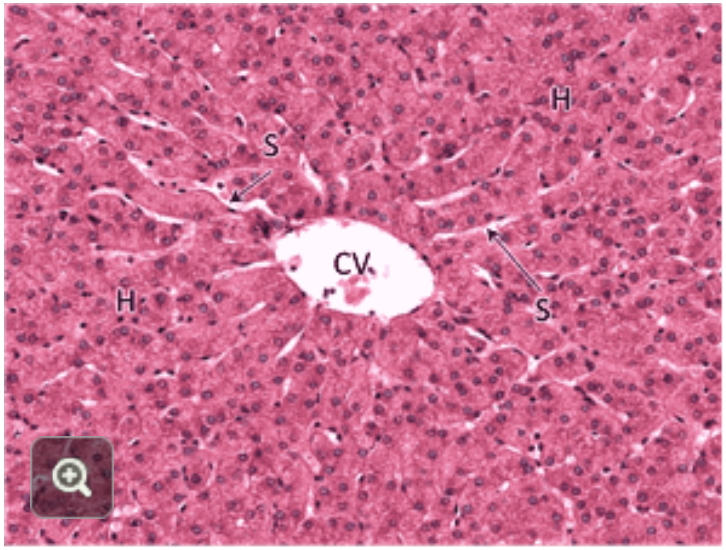

CV – **Central vein**, large venule found at center of liver lobule
H – **Hepatocytes**, radiate outward from the CV
S – **Sinusoids**, lined by endothelium, found between hepatocytes

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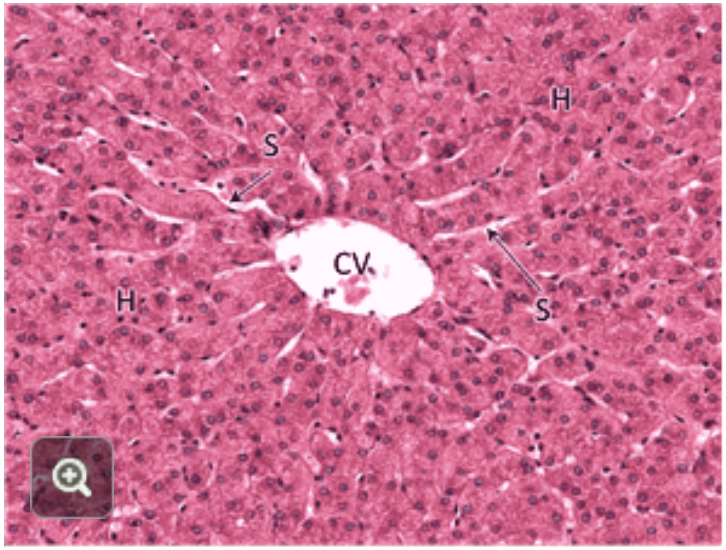

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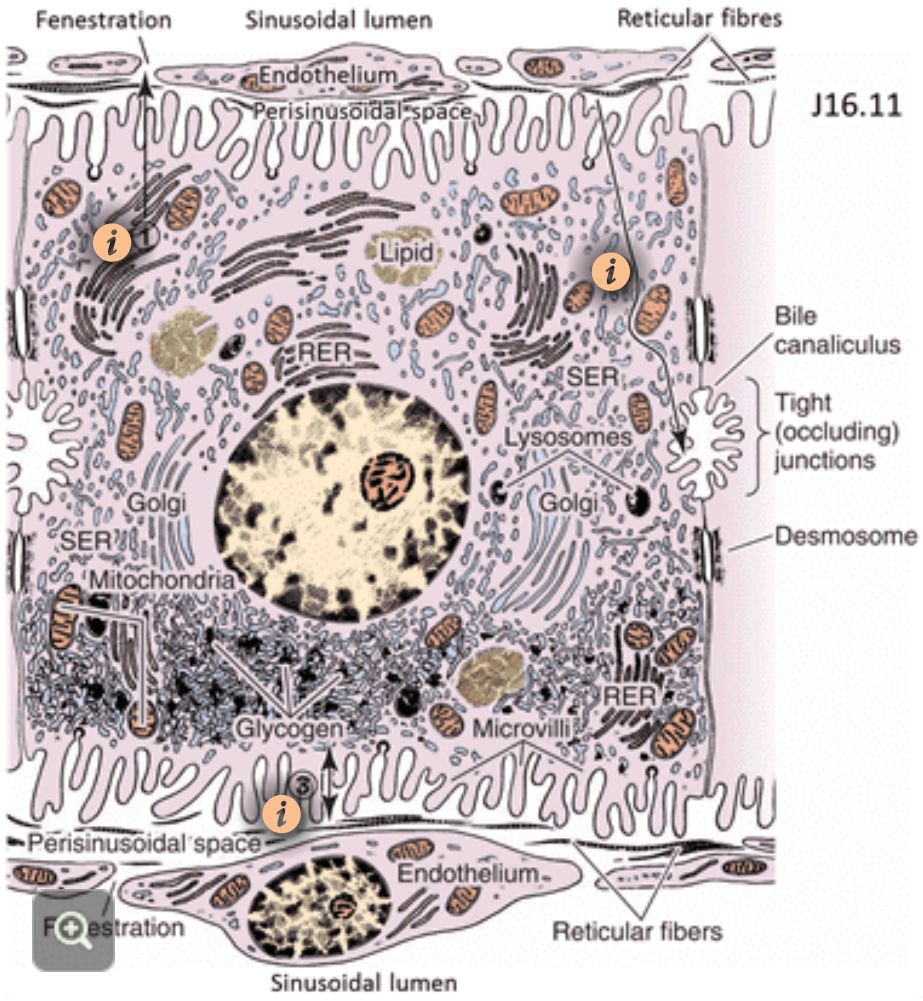
The **sinusoidal domains** of hepatocytes face the plasma-filled **perisinusoidal space** and function to **process blood and secrete plasma proteins**.

Cell junctions between the **contiguous surfaces** of hepatocytes **create a microenvironment**, the **bile canaliculus**, into which the hepatocytes **secrete bile** in an exocrine fashion.

Desmosomes and **junctional complexes** join adjacent hepatocytes. The **tight junctions** of the junctional complexes seal off the intercellular space creating the **bile canaliculus**. The surface area of the bile canaliculus is greatly increased by the presence of microvilli which extend into the canalicular lumen. Bile canaliculi form an **extensive anastomosing network** between the plates of hepatocytes **into which bile is secreted**, and along which bile flows toward the **bile ductules** of the porta hepatis.

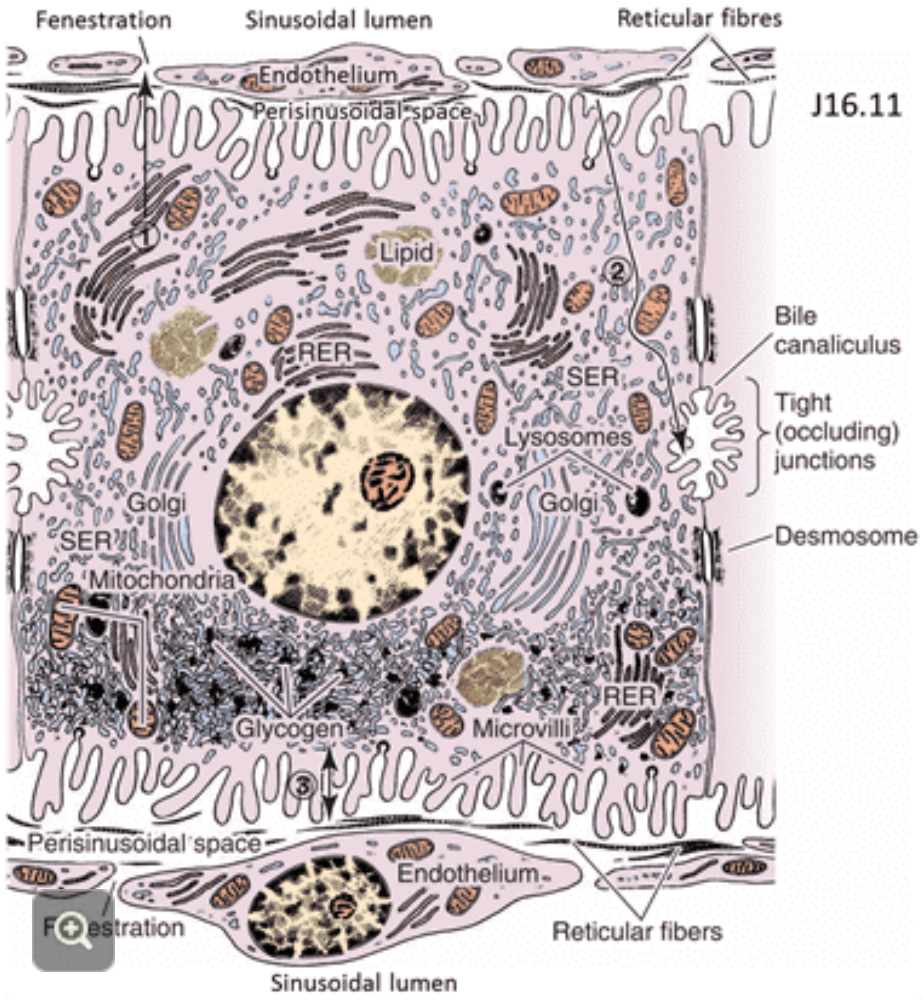
Thus bile flows in the direction opposite to that of blood; i.e. while blood flows centripetally, bile flows centrifugally.



Hepatocytes continuously produce and secrete **bile**. Bile contains bile acids and **bile salts**, electrolytes, phospholipids, cholesterol, fatty acids, and **bilirubin**.

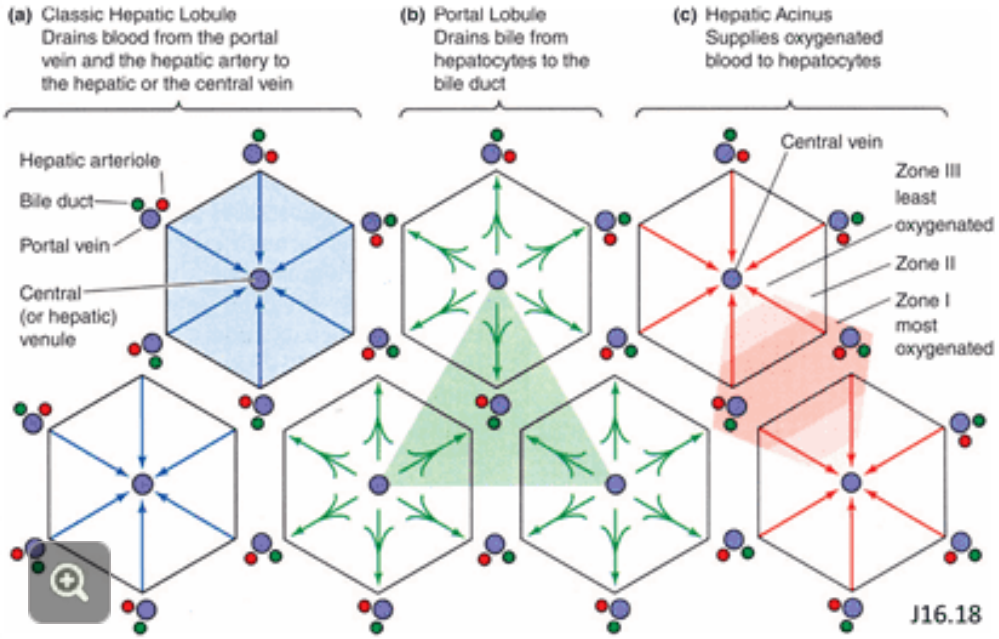
Bile salts emulsify lipids in the duodenum, thus facilitating their digestion by **lipases** secreted by the pancreas.

Senescent RBCs are phagocytosed largely by **splenic macrophages**, although some of this function is the responsibility of hepatic **Kupffer cells**. **Bilirubin** is a pigmented breakdown product of the heme thereby released. It is **carried in blood bound to albumen**, taken up by hepatocytes and **converted, in the SER, to a water-soluble form that is secreted into bile**.



Part (a) of the schematic on the right shows that the **classic hepatic lobule** centres on the **processing of blood** as it flows from the portal areas to the central vein. This emphasizes the **endocrine functions** of the liver, such as the production and release of plasma proteins into blood.

Part (b) illustrates the concept of a **portal lobule**, which emphasizes the **exocrine function** of the liver in the production and secretion of bile. In this schematic, the **bile ductule is at the centre** of a triangularly-shaped unit of liver tissue that drains bile from three adjacent classic hepatic lobules.



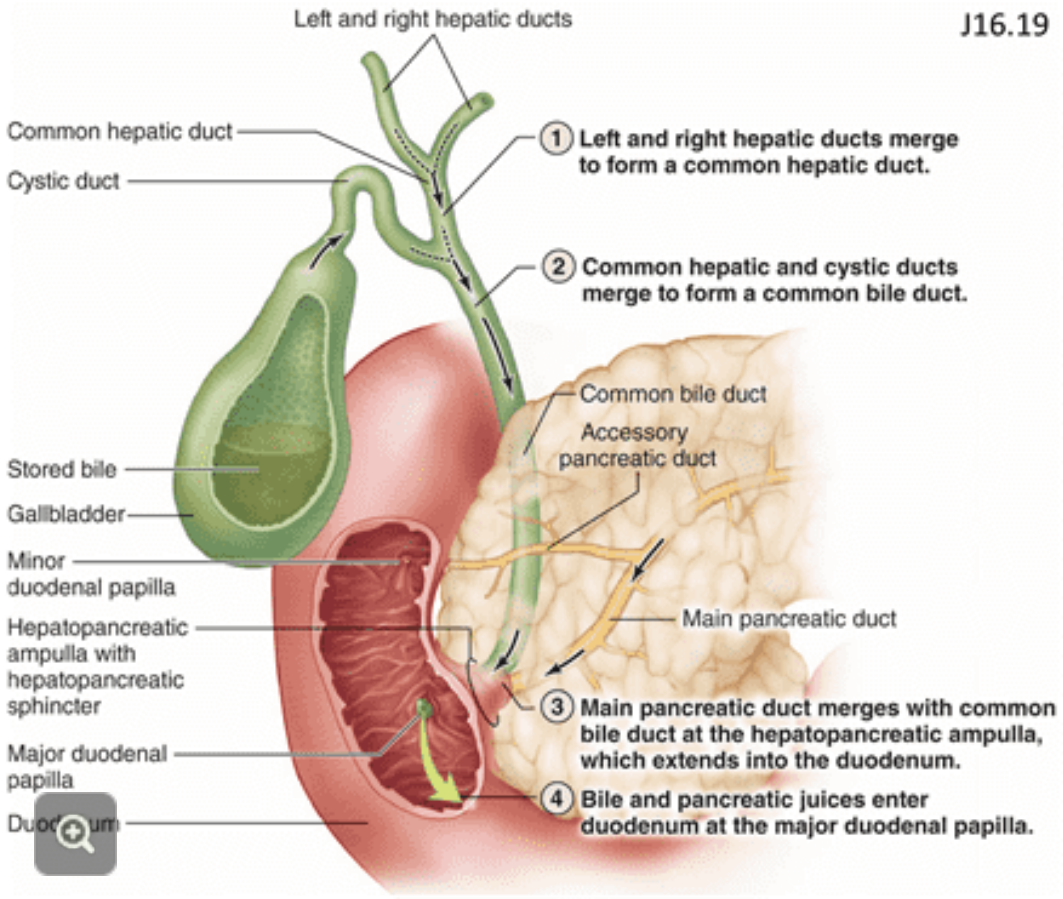
The **hepatic acinus** (c) emphasizes the **gradient in oxygen and nutrient content** of blood as it flows from the portal areas toward the central vein. The microenvironment **zone I**, closest to the portal triad, has the **highest oxygen and nutrient content**, while that of **zone III**, closest to the central vein, has the **lowest oxygen and nutrient content**. The microenvironment of Zone II is intermediate. Because of this gradient, hepatocytes in the different zones adapt their function to their microenvironment. The hepatocytes of zone I are better positioned to carry out oxidative processes, such as proteins synthesis, while those of zone III carry out glycolysis, lipid formation, and drug biotransformation. **Many pathologic changes in the liver respect these gradients; fatty accumulation and ischemic necrosis occurs first in zone III**.

Bile **canaliculi** empty into bile **canals**, which converge to form **bile ductules** in the portal areas. These coalesce to form **bile ducts**, which merge, ultimately forming the **right and left hepatic ducts**. These unite to form the **common hepatic duct** (1).

The **common hepatic duct** merges with the **cystic duct** to form the **common bile duct** (2).

At the second part of the duodenum, the common bile duct **unites with the main pancreatic duct** to form the **hepatopancreatic ampulla** (3), which opens into the lumen of the duodenum at the **major duodenal papilla** (4).

These larger ducts are lined by a **simple columnar epithelium** with a thin lamina propria and serosa. What is, in general, a thin **muscularis**, thickens as it approaches the wall of the duodenum to form the **hepato-pancreatic sphincter at the papilla**, which regulates bile flow into the duodenum.



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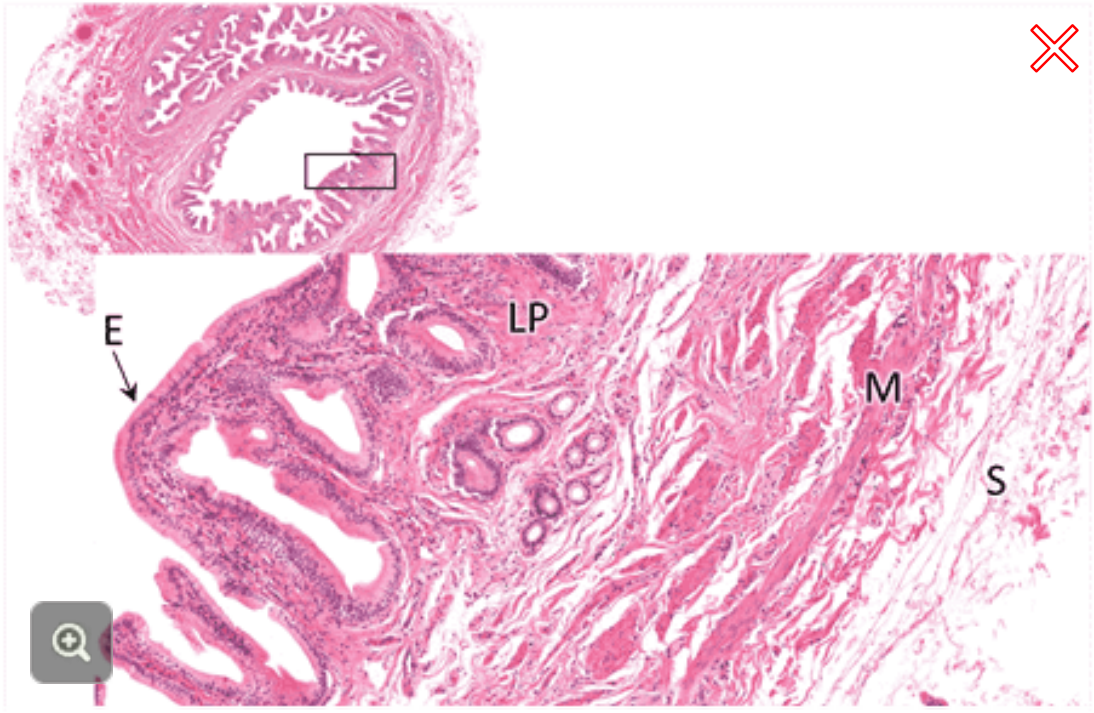
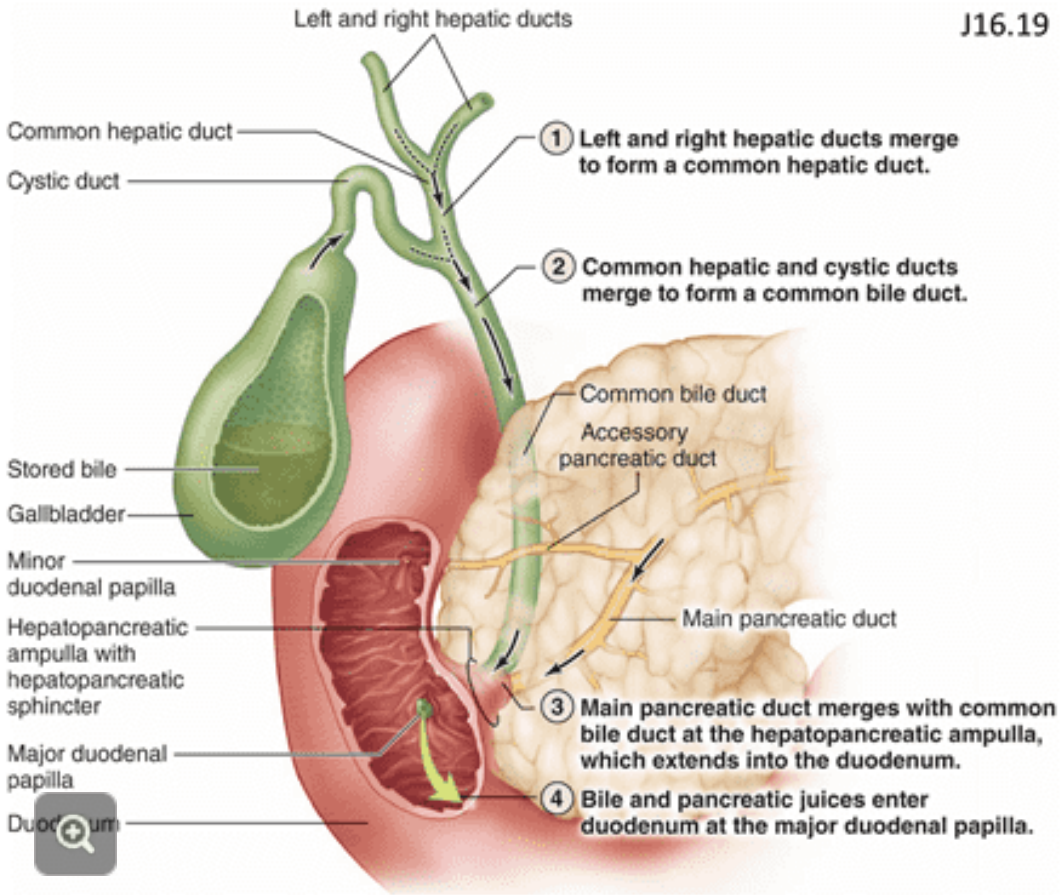


E – **Epithelium** – simple columnar epithelium with microvilli
LP – **Lamina Propria** – dense irregular CT, supports epithelium
M – **Muscularis** – thin, thickens as it approaches duodenum
S – **Serosa** – loose CT

While bile is continuously produced by the liver, it is not continuously delivered to the duodenum, but is stored in the gallbladder until needed. The gallbladder can store 30-50 mL of bile, which its mucosa **concentrates it through the absorption of Na^+ and water**.

The mucosa includes a columnar epithelium joined by **tight junctions** and with numerous **microvilli**, which reflects its absorptive function. The **smooth muscle** fibres of the muscularis run in all directions. The gallbladder is enclosed in an adventitia where it is in contact with the liver, and by a serosa where it faces the right subhepatic space.

With the arrival of lipid-containing chyme from the stomach, **enteroendocrine cells of the small intestine release cholecystokinin (CCK)**. CCK stimulates contraction of the muscularis in the wall of the gall bladder, and relaxation of the smooth muscle of the hepatopancreatic sphincter.



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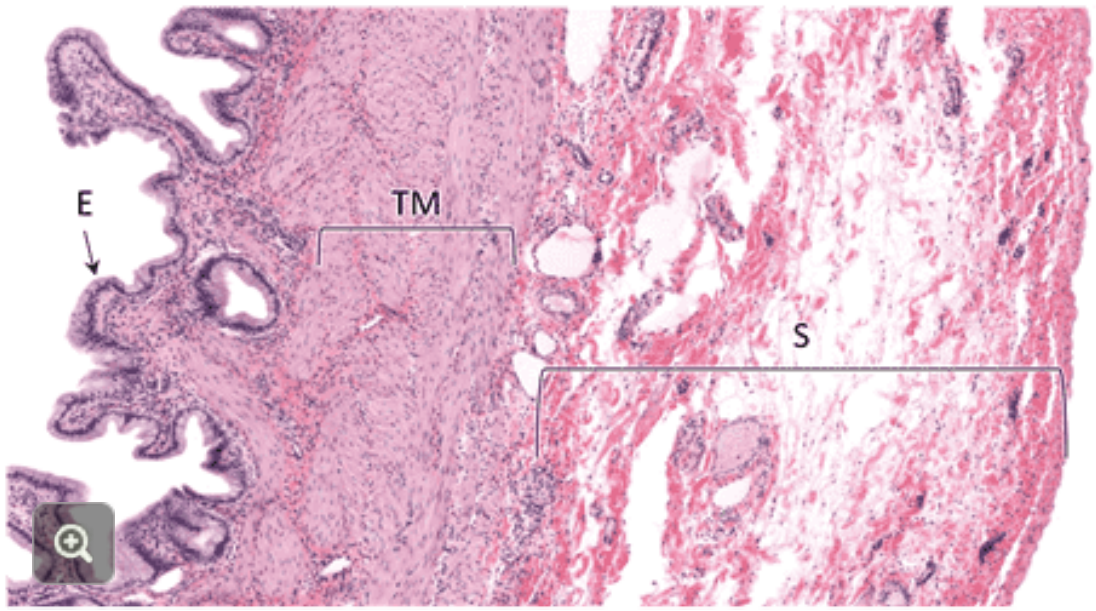


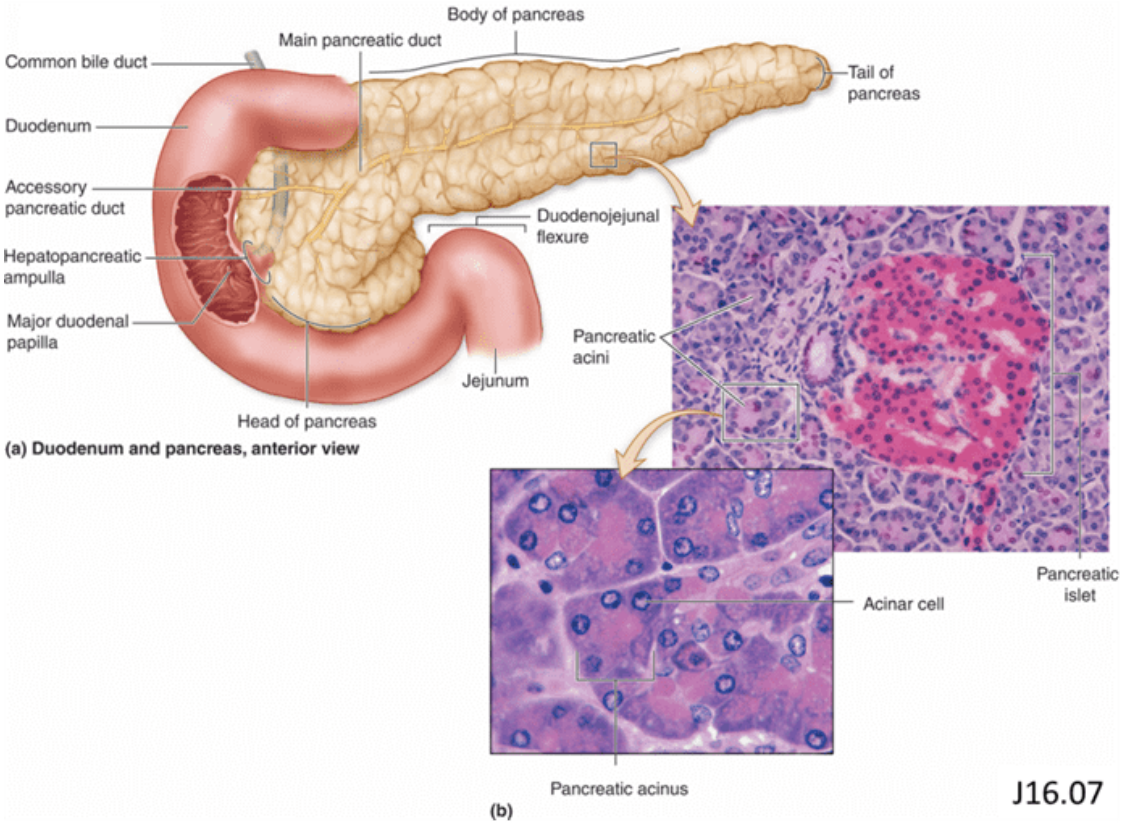
E – Epithelium – simple columnar epithelium with microvilli
TM – Tunica Muscularis – smooth muscle fibres running in all directions
S – Serosa – where the gallbladder is not attached to the liver, composed of mesothelium supported by loose CT

The pancreas is a **mixed endocrine-exocrine organ** located in the curve of the duodenum. It produces **digestive enzymes**, which it delivers to the lumen of the duodenum, and **hormones**, which enter blood.

Its thin CT capsule extends septa into the parenchyma of the organ to subdivide it into **lobules**. Within the lobules, the endocrine cells form **islets**, and exocrine cells form **acini**.

The acinar cells surround a small lumen into which they secrete their product, **inactive digestive enzymes**, including proteases, α-amylase, lipases and nucleases.

Each acinus is drained by an **intercalated duct**, the cells of which secrete a large volume of fluid containing **bicarbonate ions, HCO_3^-**. Intercalated ducts merge to form **intralobular ducts**, which in turn coalesce to form **interlobular ducts**. These empty into the **main pancreatic duct**, which opens into the **duodenal ampulla**.



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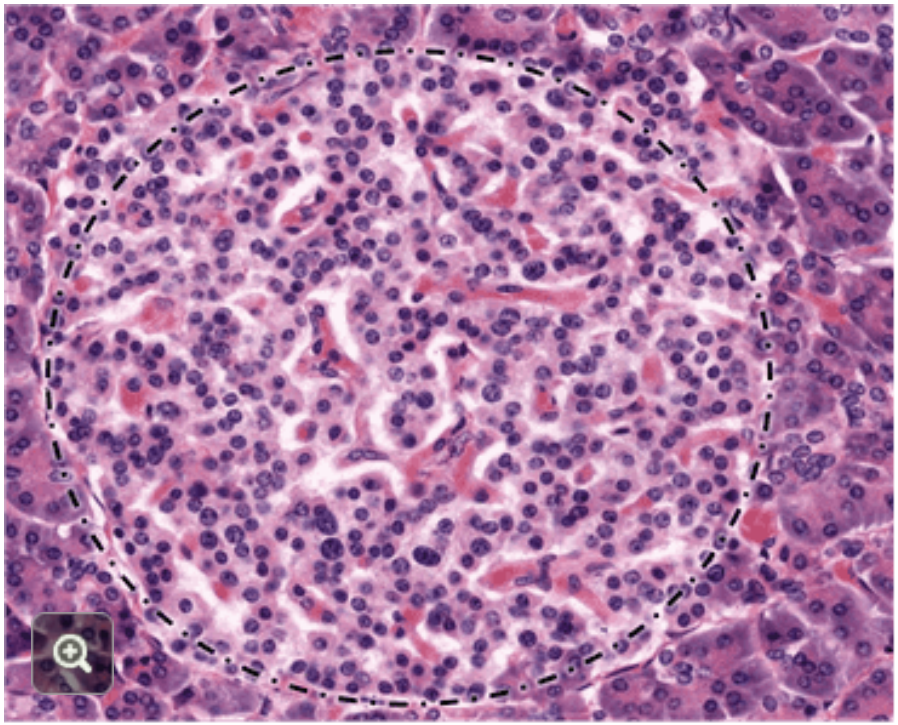
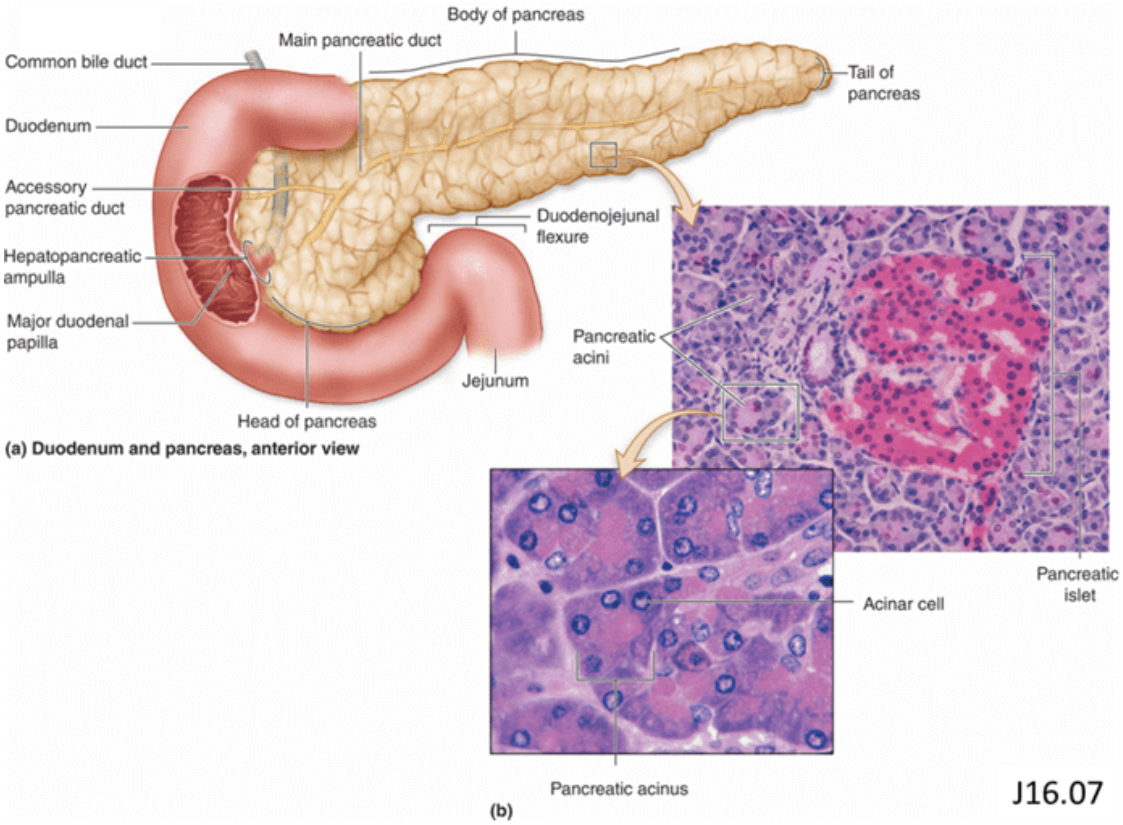


The islands of endocrine cells, or **Islets of Langerhans** are lighter in staining compared to the surrounding endocrine cells.

The arrival of chyme in the small intestine stimulates the release of **cholecystokinin (CCK) and secretin** from its enteroendocrine cells. **CCK** stimulates the release of **pancreatic proenzymes** from the acinar cells and **secretin** promotes the release of **alkaline fluid** from the intercalated ducts. **Parasympathetic input** promotes the secretion of **both** cell types. The pancreas produces **1.5 L** of alkaline pancreatic juice per day.

In the small intestine, alkaline pancreatic juice mixes with acidic chyme from the stomach. The resulting mixture is at the **appropriate pH for activation of pancreatic enzymes to occur**.



1. What does the perisinusoidal space of Disse contain?

- [ ] blood
- [ ] plasma
- [ ] bile
- [ ] lymph

SUBMIT

Which of the following are, or may be, located in the portal area?
Choose all that apply.

- [ ] a branch of the hepatic portal vein
- [ ] a lymphatic vessel
- [ ] nerve fibres
- [ ] a branch of the hepatic artery proper
- [ ] a tributary of the hepatic vein
- [ ] a bile ductule

SUBMIT

Which of the following promote the release of bicarbonate-rich fluid from the intercalated ducts of the pancreas? Choose all that apply.

- [ ] secretin
- [ ] cholecystokinin
- [ ] parasympathetic input
- [ ] sympathetic input

SUBMIT

H15 Question 4

Identify cell type A.

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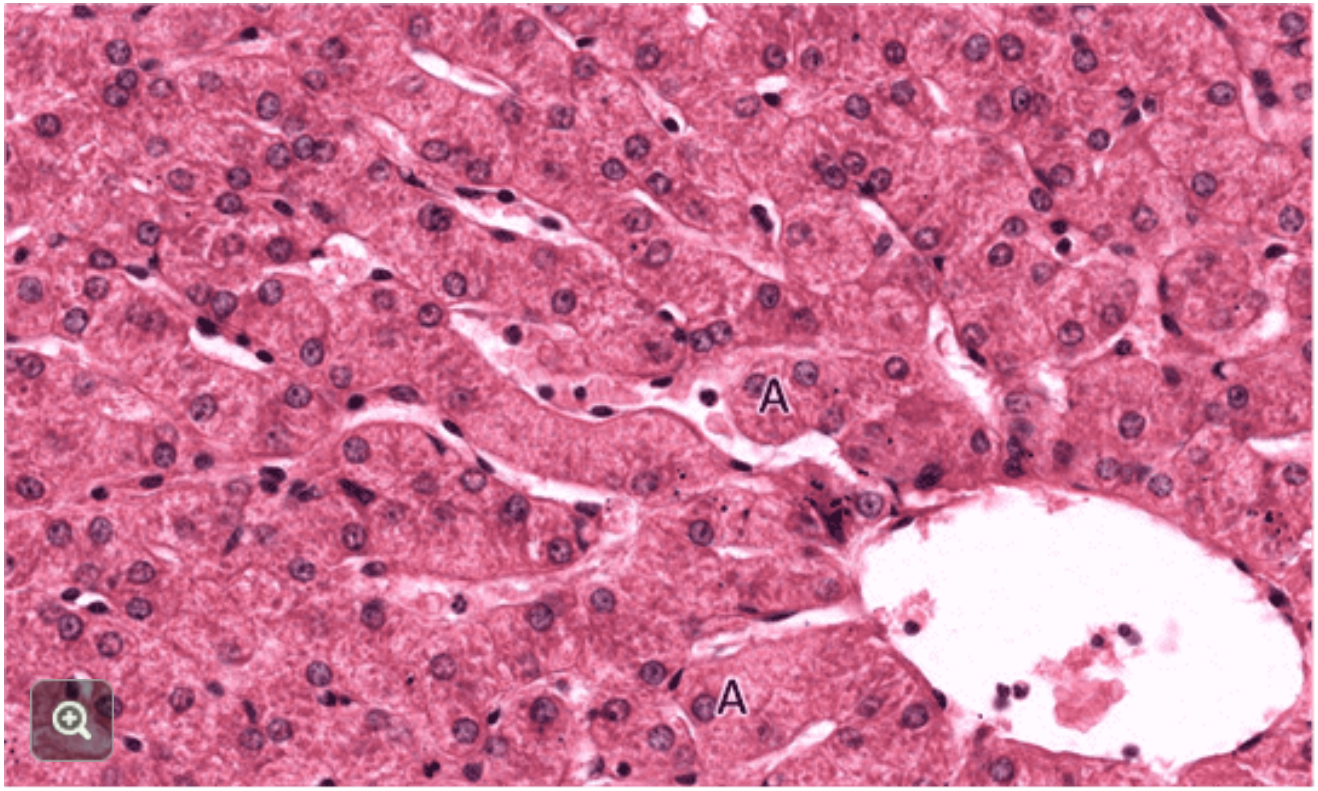

SUBMIT

H15 Question 5

Identify B.

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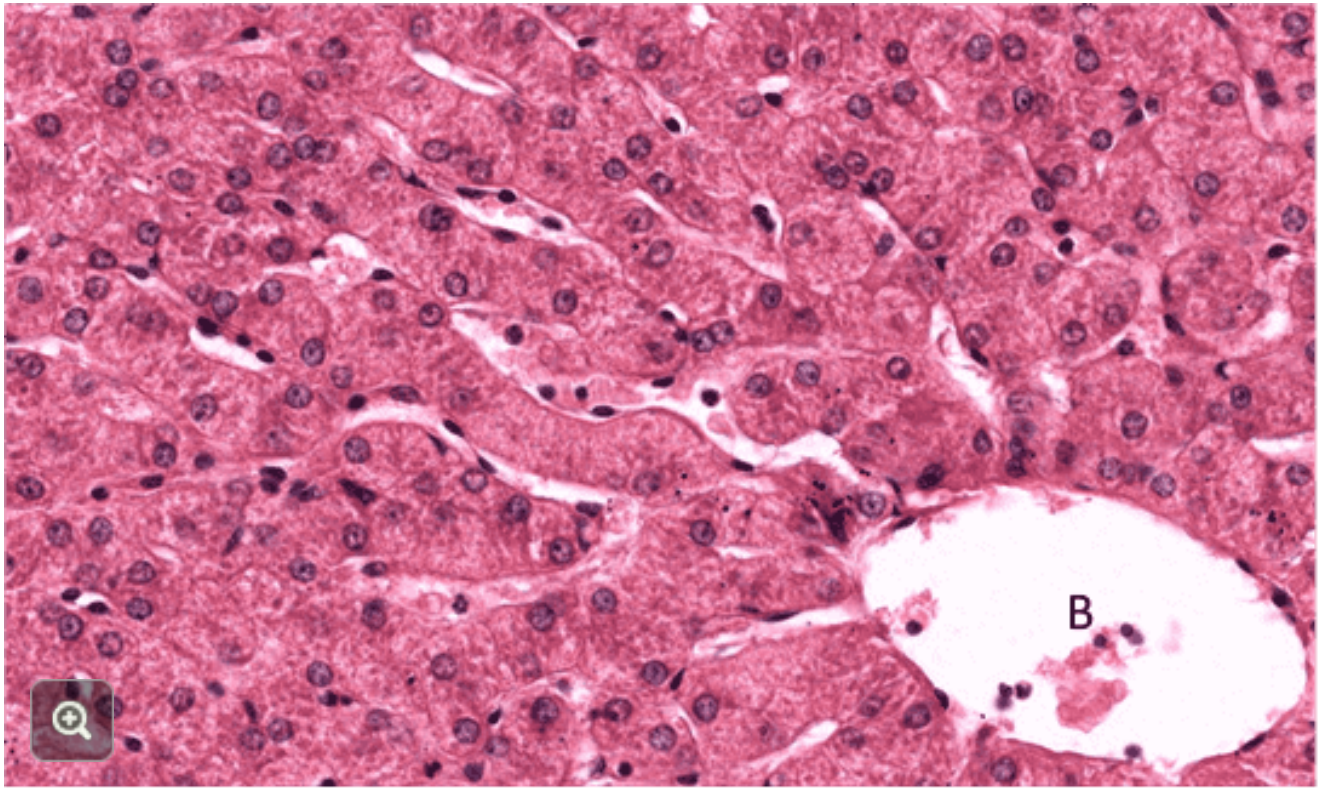

SUBMIT

Identify space C.

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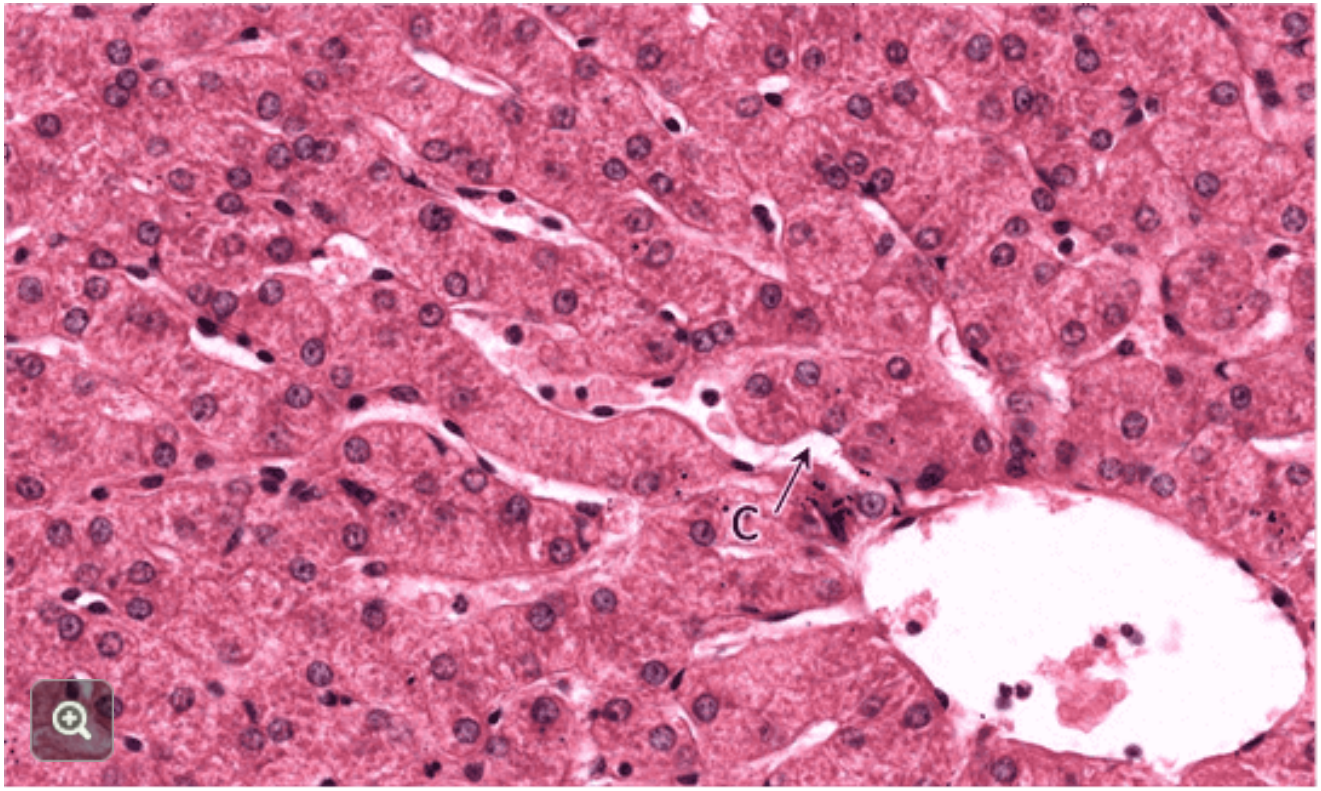

SUBMIT

H15 Question 7

Identify cell type D. Be specific.

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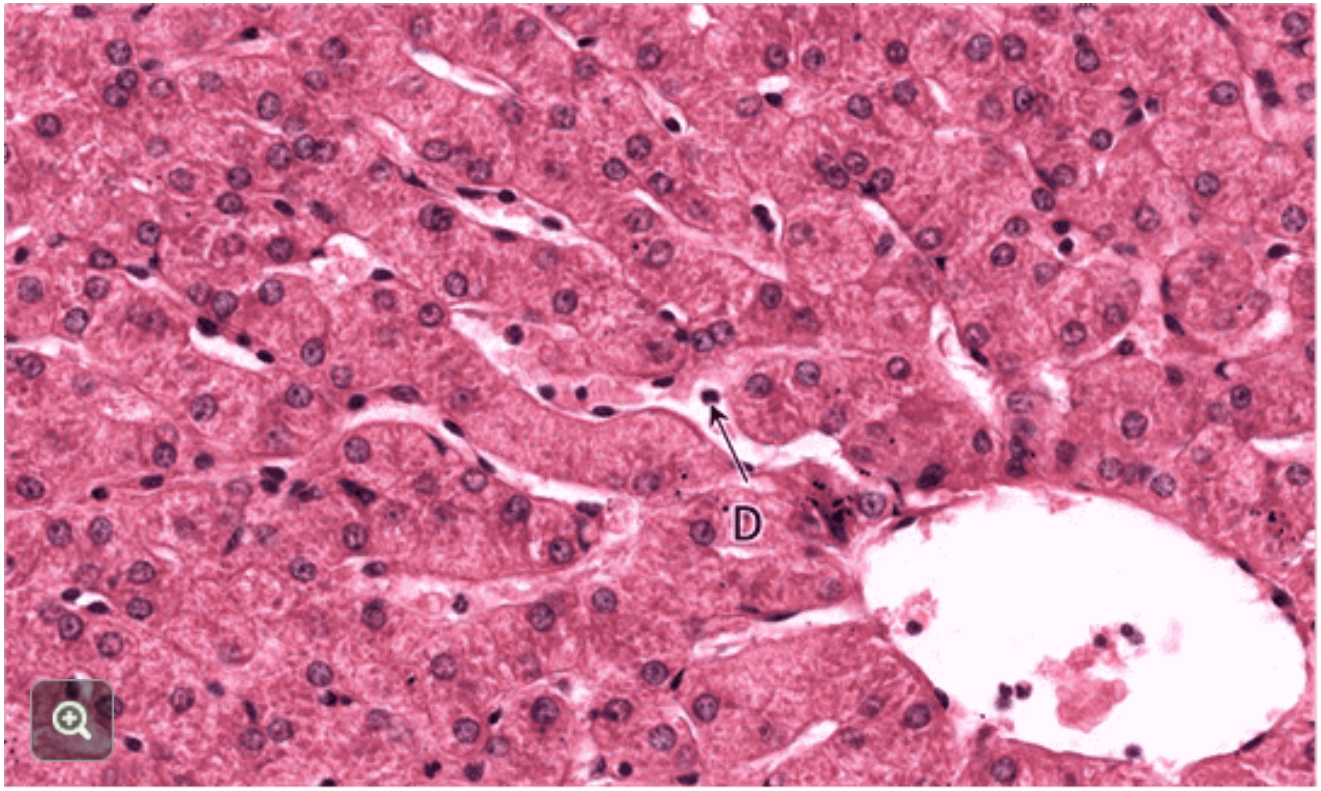

SUBMIT

Identify A.

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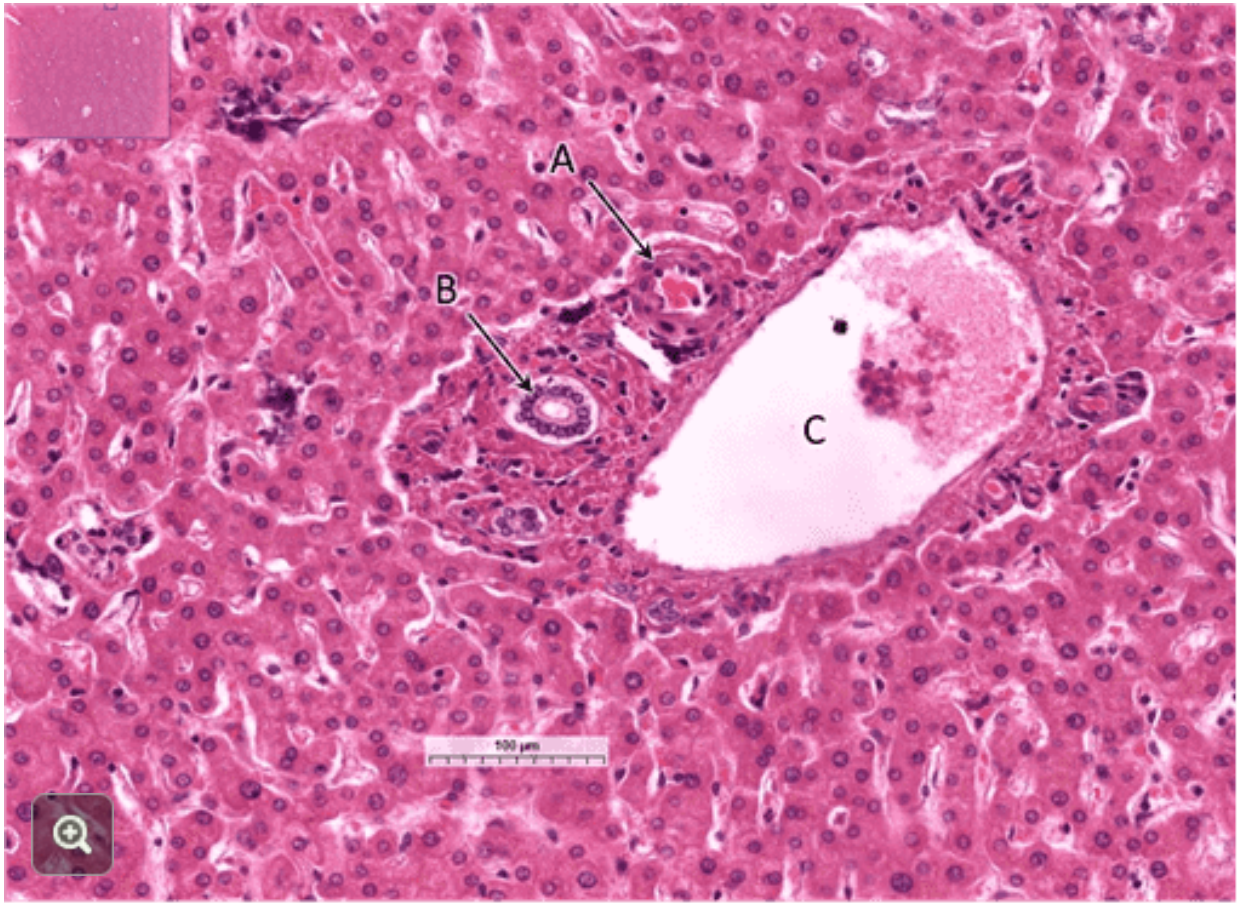

SUBMIT

H15 Question 9

Identify B.

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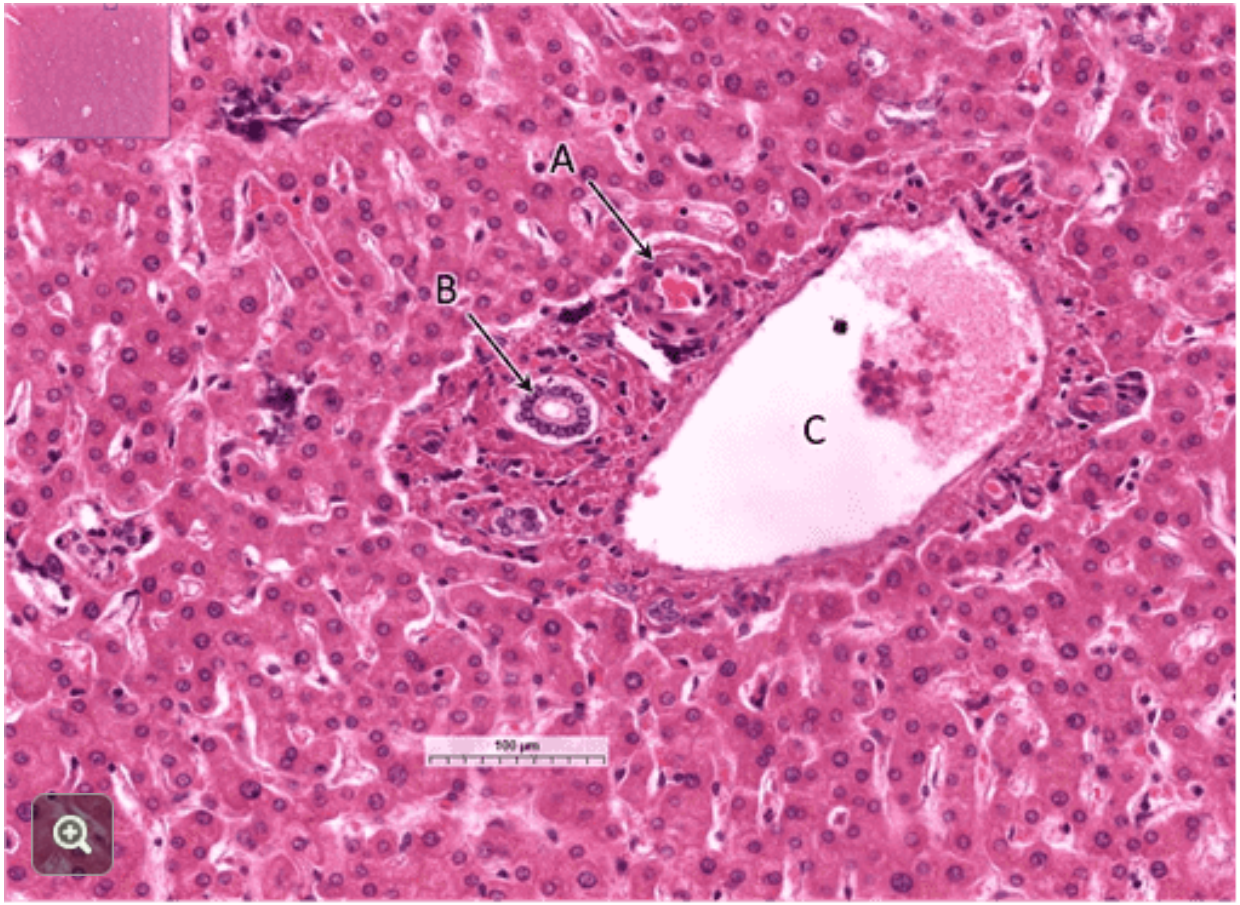

SUBMIT

Identify C.

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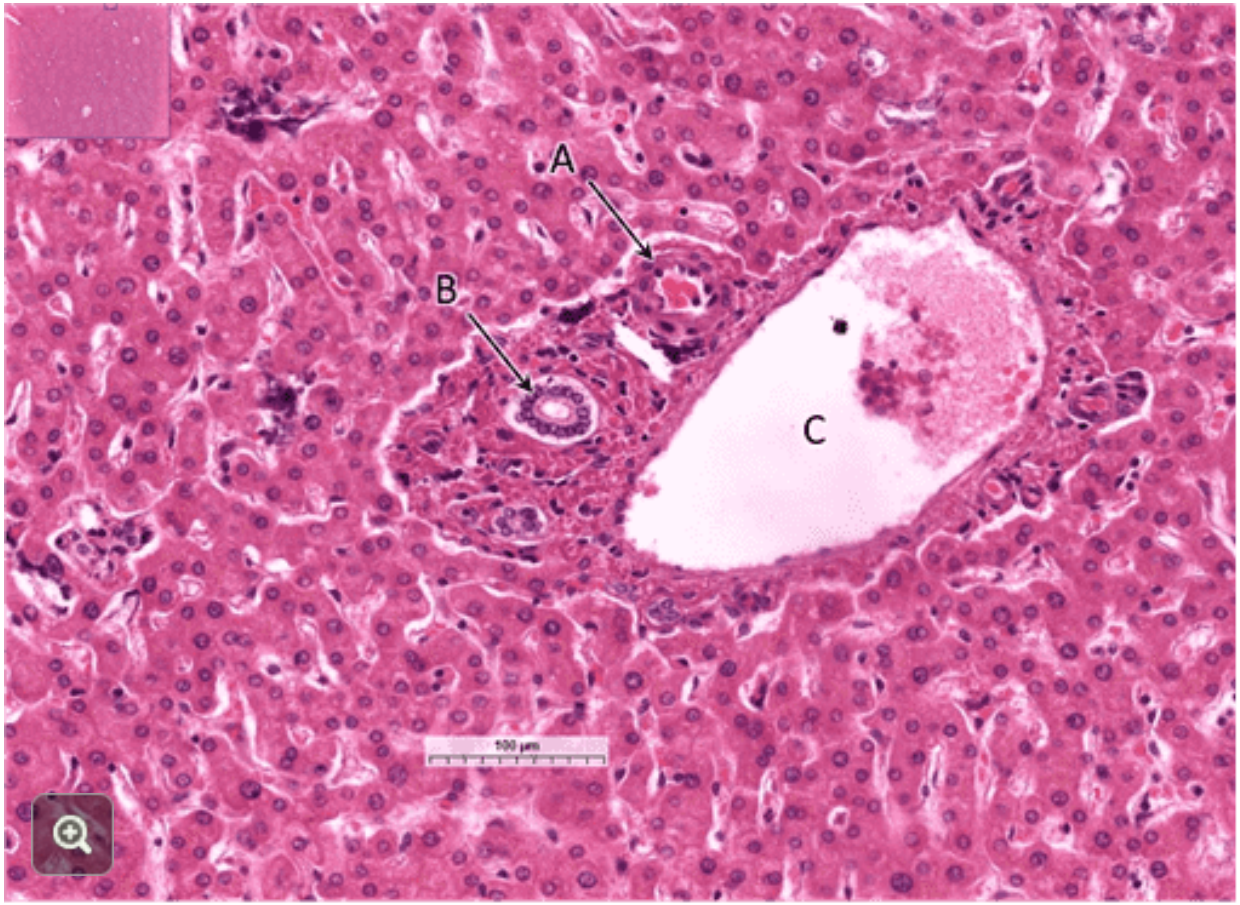

SUBMIT

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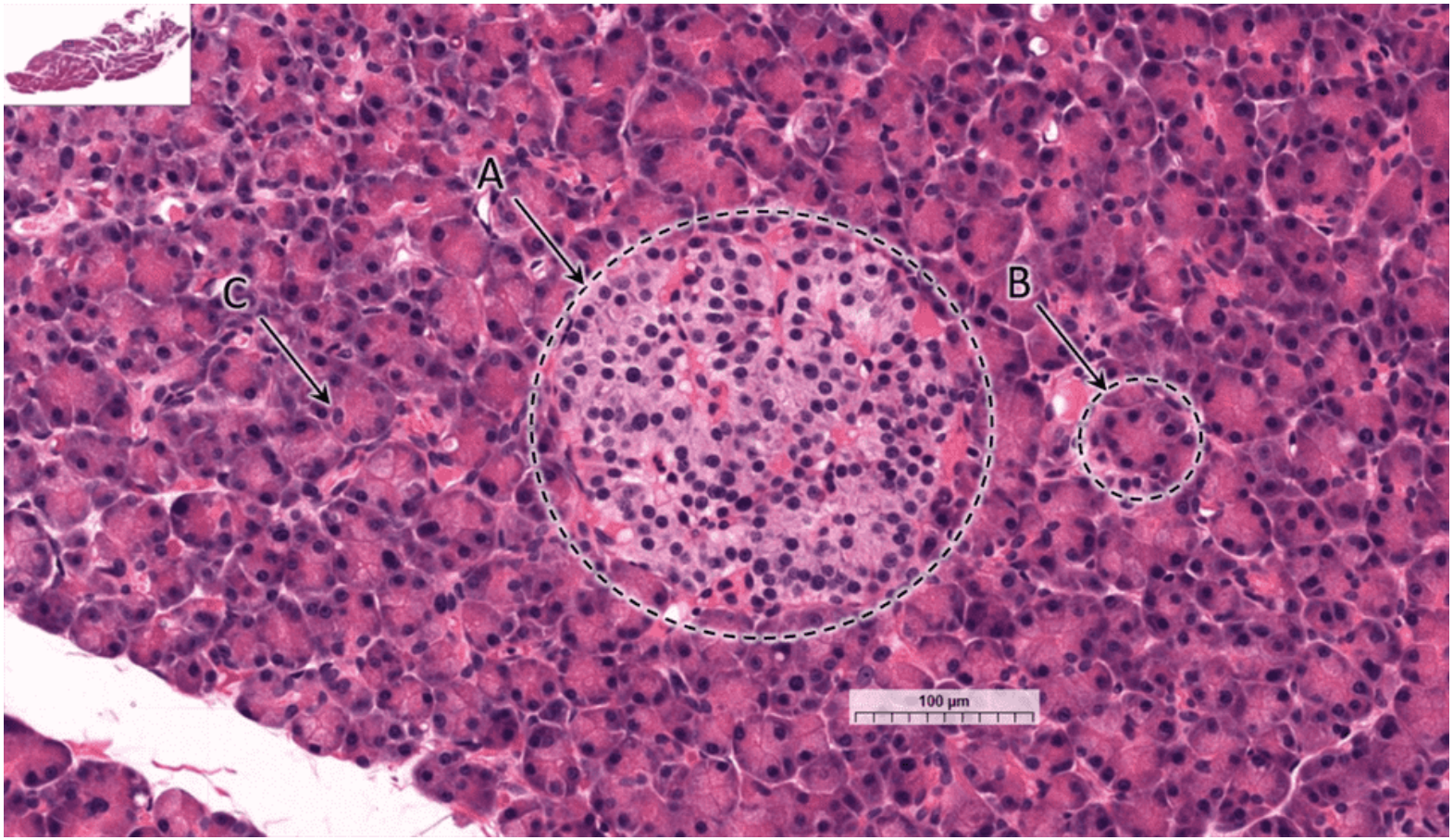

SUBMIT

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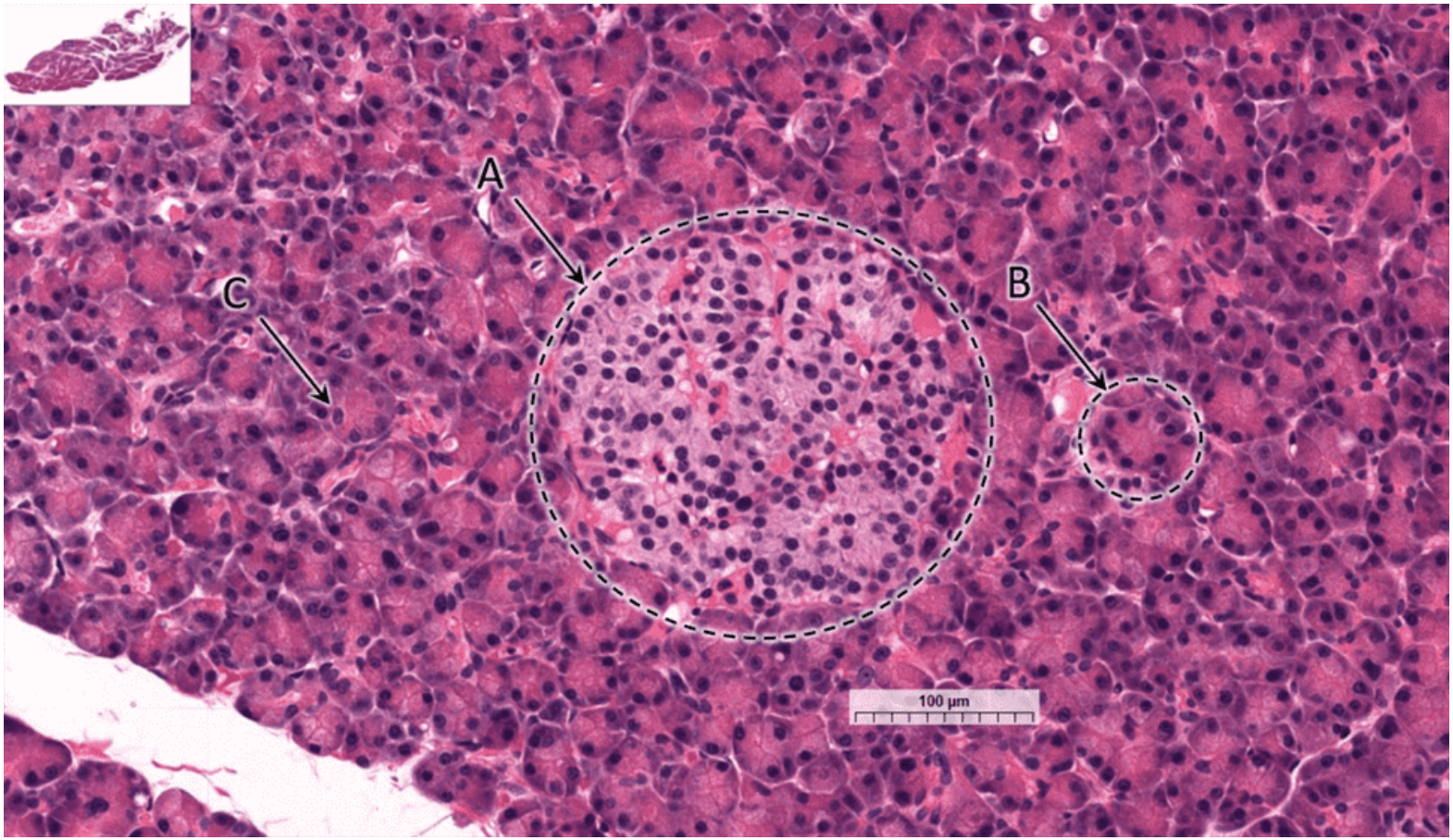
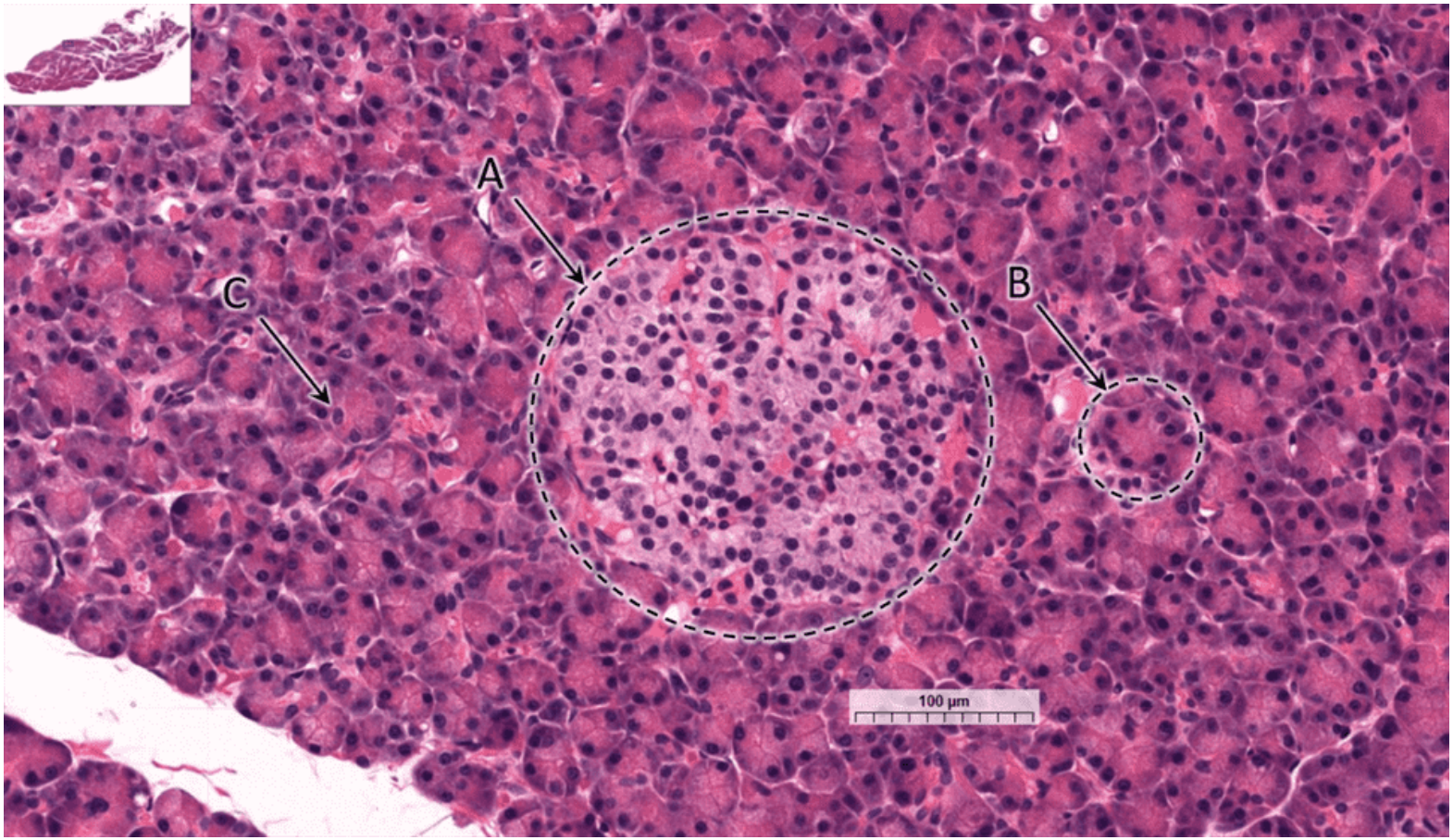


SUBMIT

Identify cell type C.

type your text here



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