AASLD Nov. 4-8, 2022

The Liver Meeting®

WASHINGTON D.C.

The Best of The Liver Meeting®

CHOLESTATIC AND AUTOIMMUNE LIVER DISEASES

About the program:

Best of The Liver Meeting 2022 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

Use of these slides:

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Telomere attrition in primary sclerosing cholangitis occurs through TGFβ-mediated repression of telomerase reverse transcriptase

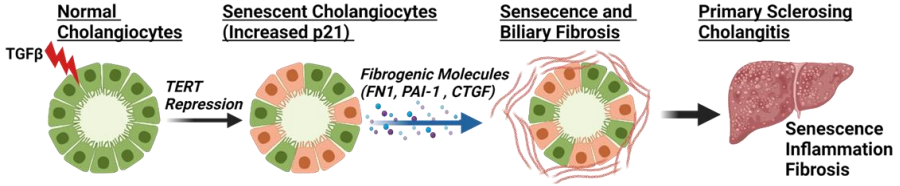
Objective

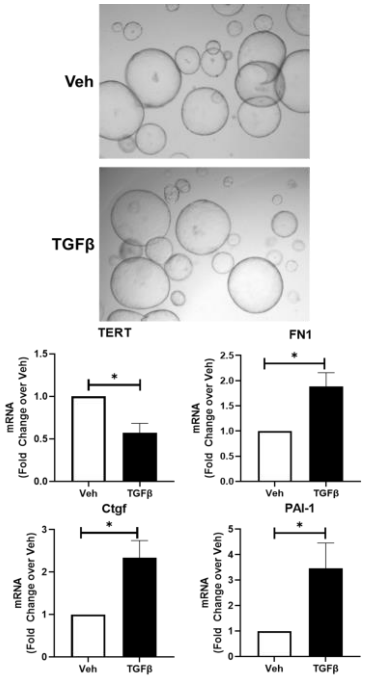
- Investigate mechanistic relationship between TGFβ signaling and telomere dysfunction in PSC.

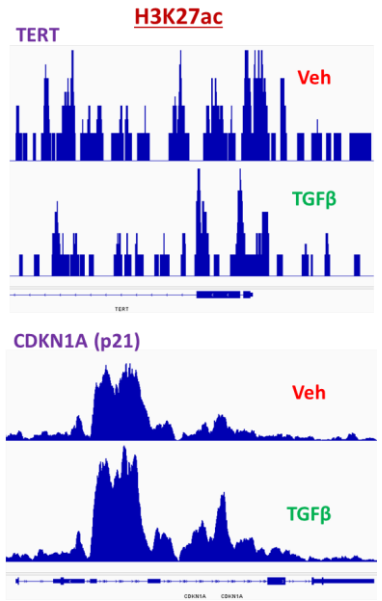
Methods

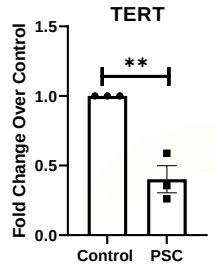
- Cholangiocyte-derived mouse organoids treated with TGFβ.
- PSC patient-derived organoids.
- Cholangiocyte-selective deletion of telomerase in mice.
- ChIP-seq on cholangiocytes treated with TGFβ.

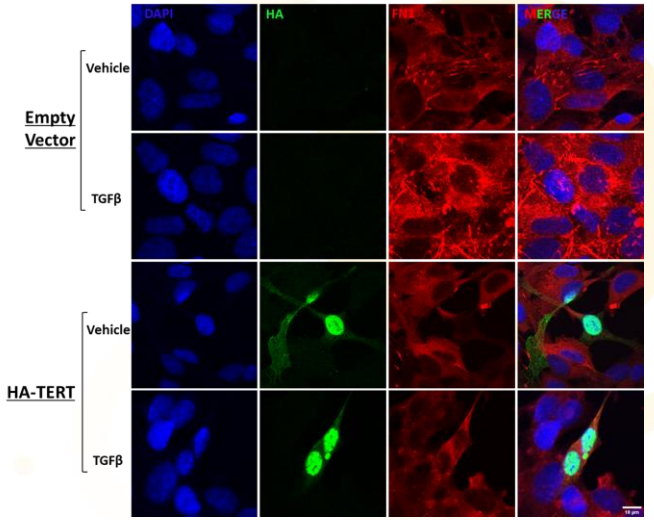
Main Findings

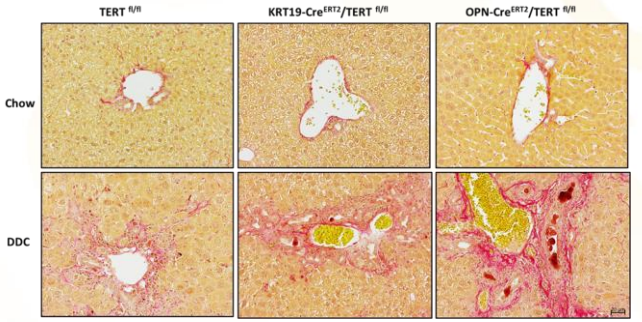












Conclusions

PSC pathogenesis is in part mediated through TGFβ-mediated TERT repression, providing a rationale for TERT-directed therapy in PSC.

Jalan-Sakrikar N, et al., Abstract 3303.

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Phosphorylation of the cMYC proto-oncogene mediates the cholangiocyte response to senescence inducing stress

Aim

- To test the hypothesis that the proto-oncogene, cMYC, functions as a “molecular switch” driving the cholangiocyte response to stress.

Methods

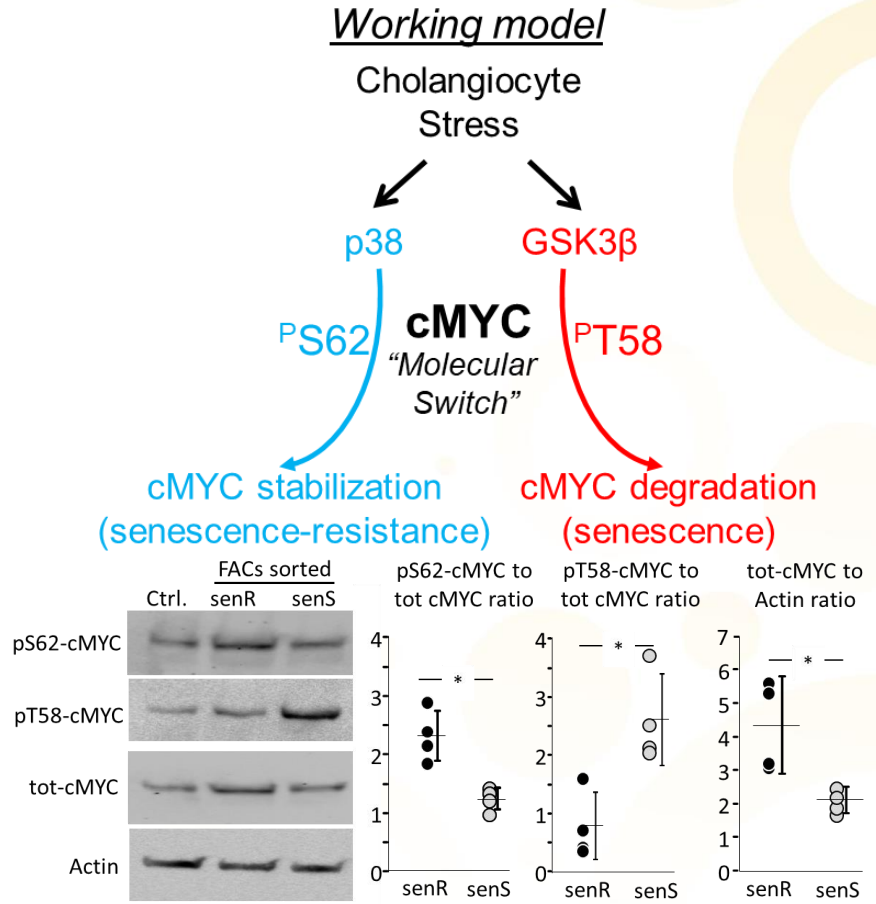
- Normal human cholangiocytes were induced to senescence with LPS, FACs sorted into senescence-resistant (senR) and senescence-sensitive (senS) populations and immunoblotted for total and phosphorylated cMYC.

Main Findings

- In senR cholangiocytes, the p38 kinase phosphorylates S62-cMYC leading to cMYC stabilization while in senS cholangiocytes, the GSK3β kinase phosphorylates T58-cMYC leading to cMYC degradation.

Conclusions

- The phosphorylation state of cMYC promotes either cholangiocyte resistance or sensitivity to experimentally induced senescence.



Splinter P, et al., Abstract 3304.

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