



Hepatic progenitor cells in chronic liver disease

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I have nothing to declare.

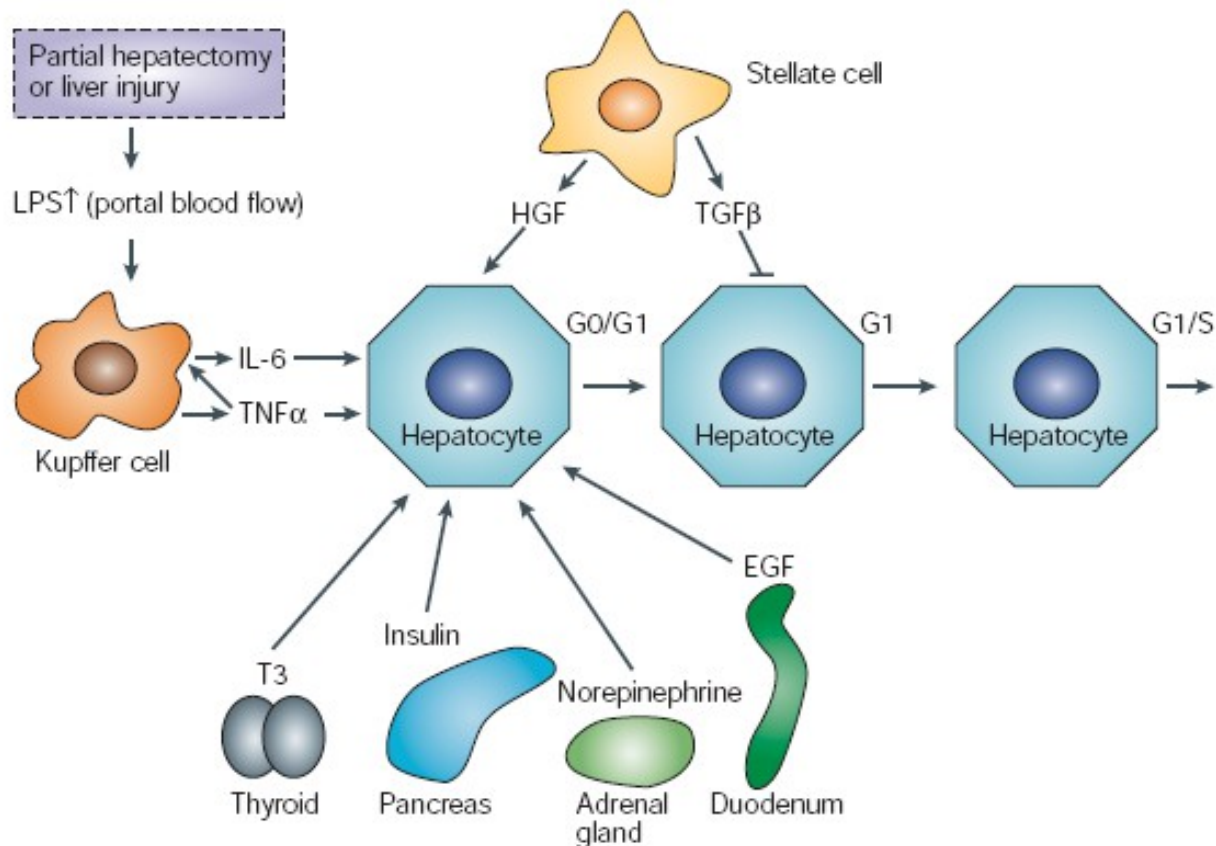
Overview

- Introduction
- Hepatic progenitor cells and their niche
- Hepatic progenitor cells and their role in cancer

Introduction

The liver: a remarkable capacity to regenerate

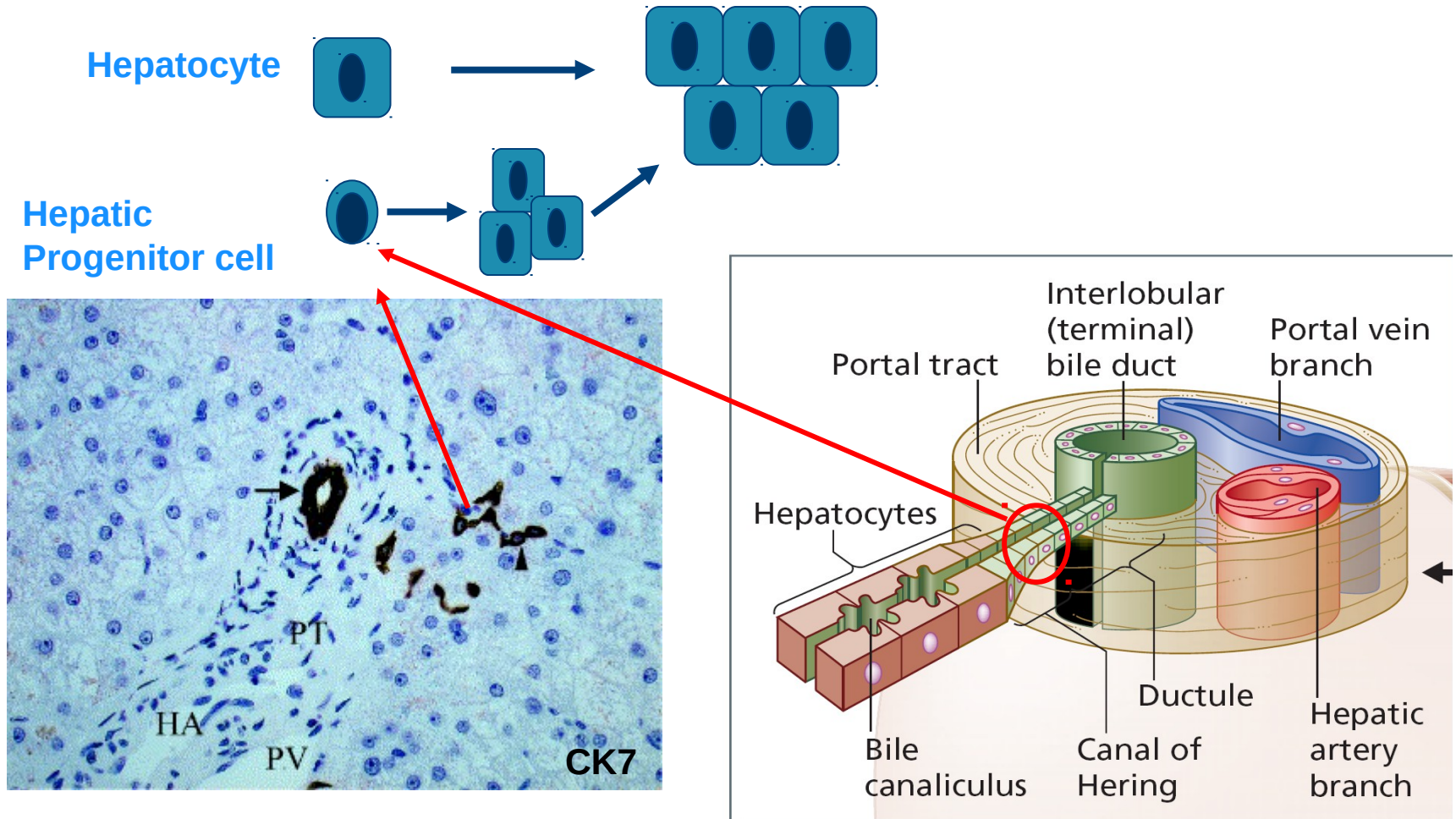
Hepatocyte mediated liver regeneration



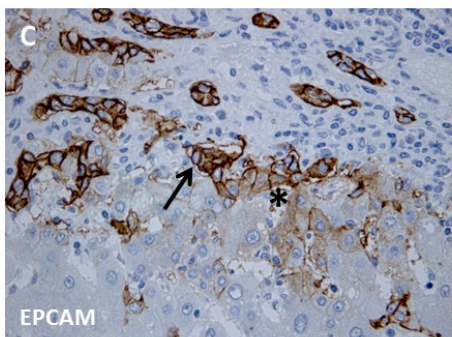
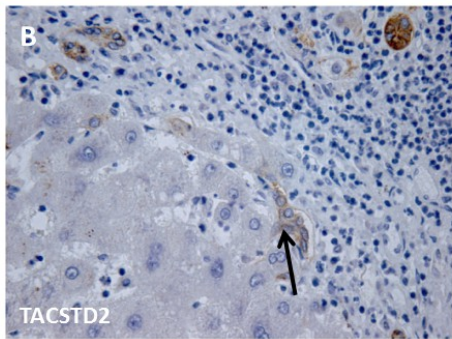
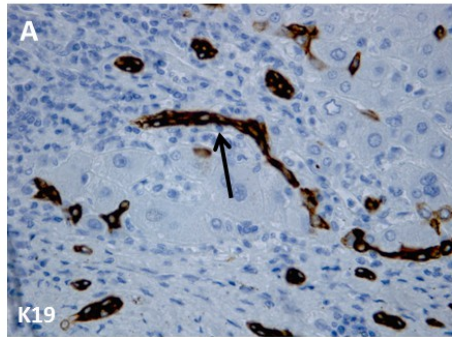
Introduction

The liver: a remarkable capacity to regenerate

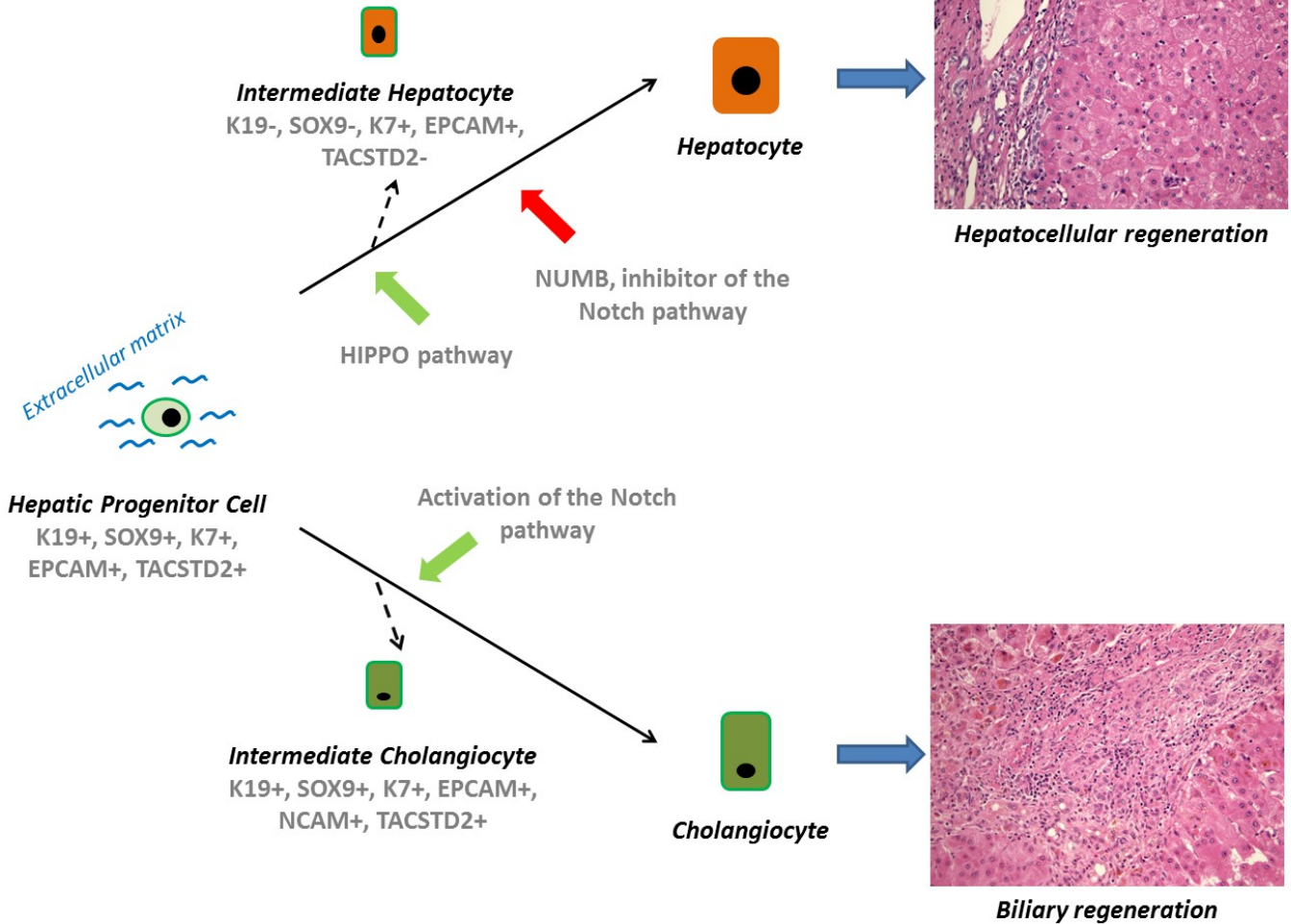
Hepatic Progenitor cell mediated liver regeneration



Introduction

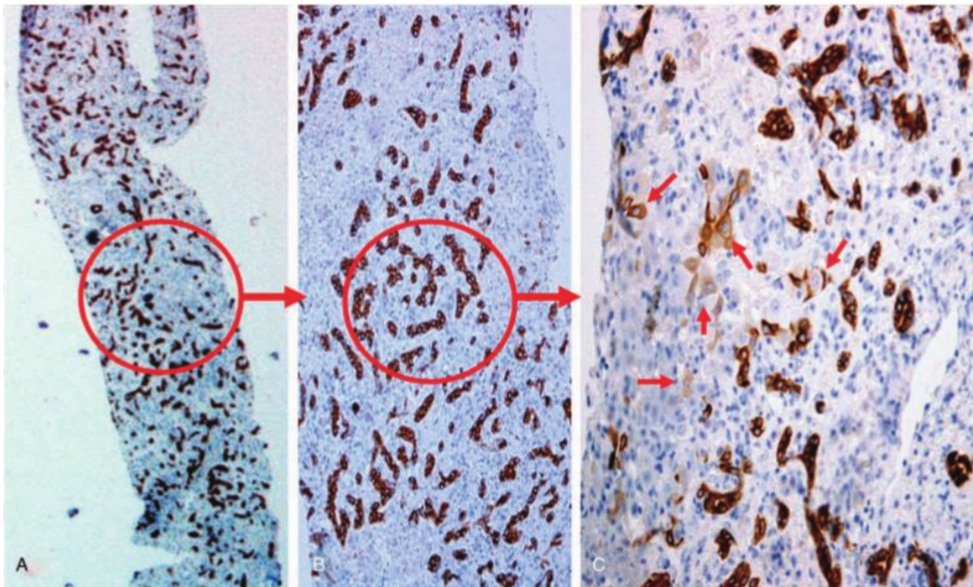


D



Introduction

HPC activation correlates with disease severity in acute liver failure



“Surviving patients compared with those who either died or were transplanted had significantly less hepatocyte loss, less HPCs activation and more mature hepatocyte proliferative activity.”

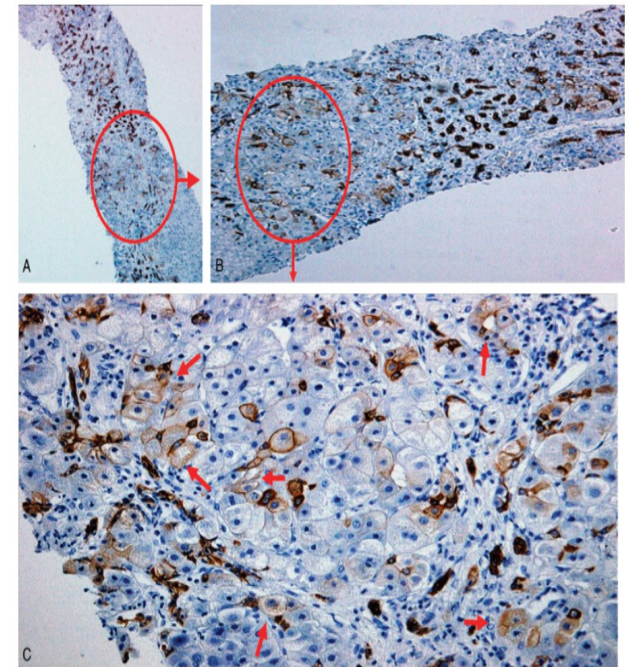
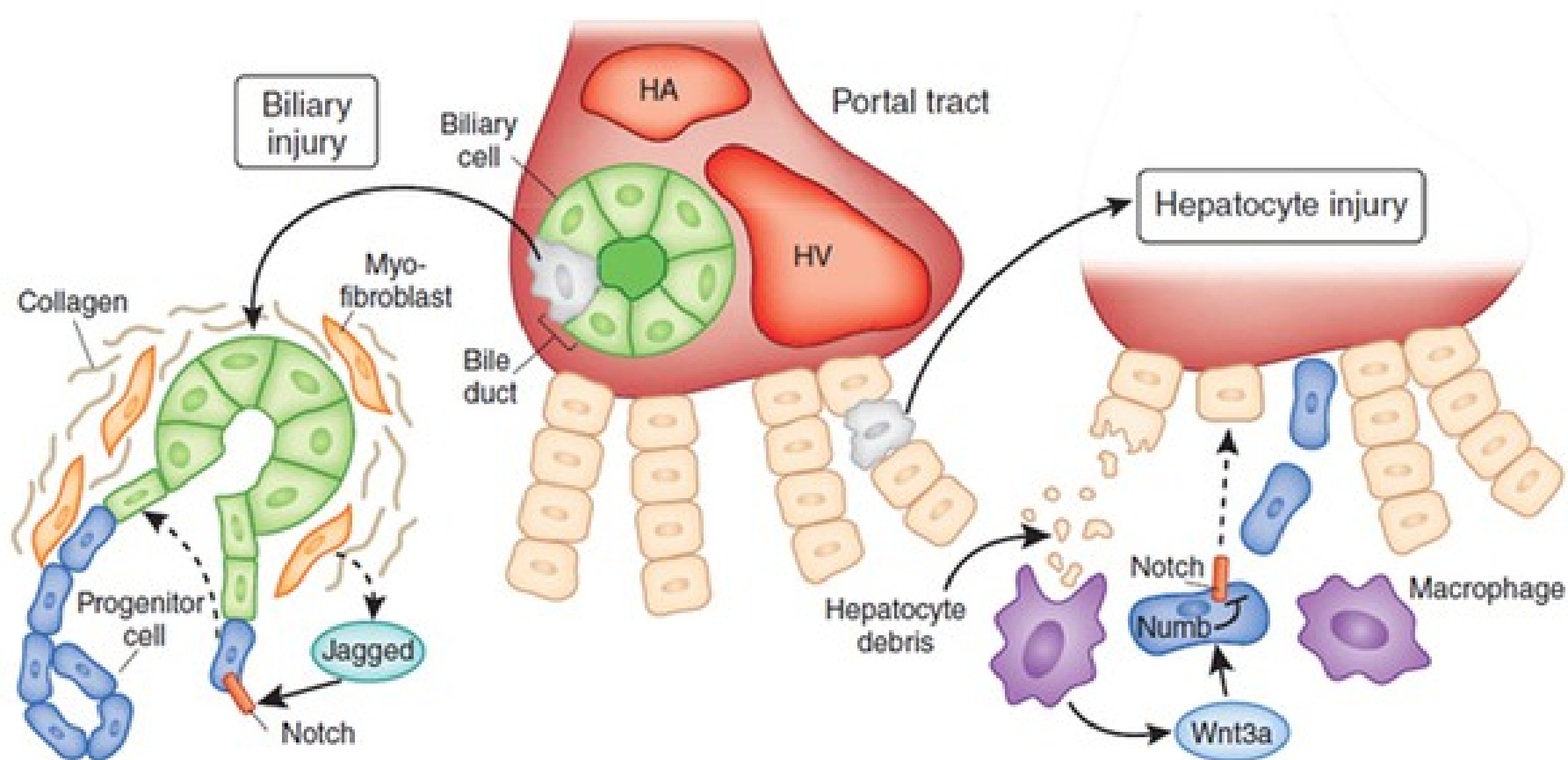


Fig. 6. (a-c) A second biopsy, taken 13 days after the first one, showed a significant increase in the number of intermediate hepatocytes [which form clusters or foci, (arrows)], suggesting further differentiation towards hepatocytes, while the degree of progenitor cell activation decreased (CK 7 staining, original magnification $\times 50$ (6a), $\times 100$ (6b) and $\times 200$ (6c)).

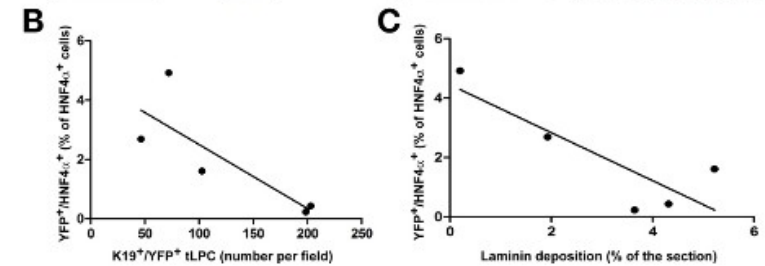
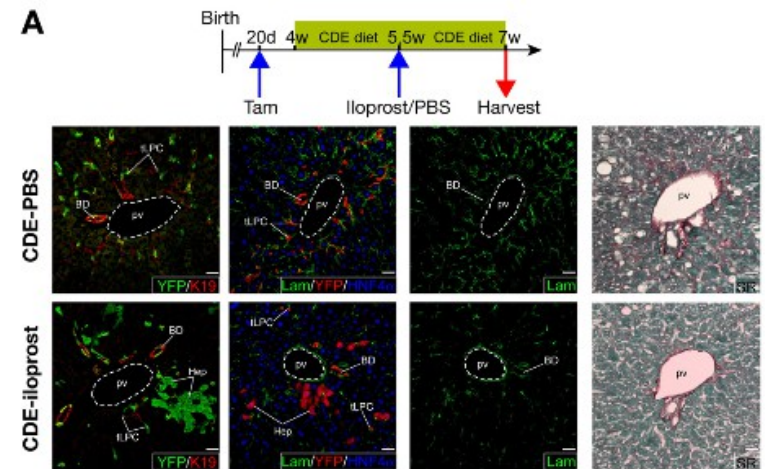
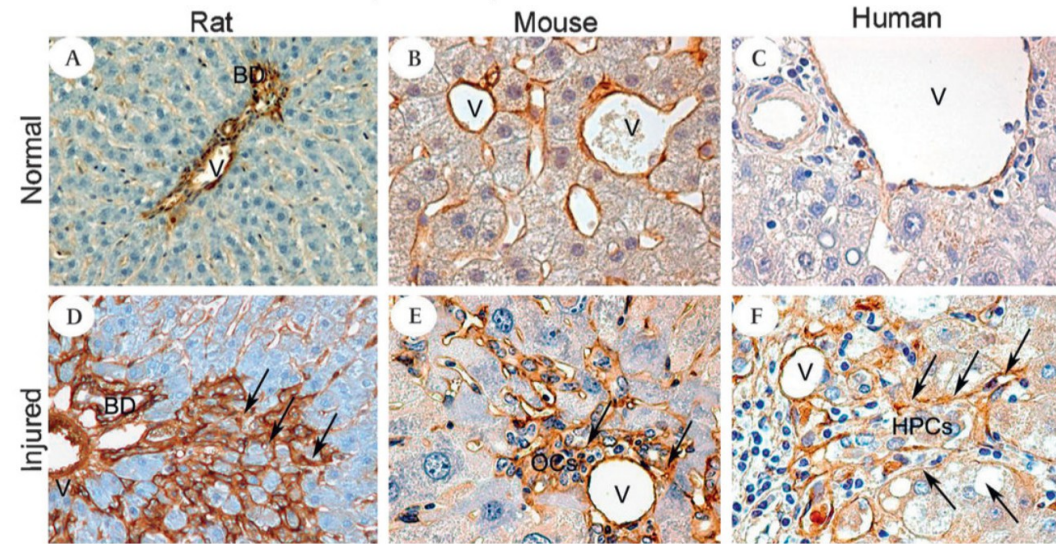
Hepatic progenitor cells and their niche

Macrophages mediate hepatocellular regeneration in mice



Hepatic progenitor cells and their niche

Laminins support biliary/HPC features



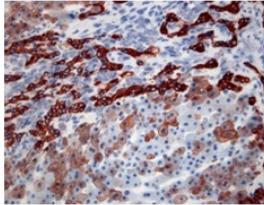
Hepatic progenitor cells and their niche

1

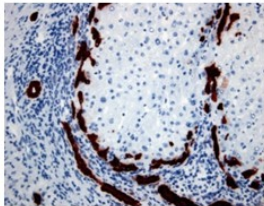
Isolation of the human

niche

Human Frozen tissue samples



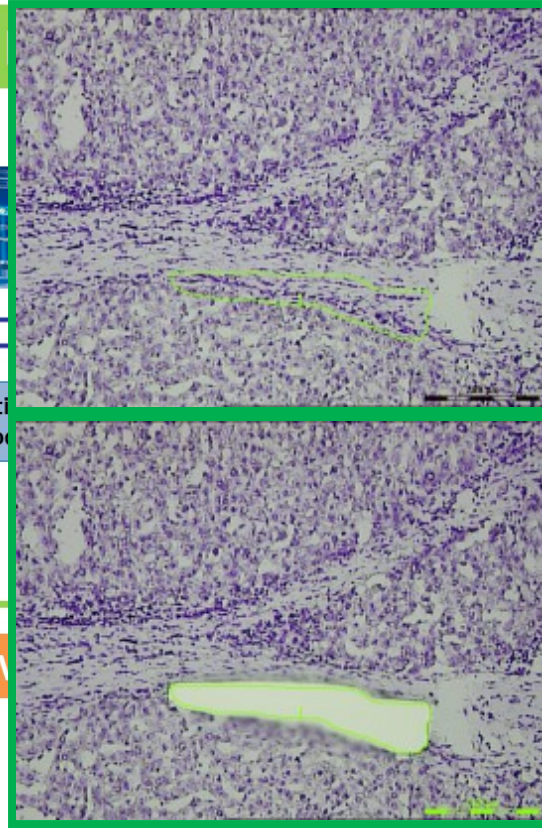
Primary Sclerosing Cholangitis
(biliary regeneration)



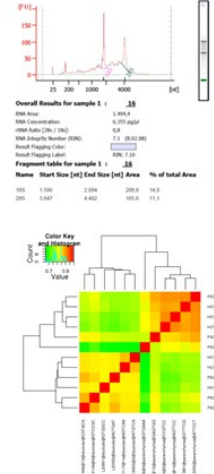
Chronic Hepatitis C
(hepatocellular regeneration)



Cell isolation
laser micro

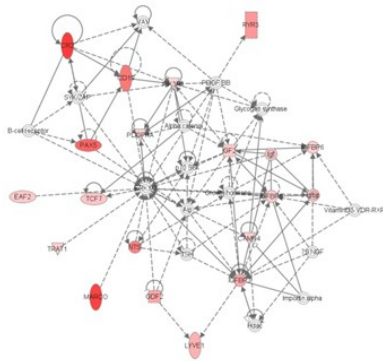


Parallel Seq
ina TruSeq



2

Pathway Analysis



3

sequencing data

Human FFPE
Tissue samples



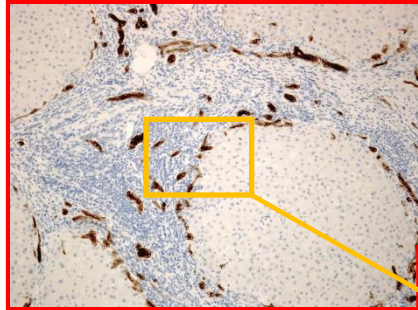
on end-stage
disease samples

(Metavir Score F4, n=40)

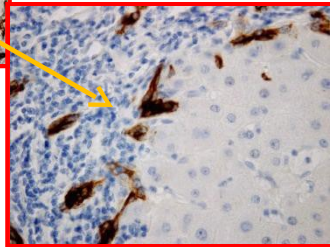
Immunohistochemistry on needle biopsies
diagnosed with early stage chronic liver disease
(Metavir Score F0-F2, n=20)

Hepatic progenitor cells and their niche

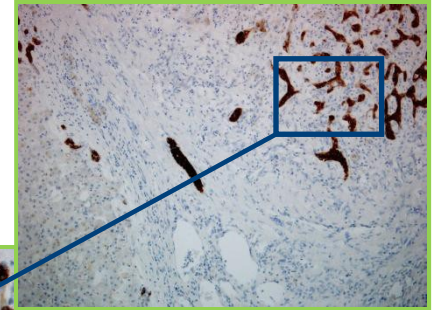
Hepatitis C



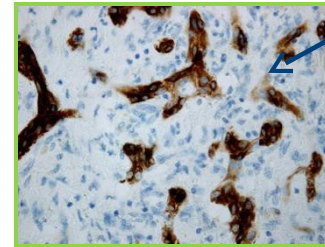
Keratin 19



Primary Sclerosing Cholangitis



Keratin 19

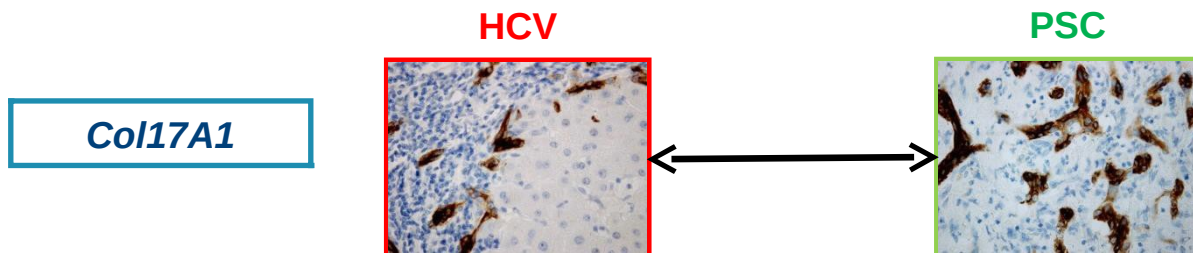


332 differentially expressed genes

- Validation of data set
- Pathway analysis
 - Transcriptional regulators
 - Networks
- Differences in extracellular matrix deposition
- Differences in HPC surrounding immune cells

Hepatic progenitor cells and their niche

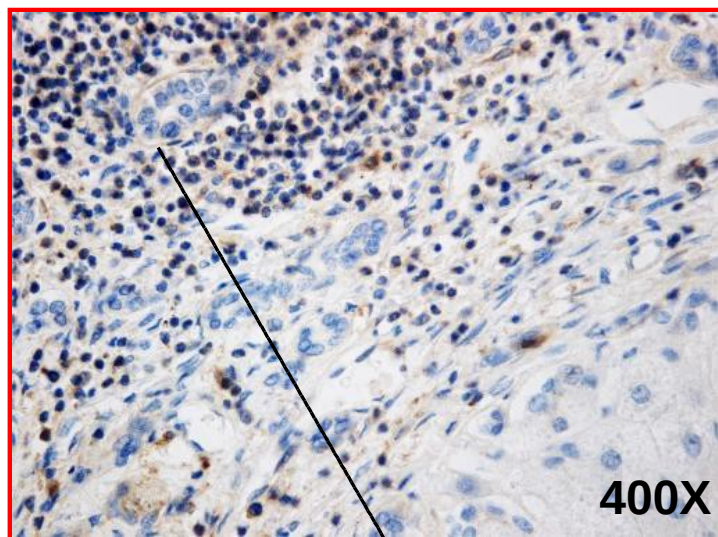
Differences in extracellular matrix deposition



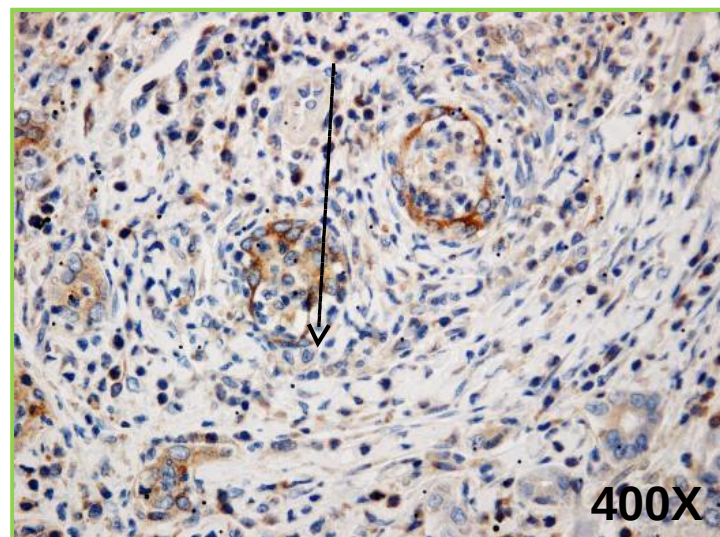
- **Laminin gamma 2**
- **Fibronectin 1**
- **Collagens**
 - COL4A6
 - COL4A1
 - COL10A1
 - COL3A1
 - COL1A1
 - COL9A2

Laminin gamma 2

Cirrhotic stage



Basal membrane of bile duct



Cytoplasmic positivity in HPCs and bile duct

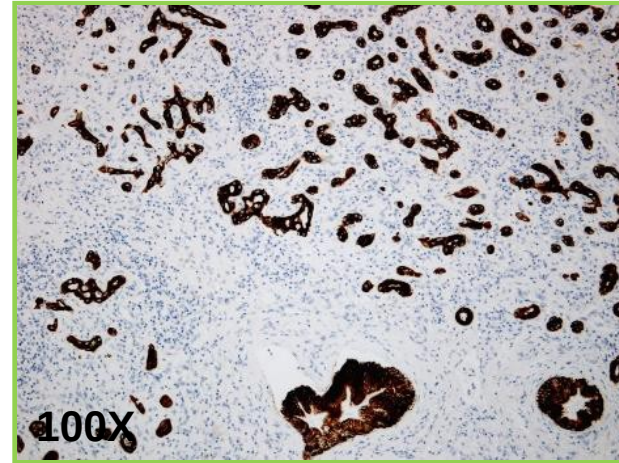
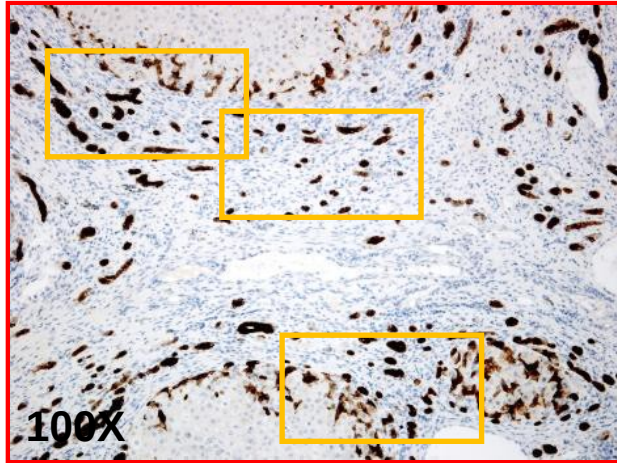
Results

Differences in extracellular matrix deposition

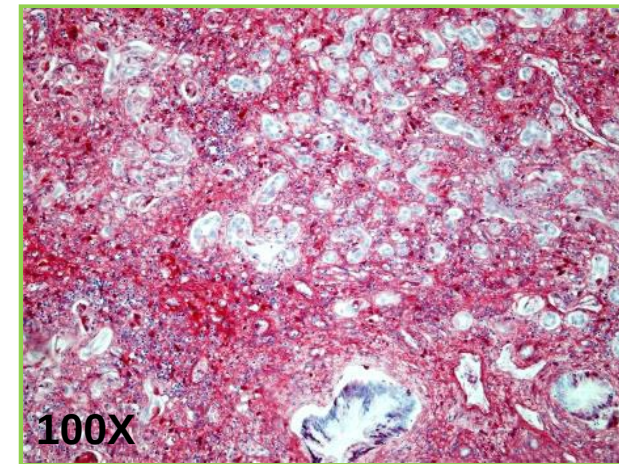
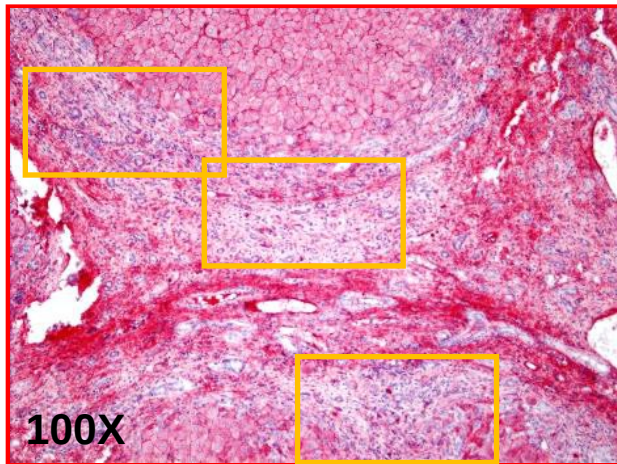
HCV

Keratin 19

PSC



Fibronectin 1



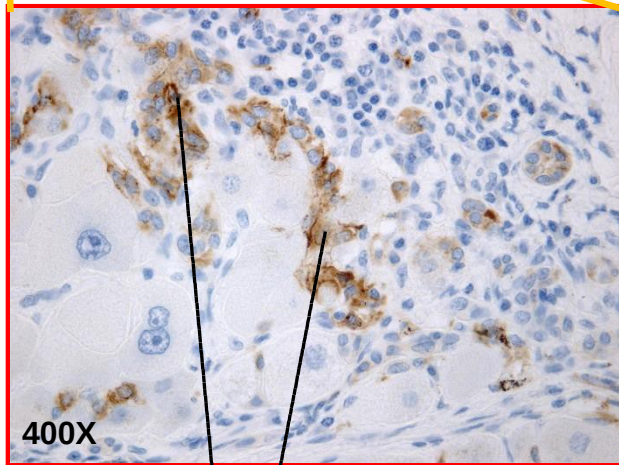
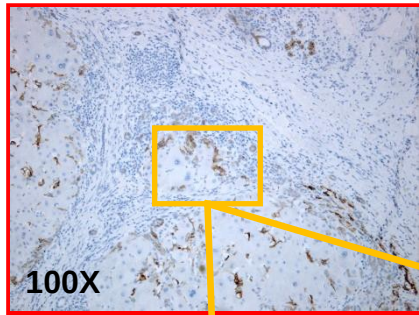
Hepatic progenitor cells and their niche

Differences in HPC surrounding immune cells

HPCs in HCV show elevated expression of 'macrophage receptor with collagenous structure'

Cirrhotic stage

HCV

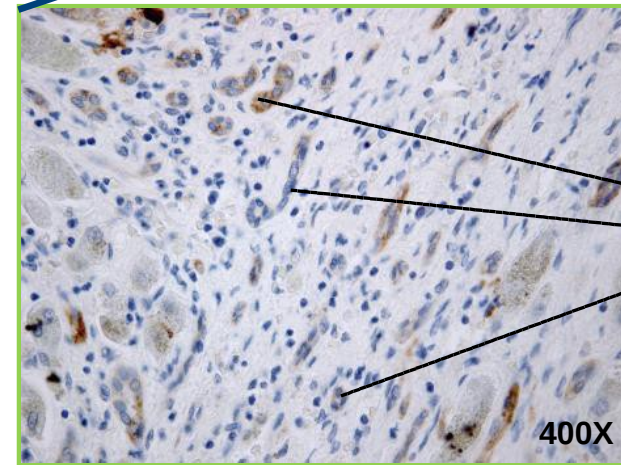
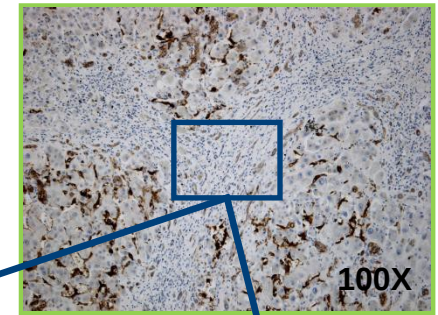


HPC

MARCO

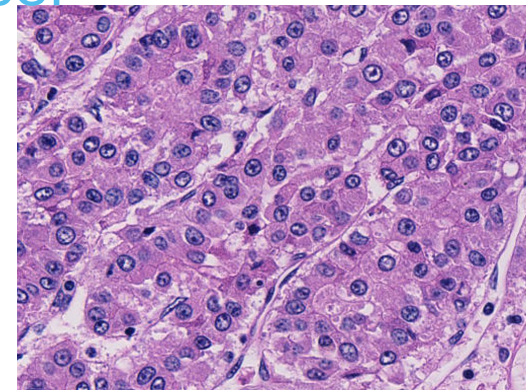
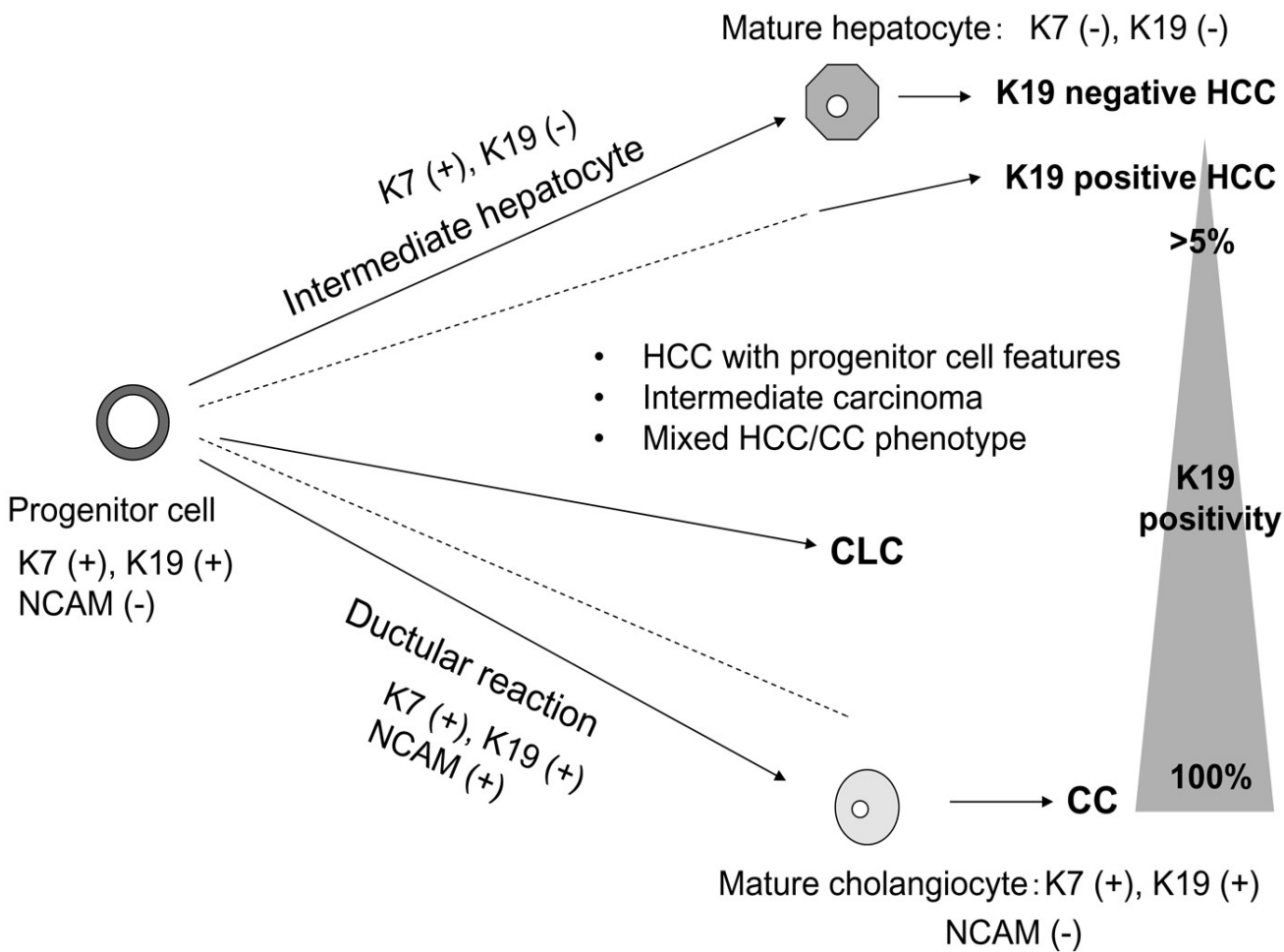


PSC

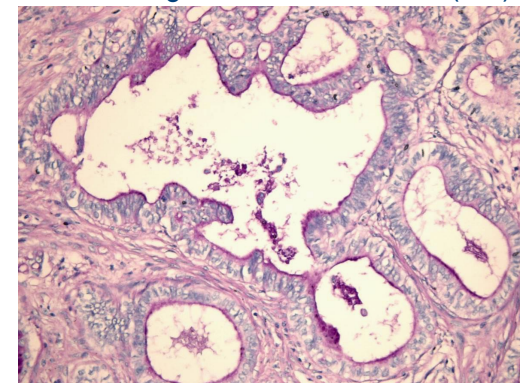


HPC

Hepatic progenitor cells and their role in cancer



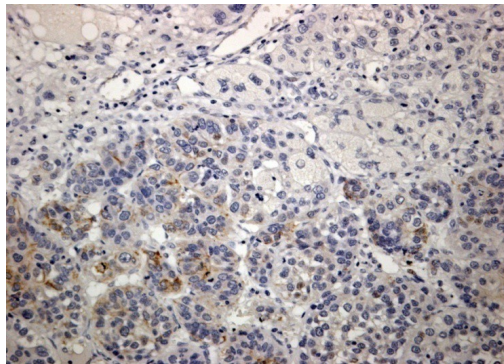
Hepatocellular carcinoma (HCC)



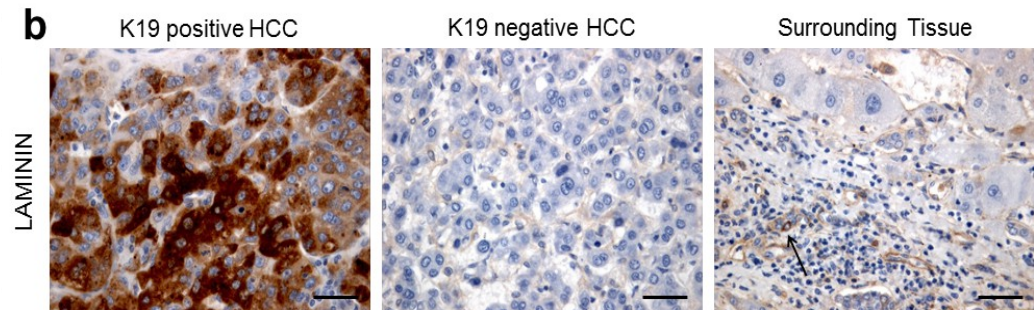
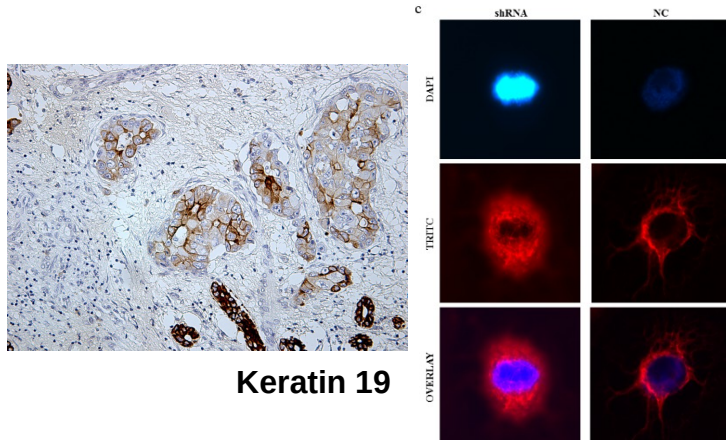
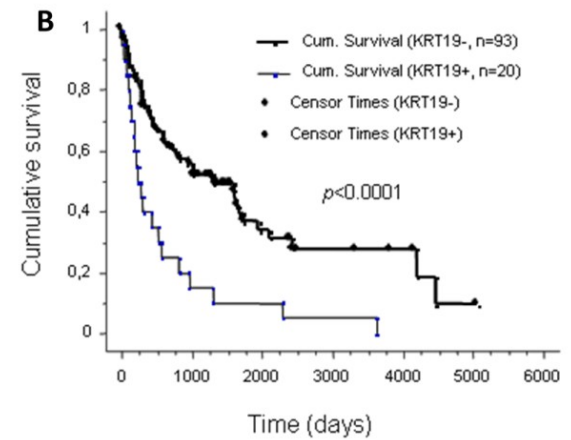
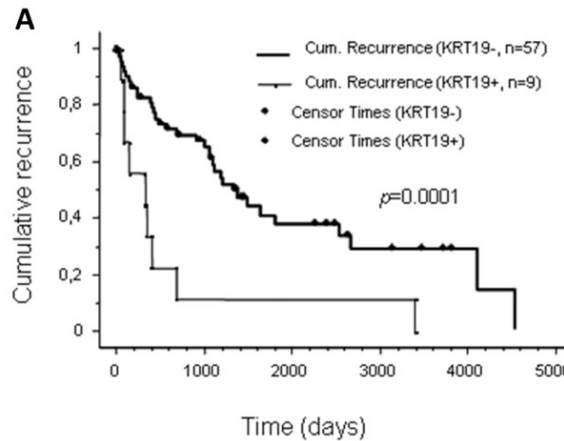
Cholangiocellular carcinoma (CC)

Hepatic progenitor cells and their role in cancer

Keratin 19, a key role player in the invasion of human HCCs

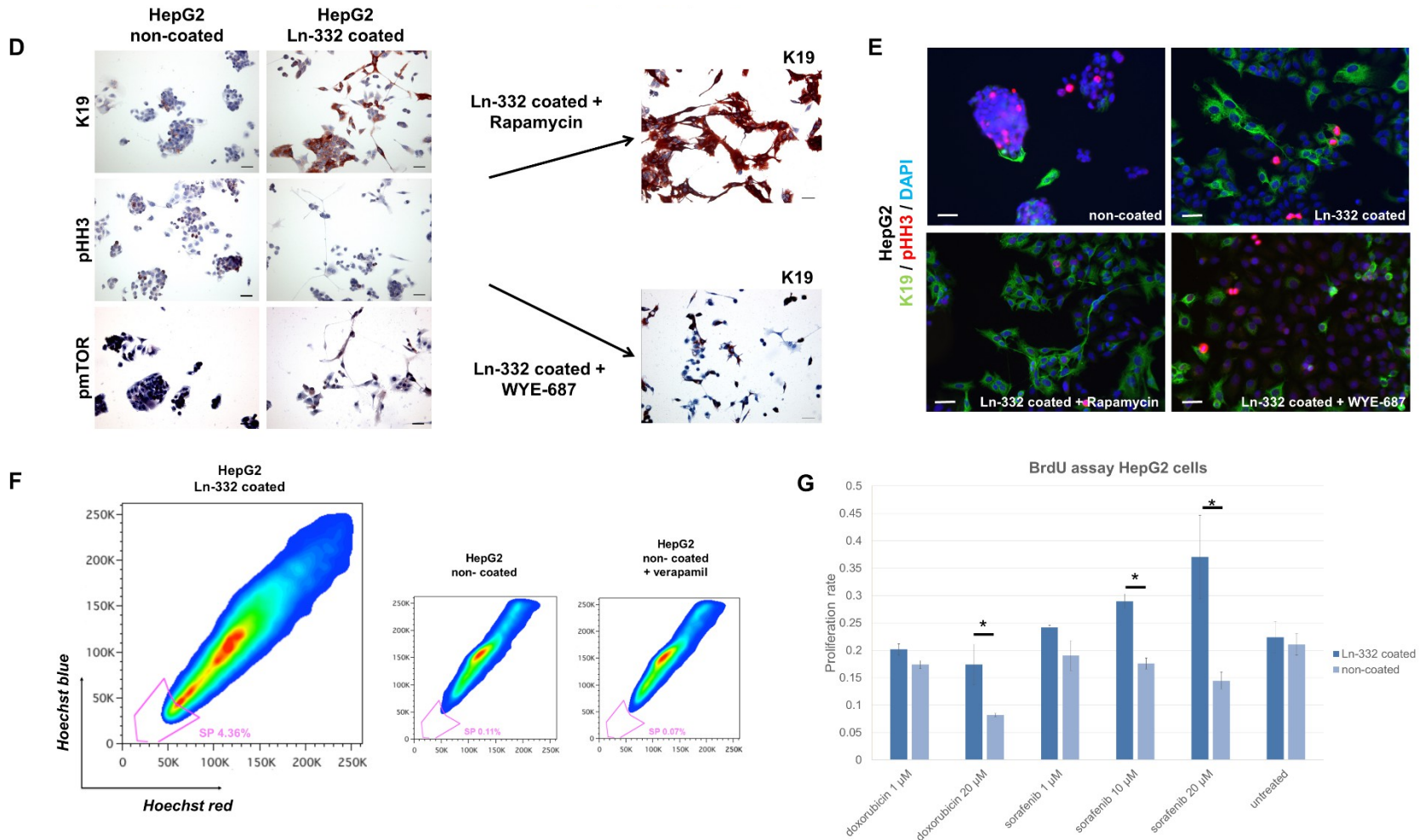


Keratin 19

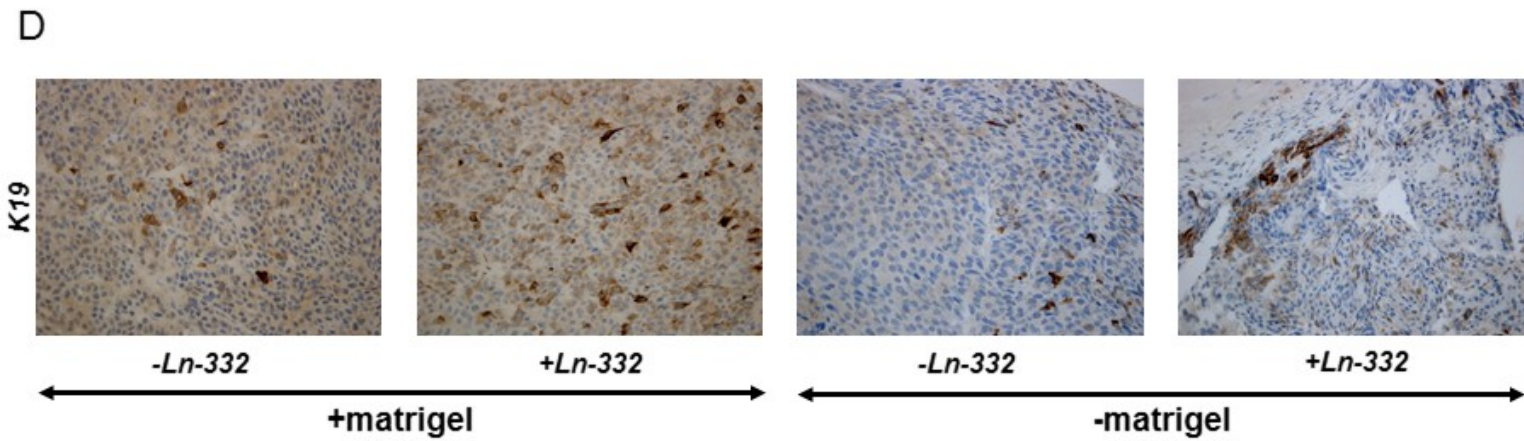
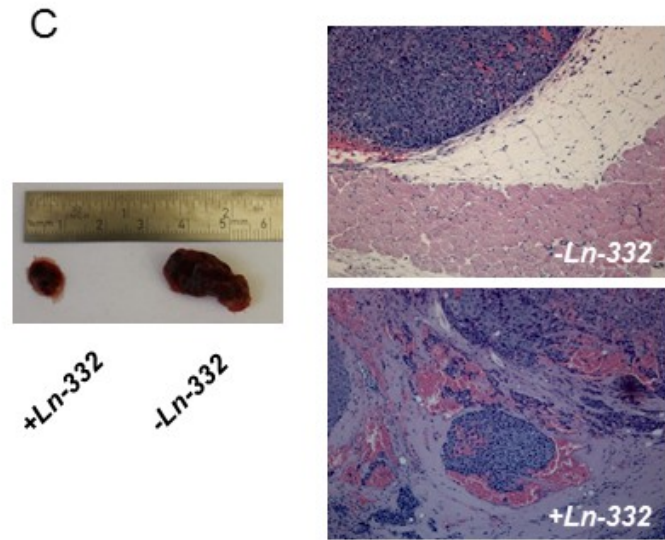
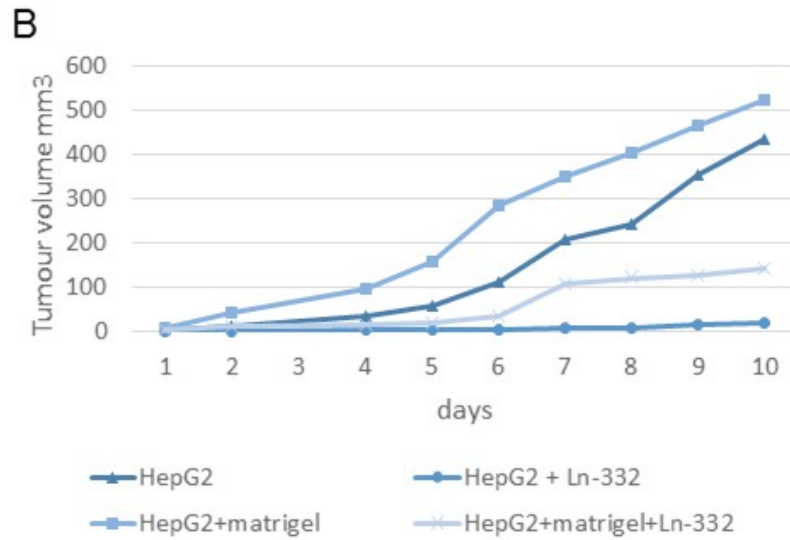


Hepatic progenitor cells and their role in cancer

Laminin-332 induces chemoresistance and quiescence



Hepatic progenitor cells and their role in cancer



Conclusion

*Understanding the complex interactions between hepatic progenitor cells and their micro-environment, brings us a step closer to **modulate and improve liver regeneration** in patients but it also helps us to apprehend **cancer behaviour**.*

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PUBLIC RELEASE: 24-NOV-2014

Cell therapy trial offers new hope to liver disease patients

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Liver disease patients could be helped by a new cell therapy to treat the condition.

Researchers from the University of Edinburgh have received funding to start testing the therapy in patients within the next year.

It will be the world's first clinical trial of a new type of cell therapy to treat liver cirrhosis, a common disease where scar tissue forms in the organ as a result of long-term damage.

The Edinburgh team has received funding from the Medical Research Council and Innovate UK to investigate the disease which claims 4000 lives in the UK each year.

Media Contact
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44-131-650-6514

[@uniofedinburgh](#)
<http://www.ed.ac.uk>

More on this News Release

Cell therapy trial offers new hope to liver disease patients
UNIVERSITY OF EDINBURGH

FUNDER
Medical Research Council Innovate UK

http://www.eurekaalert.org/pub_releases/2014-11/uoec-ctt112414.php



Thank you!



Young Belgian Association for Study of the Liver

