

Diagnosis of Hepatocellular Carcinoma

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pathCast

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The Bloomberg-Kimmel
Institute for Cancer
Immunotherapy

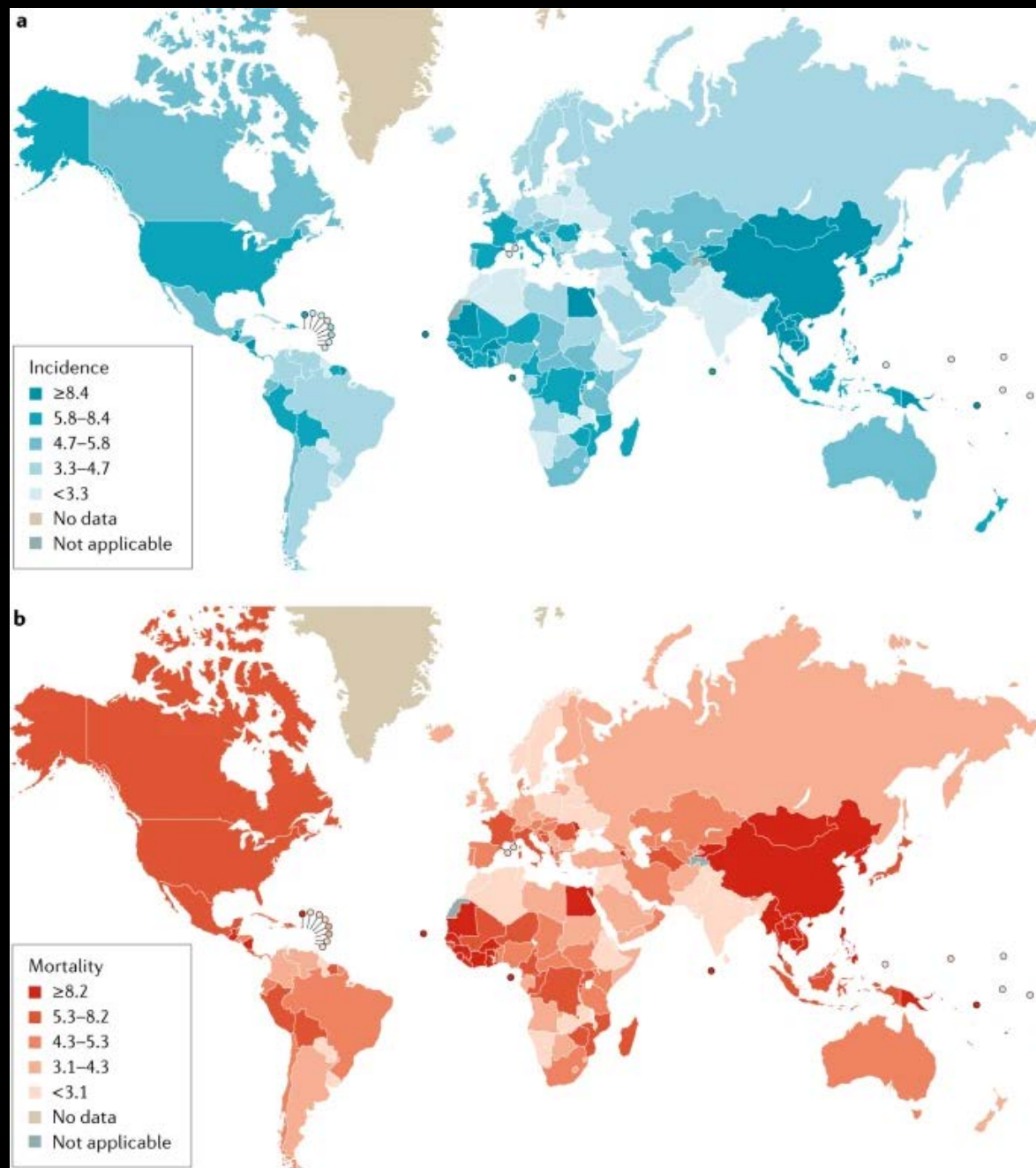


Disclosures

- Bristol Myers Squibb
- Merck SD
- Astra Zeneca
- Adaptive Biotechnologies
- Five Prime Therapeutics
- FlxBio /RAPT therapeutics
- Stand up 2 Cancer
- Roche Diagnostics / Akoya Bio
- National Institutes of Health

Objectives

- Hepatocellular carcinoma perspective
- Define the histologic and immunohistochemical features in diagnosis of hepatocellular carcinoma
- Understand concepts in utilizing the stains for
 - Liver structure
 - Hepatocytes
 - Malignant hepatocytes



Hepatocellular Carcinoma on H&E

- Loss of portal tracts / gain unpaired arterioles
- Tiny hepatocytes almost always associated with malignancy
- Architecture >> cytology

EXAMPLE 1

60 male with cirrhosis secondary to hepatitis C viral infection 7 cm liver mass.

Transplant

EXAMPLE 2

65 male with cirrhosis secondary to fatty liver disease and 4 cm liver mass. Resection

EXAMPLE 3

67 male with cirrhosis secondary to fatty liver disease 3 cm mass increasing size over 2 years. Biopsy

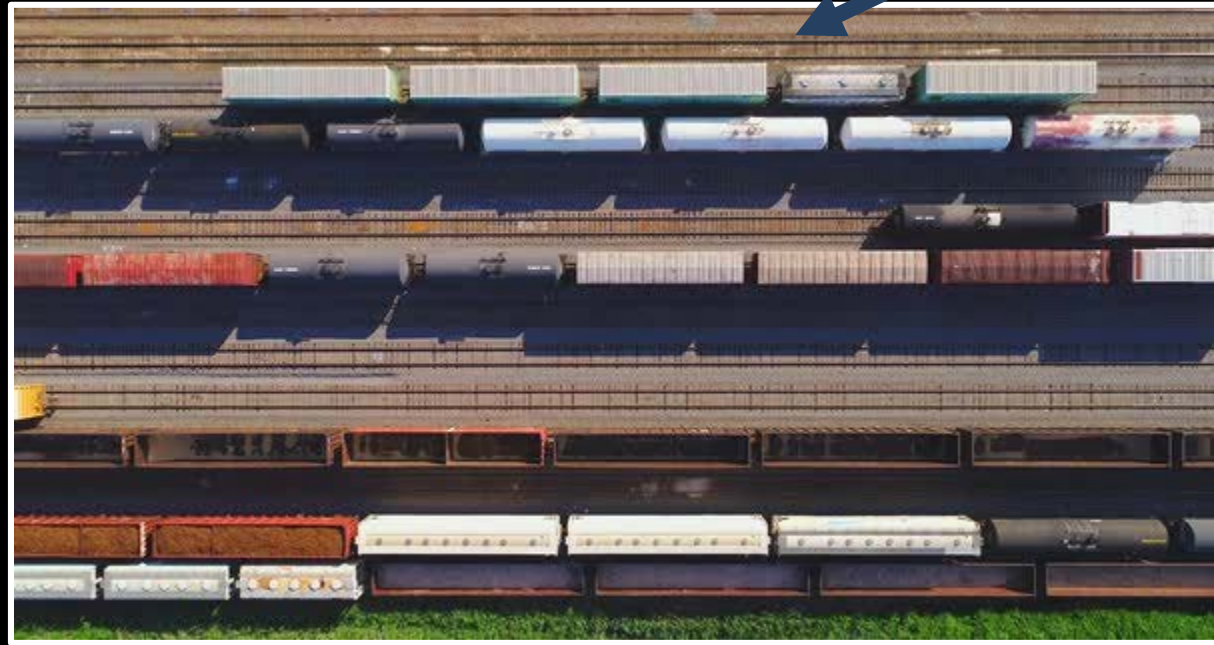
EXAMPLE 4

60 male with cirrhosis secondary to fatty liver disease 4 cm mass. Transplant

Reticulin

- Architecture assessment stain
- Present in necrotic HCC

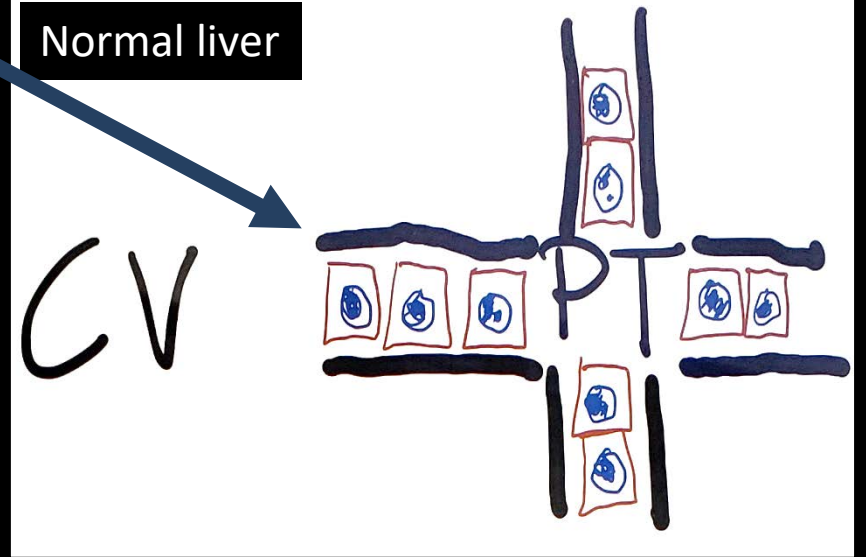
Reticulin



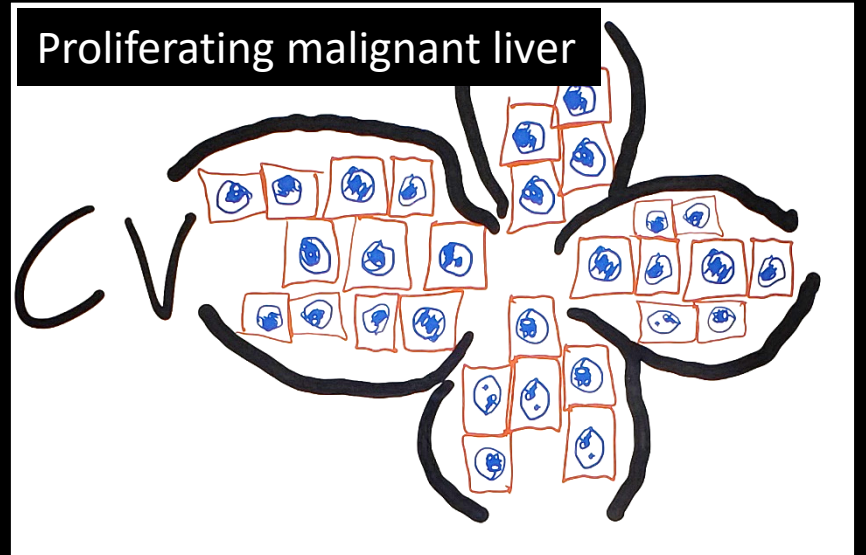
Normal liver

Reticulin fibers

Normal liver



Proliferating malignant liver



CV = Central Vein
PT = Portal tract

EXAMPLE 5*

60 male with cirrhosis secondary to fatty liver disease 4 cm mass. Transplant

*same patient as example 4

EXAMPLE 6

55 female with cirrhosis secondary to fatty liver disease 3 cm mass. Biopsy

EXAMPLE 7

48 male with cirrhosis secondary to fatty liver disease 7 cm mass. Embolization.
Transplant

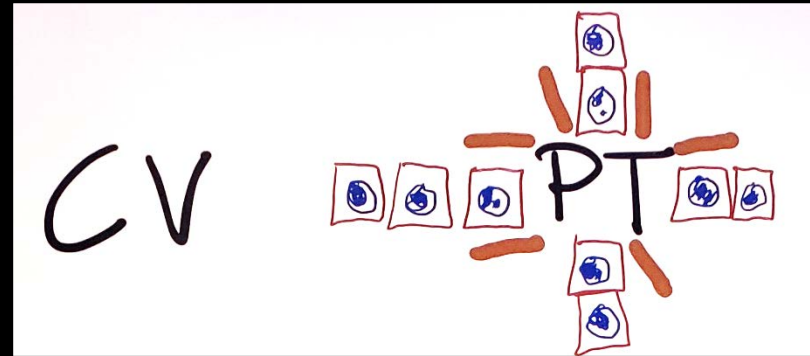
Case courtesy Natasha Larman MD, PhD
Johns Hopkins GI/Liver Pathology

Assessing Lobular Liver Structure

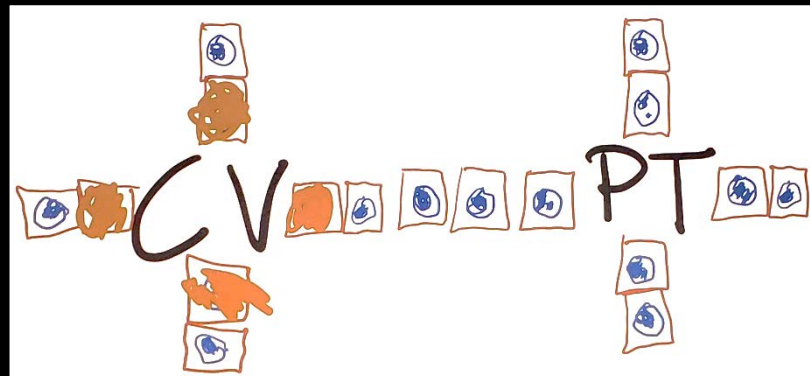
- CD 34 = periportal vascular space
- Glutamine synthase = centrilobular hepatocytes / hepatocytes around central veins

Assessing Lobular Liver Structure

- CD 34 = periportal vascular space



- Glutamine synthase = centrilobular hepatocytes / hepatocytes around central veins



CV = Central Vein
PT = Portal tract

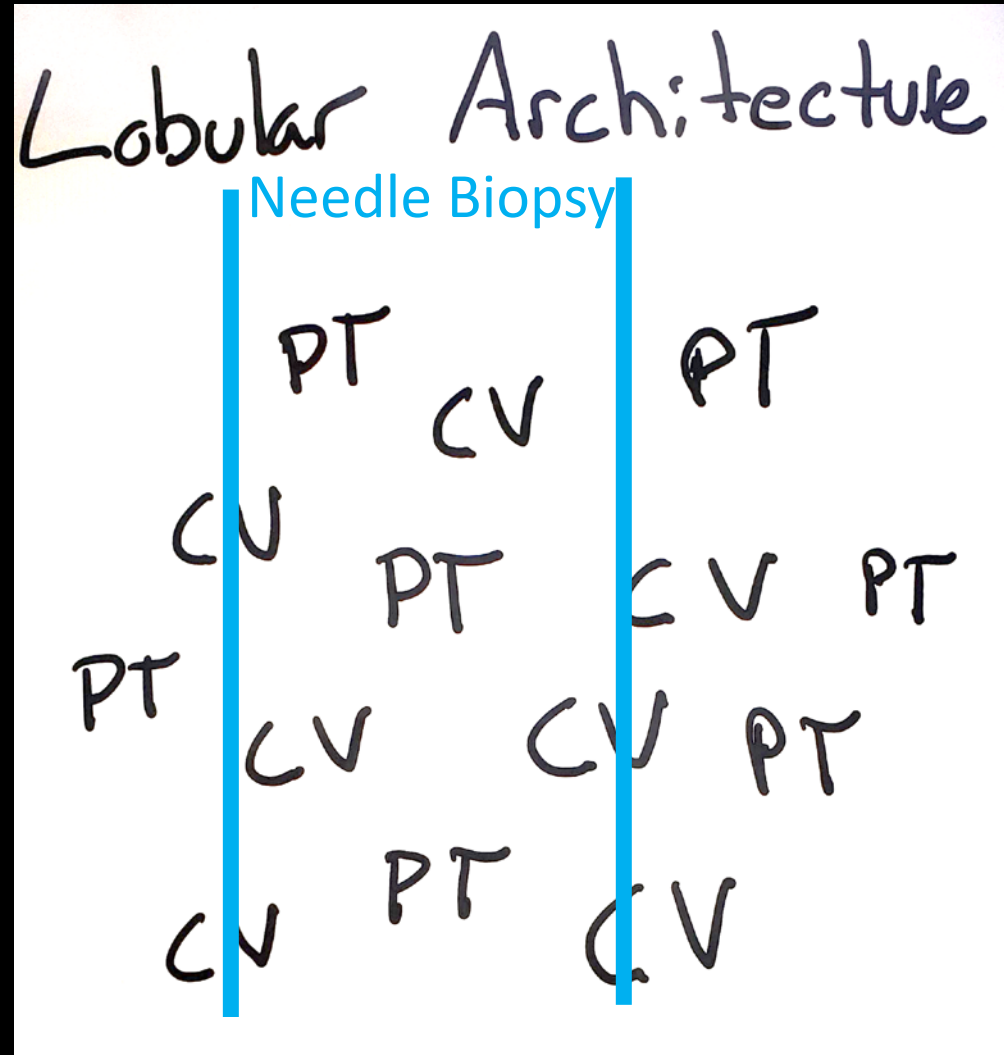
Assessing Lobular Liver Structure

Lobular Architecture

PT CV PT
CV PT CV PT
PT CV CV PT
CV PT CV

CV = Central Vein
PT = Portal tract

Assessing Lobular Liver Structure



CV = Central Vein
PT = Portal tract

EXAMPLE 8

84 female with history of small bowel neuroendocrine tumor with a 6 cm liver mass. Biopsy

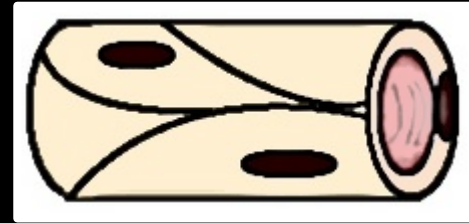
CD34

Did they hit a hepatocellular mass?

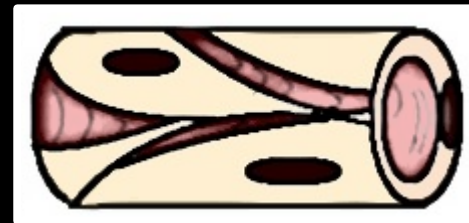
- “Capillarization” of hepatic masses

Blood Vessels

- Most capillaries have a continuous structure



- Hepatic sinusoids are discontinuous
 - Widely fenestrated lining
 - Basal lamina is absent or incomplete



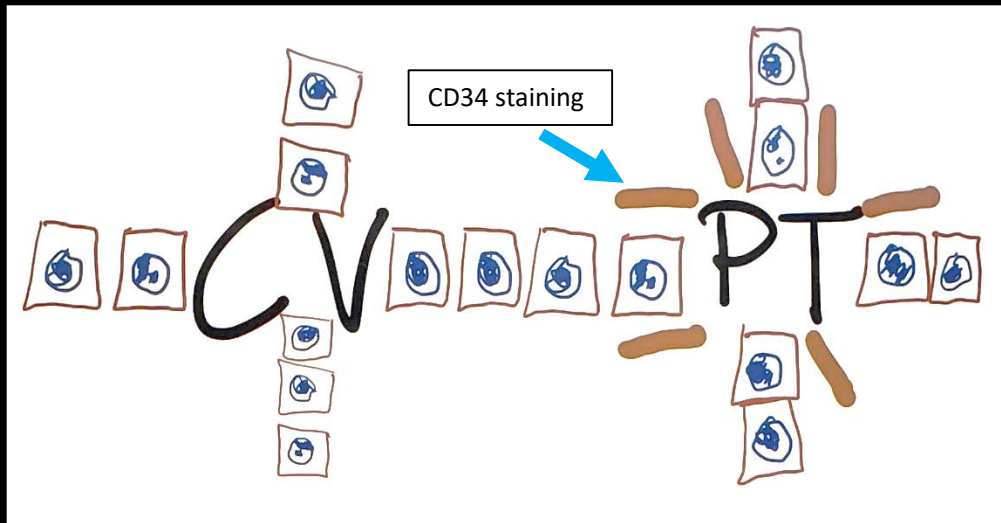
CD34

- Liver tumor
Hepatic sinus



Continuous capillary

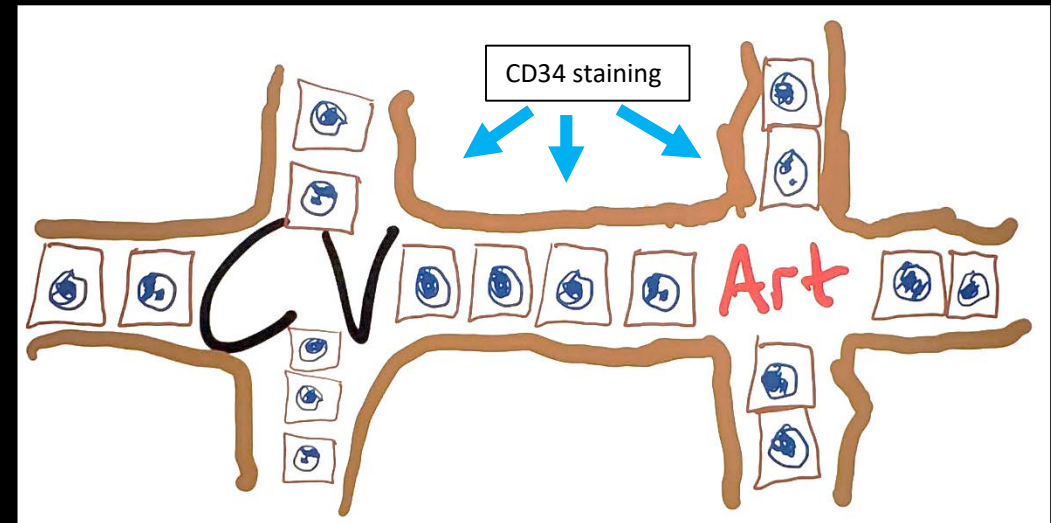
Normal Liver



"Capillarization"



Liver Tumor



CV = Central Vein
PT = Portal tract
Art = Arteriole

EXAMPLE 9

50 male with cirrhosis secondary hepatitis

C viral infection with a 3 cm mass.

Transplant

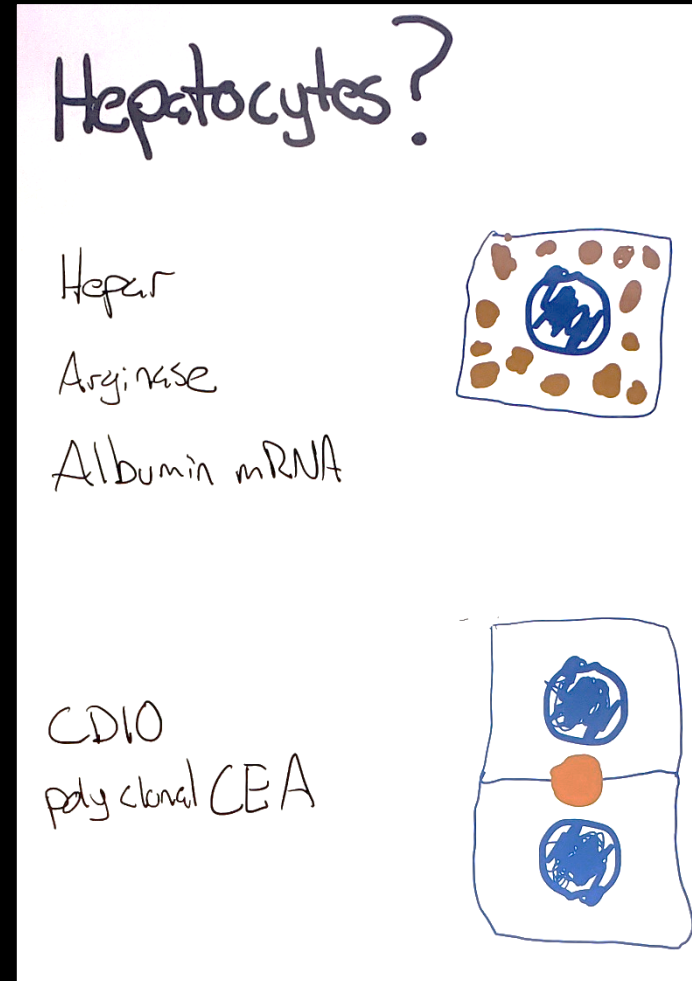
EXAMPLE 10

70 male with cirrhosis secondary hepatitis
C viral infection with a 3 cm mass. Biopsy

Hepatocyte IHC Markers

Are those hepatocytes?

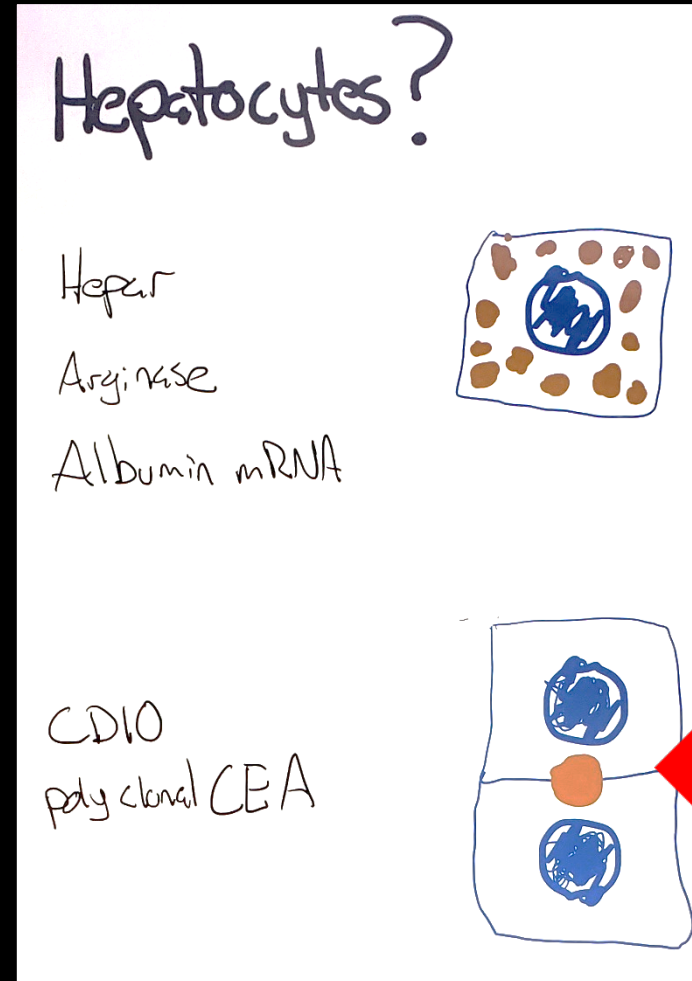
- Cytoplasmic
 - HepPar1
 - Arginase
 - Albumin ISH
- Canalicular
 - **Poly-CEA**
 - CD10



Hepatocyte IHC Markers

Are those hepatocytes?

- Cytoplasmic
 - HepPar1
 - Arginase
 - Albumin ISH
- Canalicular
 - **Poly-CEA**
 - CD10



EXAMPLE 11

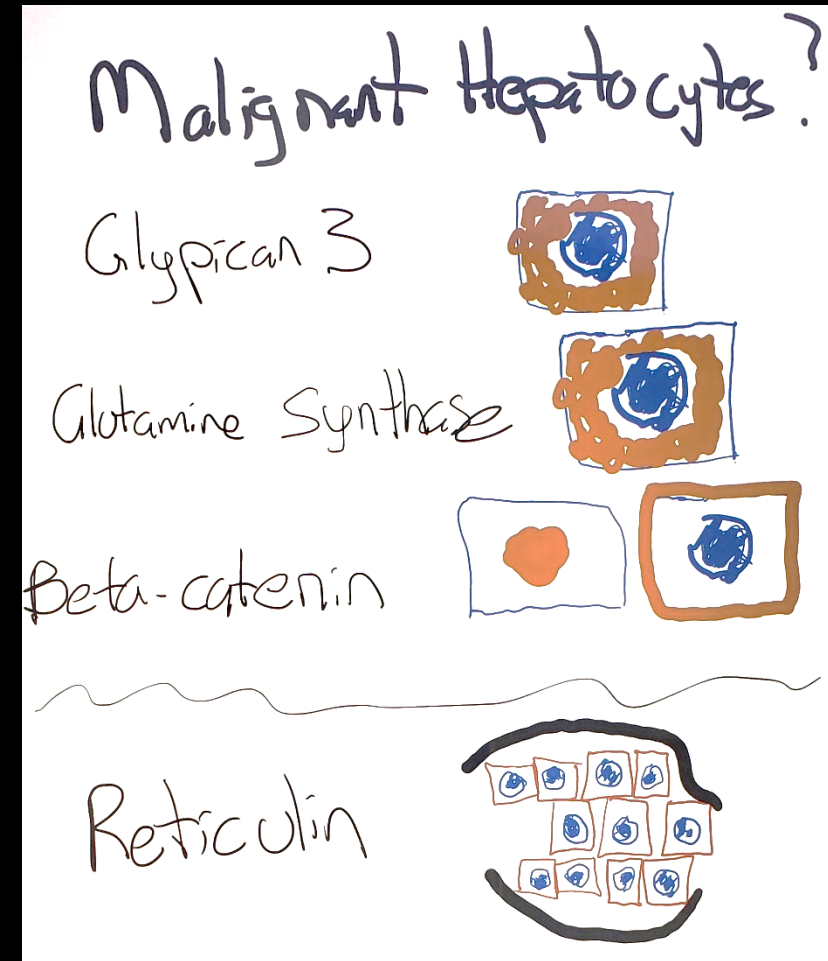
70 male with cirrhosis secondary hepatitis
C viral infection with a 3 cm mass. Biopsy

Hepatocyte IHC Markers

Are those **MALIGNANT** hepatocytes

- Cytoplasmic
 - Glypican 3
 - *Glutamine synthesis!*
- Nuclear
 - *Beta-catenin!*

! Careful. Many caveats. might label a hepatic adenoma



Example workflow...

EXAMPLE 12

75 male with cirrhosis secondary to fatty
liver disease 4 cm mass. Biopsy

Review the Objectives

- Hepatocellular carcinoma perspective
- Define the histologic and immunohistochemical features in diagnosis of hepatocellular carcinoma
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What primary liver lesions did we not cover?

- Hepatocyte
 - Well differentiated hepatocellular carcinoma vs adenoma sometime focal nodular hyperplasia
 - Hepatic neoplasm of undetermined malignant significance
 - Adenoma classification
 - Hepatic lobar / segmental atrophy
- Cholangiocarcinoma
 - Cholangiocarcinoma vs metastatic cancer
 - Utility of albumin-ISH
 - Cholangiocarcinoma vs inflamed biliary proliferation

The End
Thank you for your attention!

