S. S. College, Jehanabad

Department: Zoology

Class: M.Sc. Semester II

Subject: Zoology

Topic: Mammalian histology - Liver

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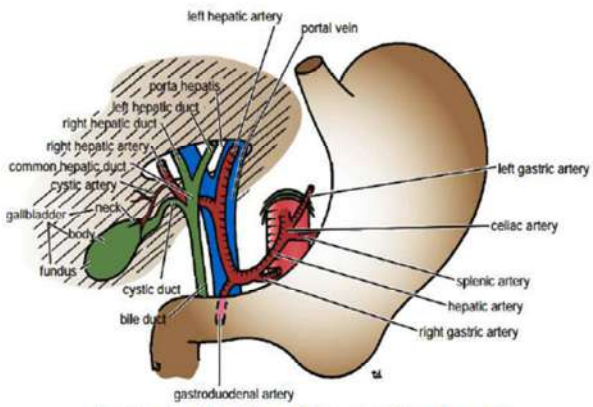
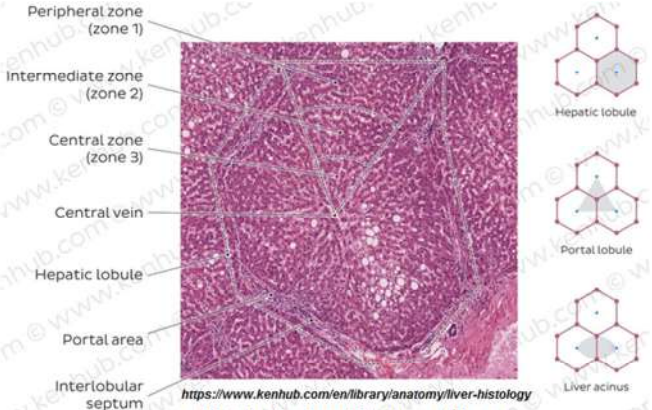
MAMMALIAN HISTOLOGY - LIVER

The liver is the most vital and largest internal organ in the mammalian body, weighing approximately 1.5kg in human. Embryologically, it develops from the foregut and spans the upper right and part of left abdominal quadrants. Anatomically, it has lobular structure and lies in the abdominal cavity below diaphragm in human. It consists of four lobes; two larger ones, which are right and left, and two smaller ones which are quadrate and caudate. Histologically, it has a complex microscopic structure that can be viewed from several different angles. Physiologically, the liver also performs many essential functions and therefore it is said to be one's best friend when you are enjoying some beers with your friends. The circulatory system of the liver is different from that of other organs. Roughly 75% of the blood entering in liver through the portal vein is the venous blood returning back from the small intestine, stomach, pancreas, and spleen. From this portal venous blood all nutrients along with drugs and other potentially harmful substances are absorbed. The remaining 25% of the arterial blood received by liver is the oxygenated blood being carried from the pulmonary system to the liver by the hepatic artery. The blood contents of the hepatic artery as well as hepatic portal vein empty into sinusoids. Sinusoidal blood moves towards the central vein of each lobule and empties its content. Hepatic veins carry deoxygenated blood from liver to the inferior vena cava.



Anatomical location of liver and blood supply



Histological architecture of liver

Functions and physiology

The liver performs several important functions in the human body, such as given below:

- Plasma protein synthesis - albumins, lipoproteins, glycoproteins, prothrombin, fibrinogen
- Vitamin storage and modification - vitamins A, D, and K
- Iron storage and metabolism - transferrin, haptoglobin, hemopexin, ferritin
- Drugs and toxins degradation
- Bile production
- Carbohydrate metabolism

Histological components

The liver consists of the following major histological components:

Parenchyma: It is represented by hepatocytes.

Stroma: It is a continuation of the surrounding capsule of Glisson. It consists of connective tissue and contains the vessels. The capsule is also covered by a layer of mesothelium, arising from the peritoneum covering the liver. The connective tissue of the stroma is type III collagen (reticulin), which forms a meshwork that provides integrity for the hepatocytes and sinusoids.

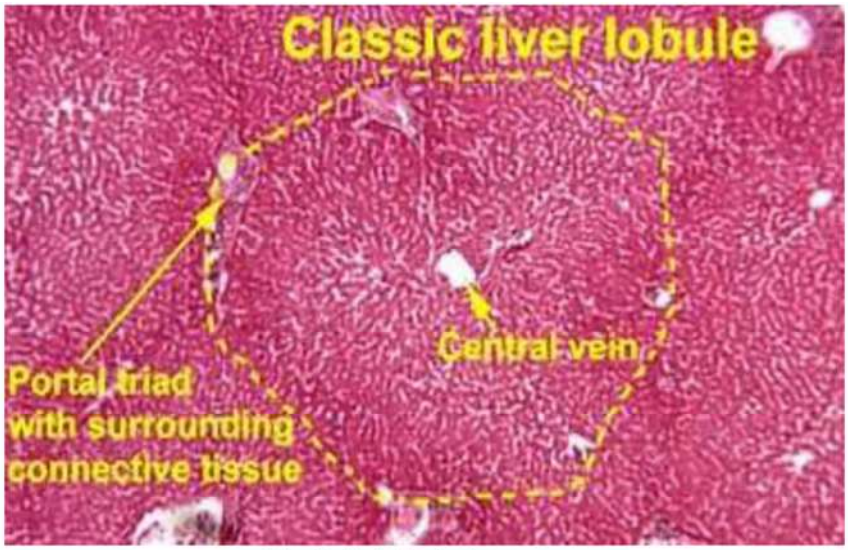
Sinusoids: These are capillaries travelling between hepatocytes.

Spaces of Disse (perisinusoidal spaces): These are located between the hepatocytes and the sinusoids.

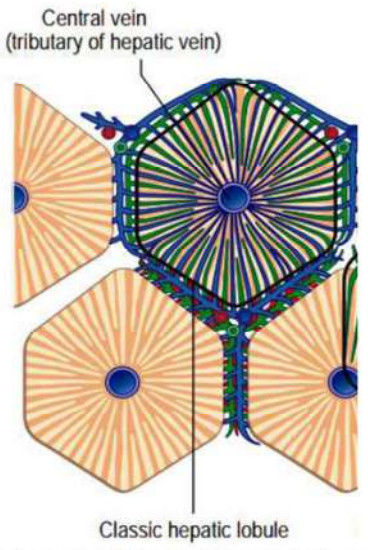
Structure

As described above, histologically liver consists of a large number of microscopic functional units that work in unison to ensure the overall, proper activity of the entire organ. These functional units are hepatic lobule, portal lobule and liver acinus.

Hepatic lobule: It is also trivially known as classic lobule. It is an independent venous unit consisting of hexagonal plates of hepatocytes stacked on top of each other. Within each plate, the hepatocytes radiate outwards from a central vein. As they extend towards the periphery, the hepatocytes are arranged into strips, similar to the spokes of a cartwheel known as ***hepatic lamina***. Spaces between the hepatic lamina are called ***hepatic lacunae***, which are occupied by ***hepatic sinusoids***. Hepatic sinusoids travel between the strips of hepatocytes, draining into the central vein. One portal canal is located at each corner of the hexagonal classic lobule, making a total of six for each lobule. These portal canals are composed of the portal triads, which are surrounded by loose stromal connective tissue. A periportal space (space of Mall), where lymph is produced, is sandwiched between the connective tissue of the portal canals and the hepatocytes. While connective tissue is present around the portal canals, the interlobular quantity is very small in humans. This can make routine histological visualizations of the classic lobule difficult.

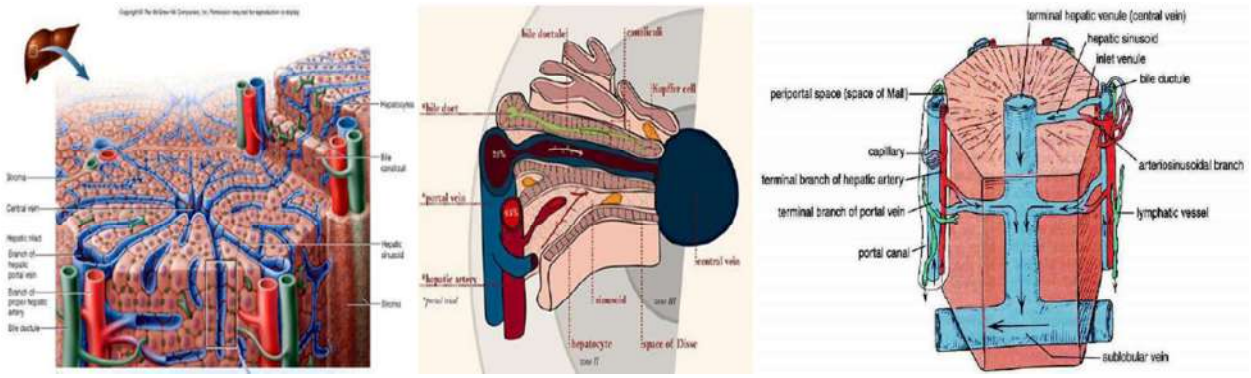


Classical lobule of a liver



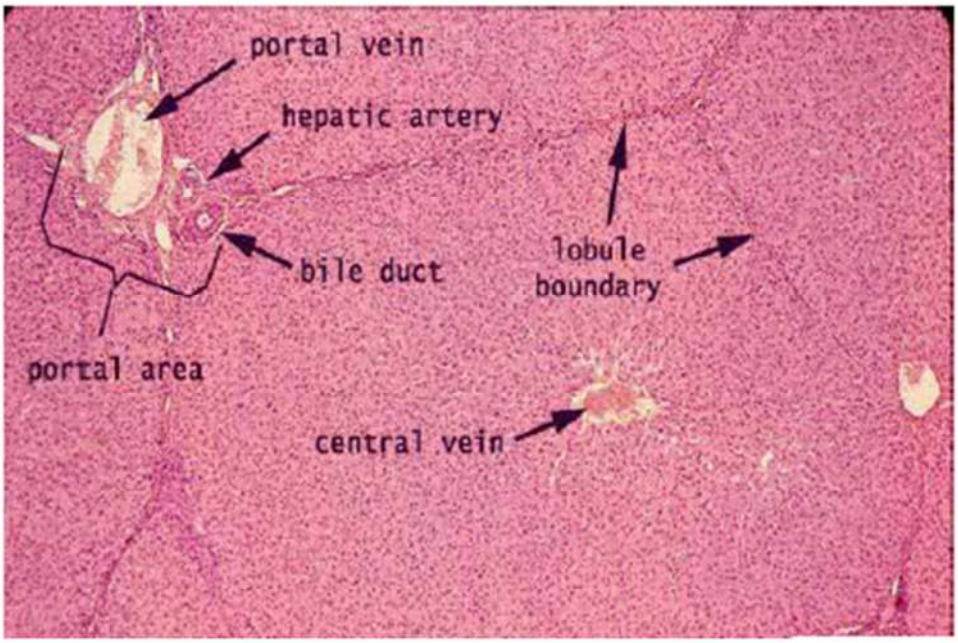
Schematic of classical lobule of a liver

It boasts wide diameter capillaries. The wall of the capillaries is fenestrated and made up of flattened endothelial cells. Kupffer cells and pit cells are attached to the endothelial surface. Hepatic sinusoids receive a mixture of blood from the portal vein and the hepatic artery of adjacent portal area. They are interlaminar and centripetal in direction. The blood flows towards **central vein → sublobular vein → hepatic vein → inferior venacava**.



Portal lobule: While the classic lobule view focuses on the blood supply and hepatic mass arrangement, the portal lobule view underlines the exocrine function of the liver i.e. bile secretion. Peripherally, each lobule has 3 to 6 portal areas with more fibrous connective tissue, each of which contains interlobular structures that comprise the portal triad. They include:

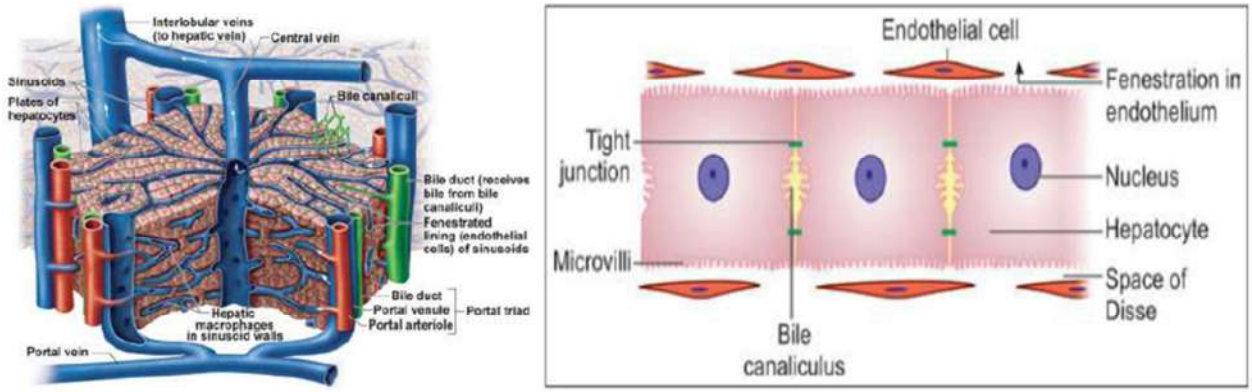
- A venule branch of the portal vein, with blood rich in nutrients but low in O_2.
- An ateriole branch of the hepatic artery that supplies O_2.
- One or two small bile ductules of cuboidal epithelium, branches of the bile conducting system. The area covered by the triangle represents the hepatic regions that secrete bile into the same bile duct.



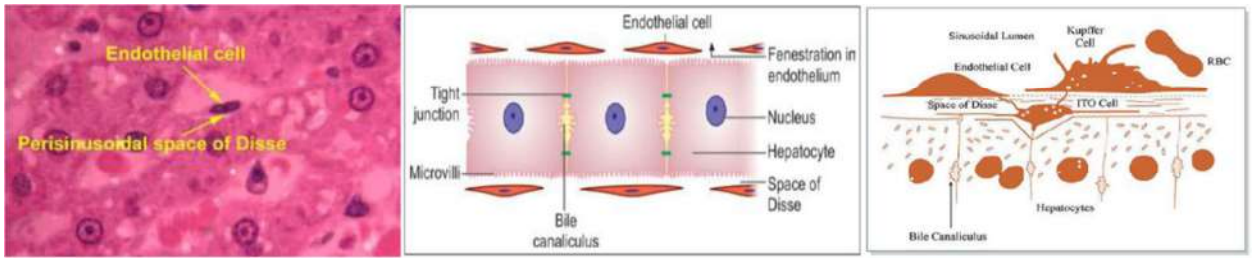
Portal lobule

Hepatic regions contain liver cells and bile canaliculi that are responsible for production, secretion and transportation of bile in the hepatic regions.

Bile canaliculi: It is formed by spaces present between the plasma membranes of adjacent liver cells. It forms hexagonal networks around the liver cells. Borders around the canaliculi are sealed by tight junctions, which form the blood-bile barrier. The canaliculi pass to periphery of the hepatic lobules where they form interlobular ***canal of Herring*** that finally drains into the interlobular duct of the portal area. Bile canaliculi are intralaminar and centrifugal in direction.



Space of Disse or Perisinusoidal space: It is the potential space between the wall of sinusoids and laminae of the liver cells. It is filled with blood plasma and chylomicrons that percolate through the wall of sinusoids. It is characterized by the presence of Ito cells.



Ito cells: As shown in figure above, these cells are located in the space of Disse. These are of irregular outline with numerous lipid vesicles. Their mains functions are;

- to secrete collagenous matrix.
- to provide growth factor for regeneration of damaged liver cells.
- to store Vitamin A in their lipid vesicles.

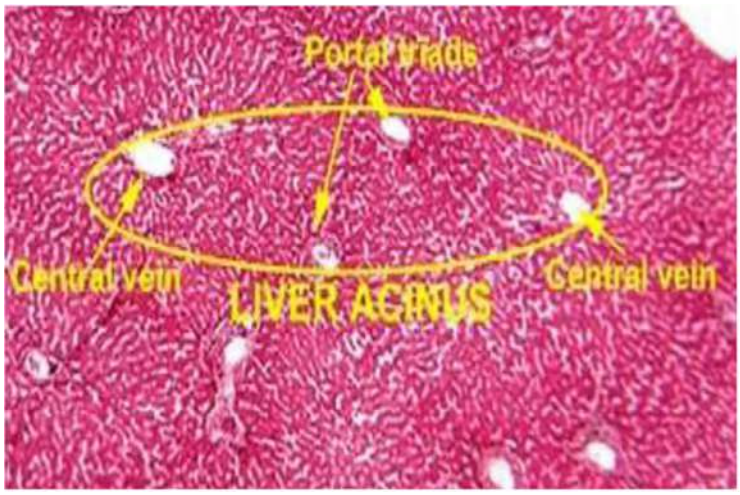
Space of Mall: It is potential space between the Glisson's capsule of portal area and the hepatic plates of the cells. It is the begining point of lymphatics of liver.

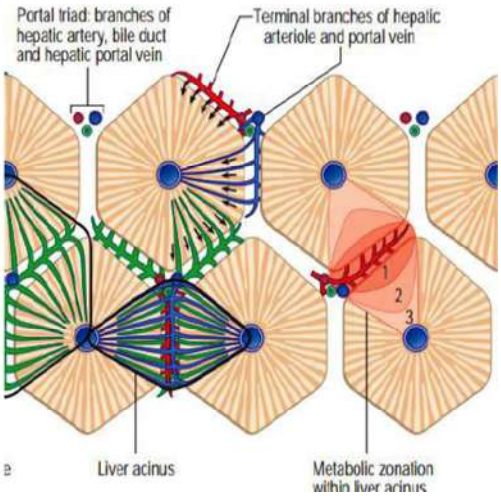
Hepatic acinus or hepatic acinus of Rappaport

Hepatic acini are diamond shaped area of liver parenchyma. It forms structural and metabolic functions of the liver. Backbone of liver acinus is formed by the terminal vessels of numerous

branches originated at right angles from blood vessels of portal area. It can be divided into three zones based on the gradient of blood supply:

- ***Zone 1:*** It is well oxygenated area around the vascular backbone.
- ***Zone 2:*** It is intermediate zone and is moderately oxygenated.
- ***Zone 3:*** It is close to the central vein and the least oxygenated. It is most susceptible to anoxic injury.





Cells of the liver

Hepatocytes: Hepatocytes constitute a major fraction of hepatic cell population. These are cuboidal or polyhedral in shape with round central nuclei and eosinophilic cytoplasm which is rich in mitochondria. These cells are arranged in single-cell cords or plates. These hepatocytes are linked together via intercellular adhesion complexes and tight junctions. Their one side faces the persinusoidal space, while the other faces the bile canaliculi and covered with microvilli. Binucleated cells with large polyploid nuclei are commonly seen in adult liver. Hepatocytes are responsible for most of the liver functions such as metabolism, detoxification, synthesis, and storage of nutrients, carbohydrates, fats, and vitamins. They are also involved in secretory and excretory functions along with other hepatic cells. These functions are performed by different hepatocytes residing in different zones of hepatic lobules. Cytoplasmic characteristics of hepatocytes are as follows;

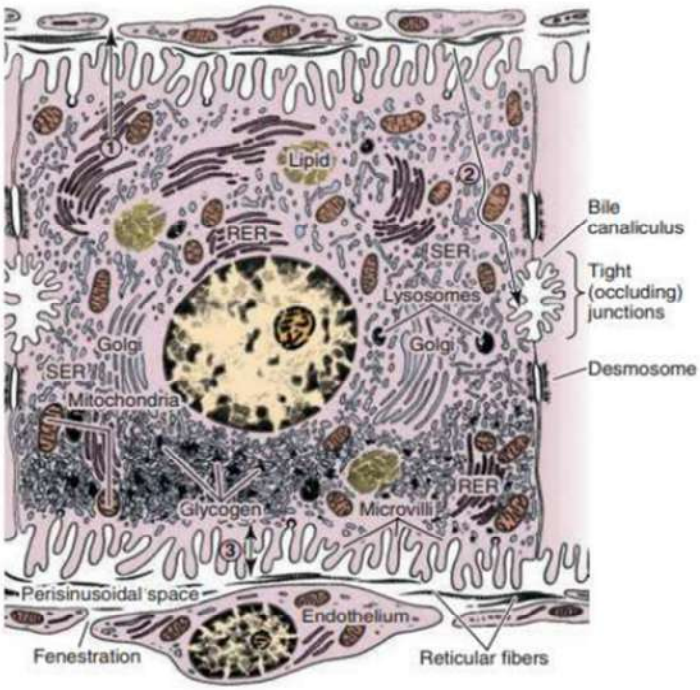
- *Smooth endoplasmic reticulum (sER)*, which is essential in toxin degradation and conjugation, as well as cholesterol synthesis.
- *Mitochondria* (up to 1000/cell)
- *Golgi network*, which is composed of approximately 50 small Golgi units. They contain granules with very low density lipoprotein and bile precursors.
- *Peroxisomes*, which contain oxidases and catalases. These enzymes are responsible for detoxification reactions taking place in the liver, for example, that of alcohol.
- *Glycogen deposits, which are lost in during H&E preparations, leaving irregular stained areas.*
- *Lipid droplets*

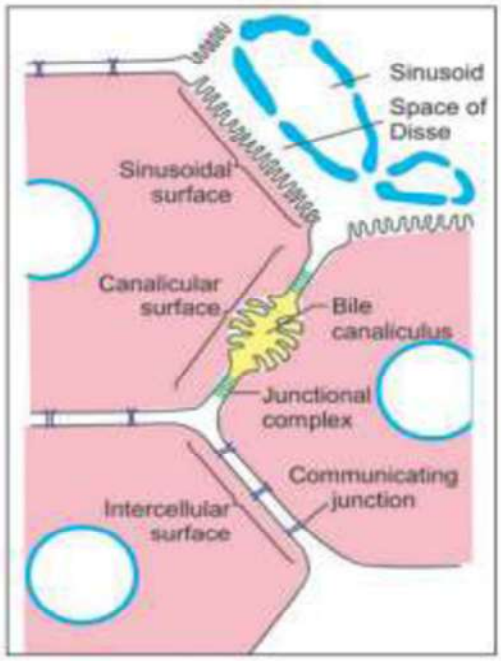
– *Lysosomes*, which are responsible for iron storage under the form of ferritin.

Kupffer cells: Kupffer cells are resident macrophages in liver with largest population. They are attached to the luminal surface of the sinusoidal endothelium. These cells are essential for the phagocytosis of foreign particles, infecting organism as well as cytokines products.

Hepatic stellate cells: These cells are located within persinusoidal space of Disse, in the recesses between hepatocytes. These cells are associated with several functions such as secretion of cytokines, storage of vitamin A and synthesis of hepatic extracellular matrix. They gets activated during liver injury and play a key role in progression of fibrosis.

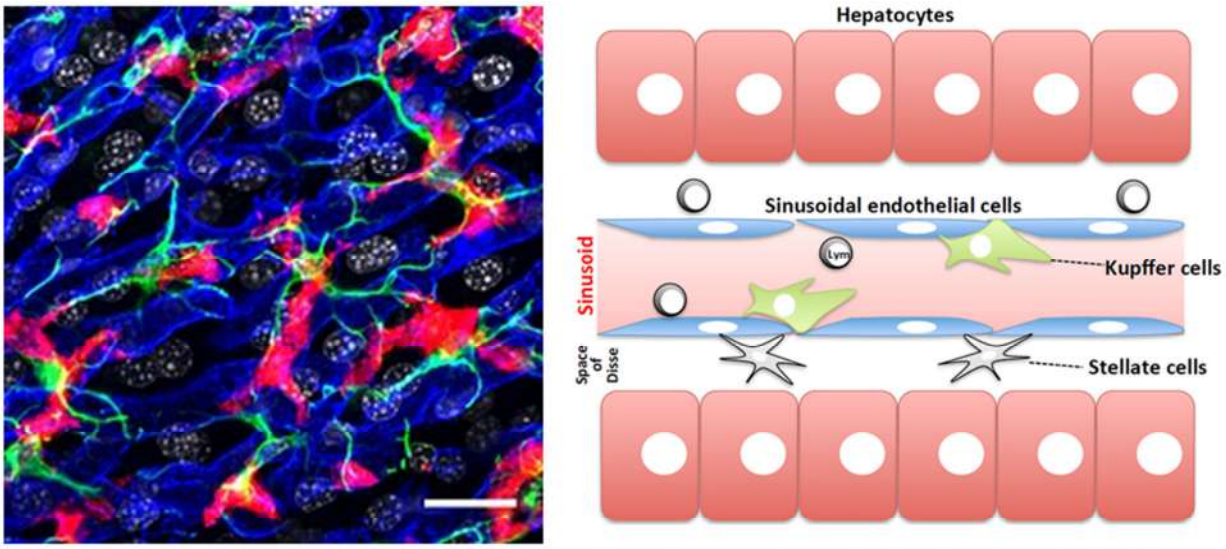
Biliary epithelial cells: These cells line the bile duct in portal triads. They are also known as the **cholangiocytes**. The connecting duct between bile duct and bile canaliculi (canal of Herring) along with hepatocytes are also lined by these biliary cells. They are involved in modifying bile composition by altering solute and water content. It has also now become evident that during liver transplantation, the biliary epithilium is an important target for leucocytes of the graft recipient.





Endothelial cells: These cells are largest group of non-parenchymal cells of liver and line the intrahepatic circulatory vessels of liver and provide a large surface area for nutrient absorption. They form a pathogenic and selective barrier during separation of hepatocytes from sinusoidal blood by exchange of molecules.

Lymphocytes: Lymphocytes are present everywhere in the liver parenchymal sinusoids. These lymphocytes are also a part of innate immune system and selectively rich in NKT cells and natural killer cells providing defense against invading pathogens.



Confocal microscopy picture showing the steady-state location and interactions between **Kupffer cells** (Red), **hepatic stellate cells** (green) and **liver sinusoidal endothelial cells** (blue). Cell nuclei are in grey, and schematic representation of the same (right).

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