Fibroblast activation protein alpha (FAP) in severe fatty liver disease (NASH)

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FAP in human liver

- Expression increases massively in chronic injury
- Both liver and serum FAP up with fibrosis severity
- Fibrosis, insulin resistance and fibrinolysis roles.

FAP in mouse liver

WT

FAP gki

Cirrhosis

Fibronectin

FAP

Merge

Cirrhosis

Non-diseased

Cirrhosis

FAP Enzyme Activity

Non-Diseased

Alcoholic Cirrhosis

Biliary Cirrhosis

Human Liver

Non-diseased

Cirrhosis
FAP in NASH fibrosis; key substrates

- Collagens, a2-anti-plasmin and FGF21 are degraded by FAP in humans.

- FGF21 up 3x with FAP i.
Need selective potent protease inhibition

Dipeptidyl peptidase activity

Endopeptidase activity

DPP4

FAP

PEP

Mark Gorrell