Morphological and Mechanical Characterization of Primary Hepatic Stellate Cells

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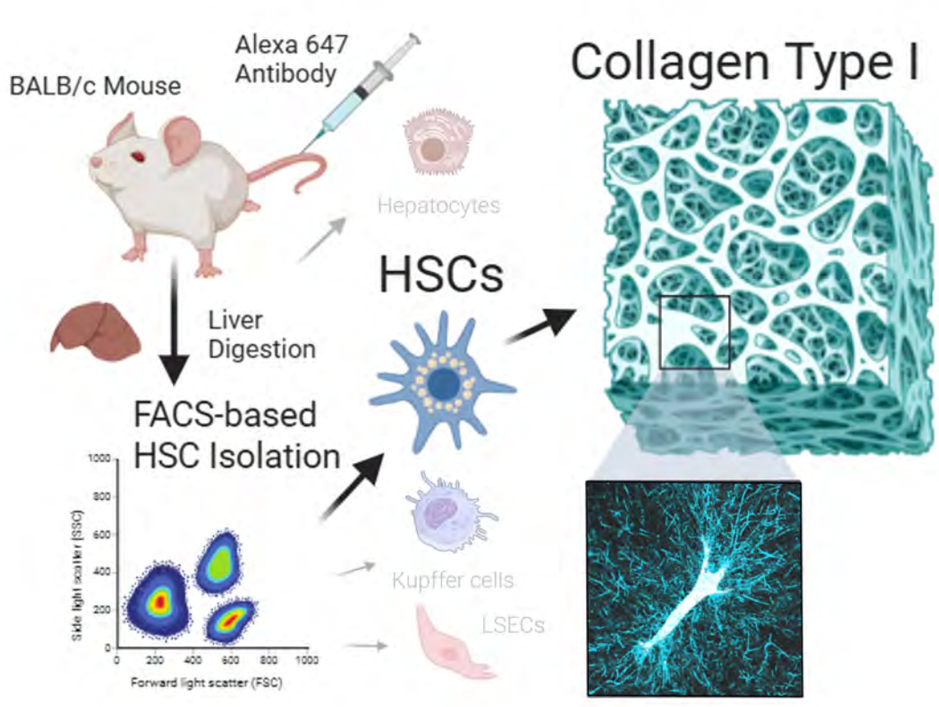
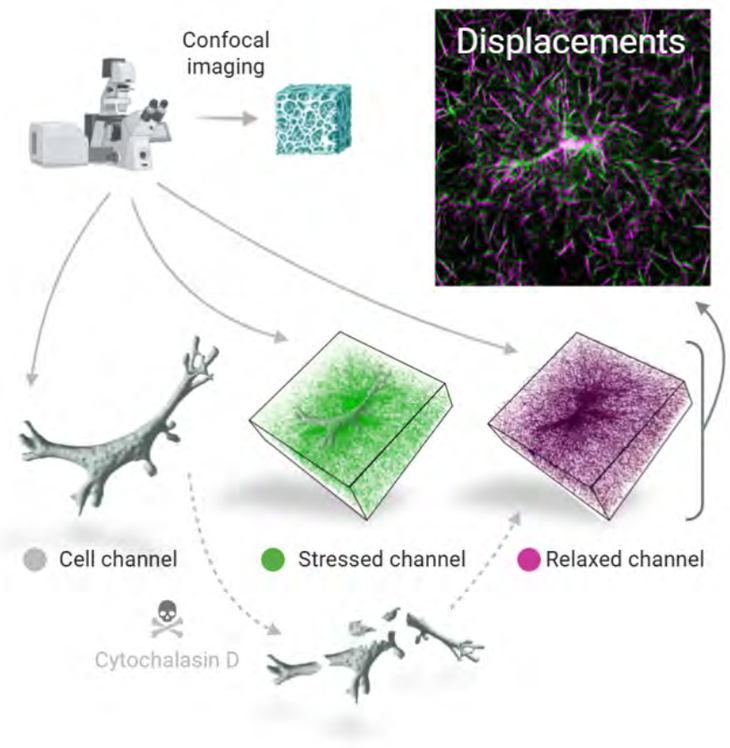
Background

- **Hepatic stellate cells (HSCs)** play a pivotal role in **liver fibrosis**. Liver damage triggers the transition from quiescent HSCs to activated, smooth muscle cell-like aHSCs. aHSCs induce **ECM remodeling**, causing scar tissue formation. aHSCs also acquire a highly **contractile** phenotype, which can lead to **portal hypertension**[1,2,3].
- By using **freshly isolated mouse HSCs**[4], cells remain **quiescent** until stimulation induces a transition to an activated phenotype.
- Using **single-cell 3D traction force microscopy** allows us to precisely monitor the changes in cell contractility during the initiation of HSC activation.
- This approach allows us to evaluate the effect of **compounds targeting portal hypertension** and determine the role of **alpha smooth muscle cell actin**.

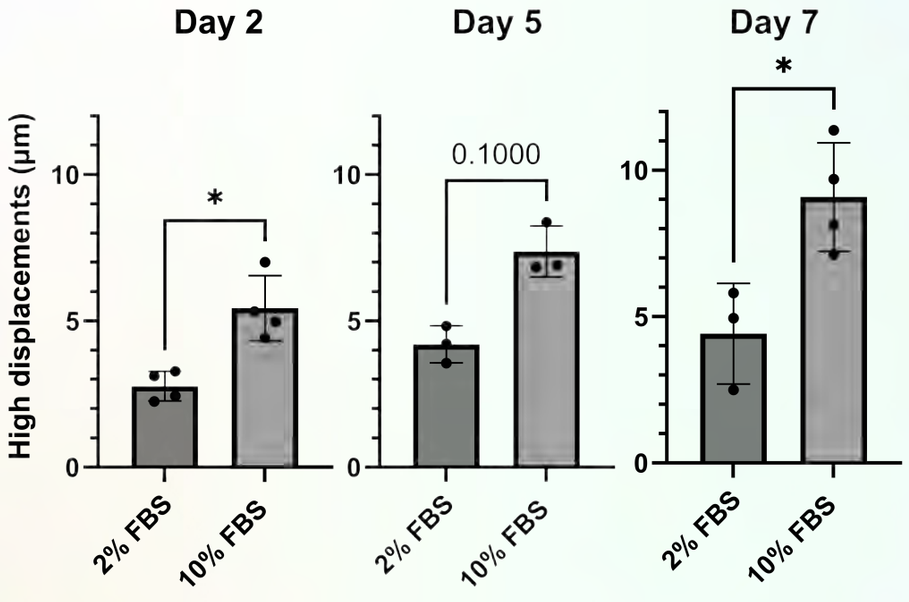
Sample Preparation

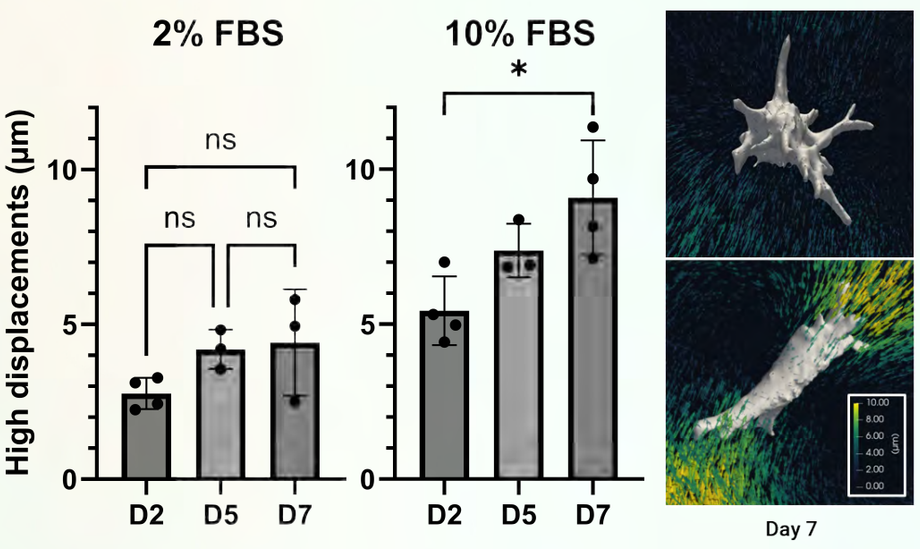


3D Traction Force Microscopy

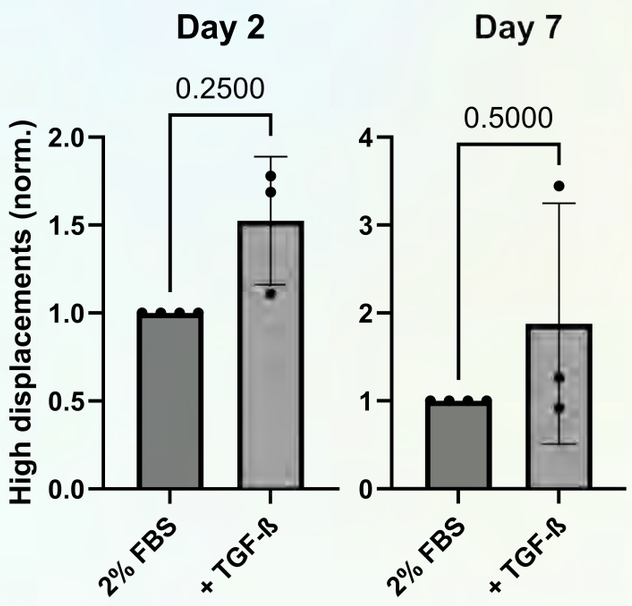


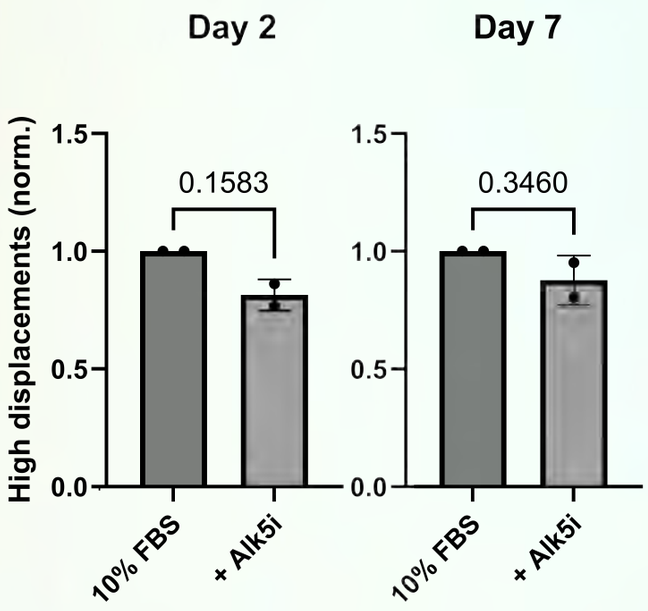
Response of quiescent HSCs to activation factors is time and concentration dependent



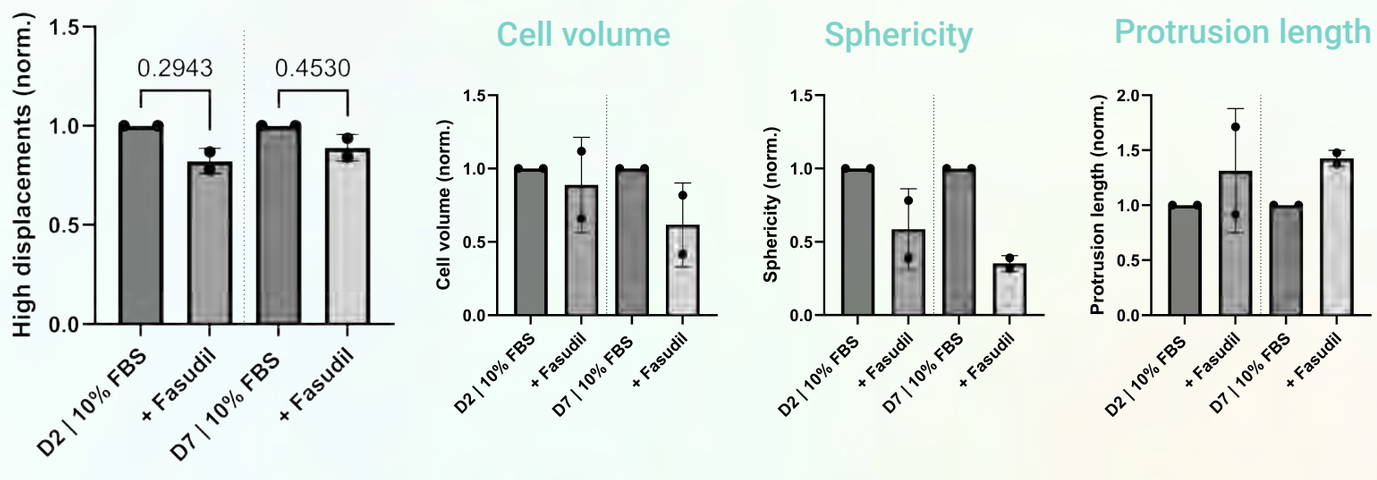


Modulation of TGF-ß signaling affects contractility of quiescent HSCs

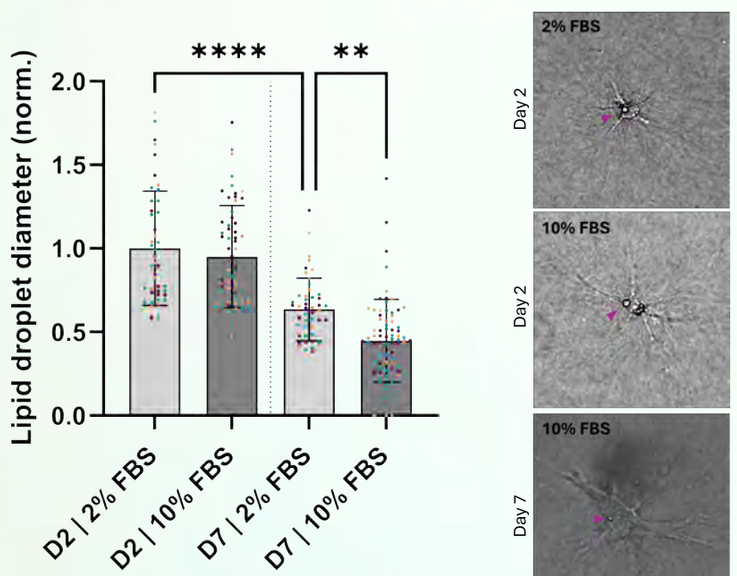


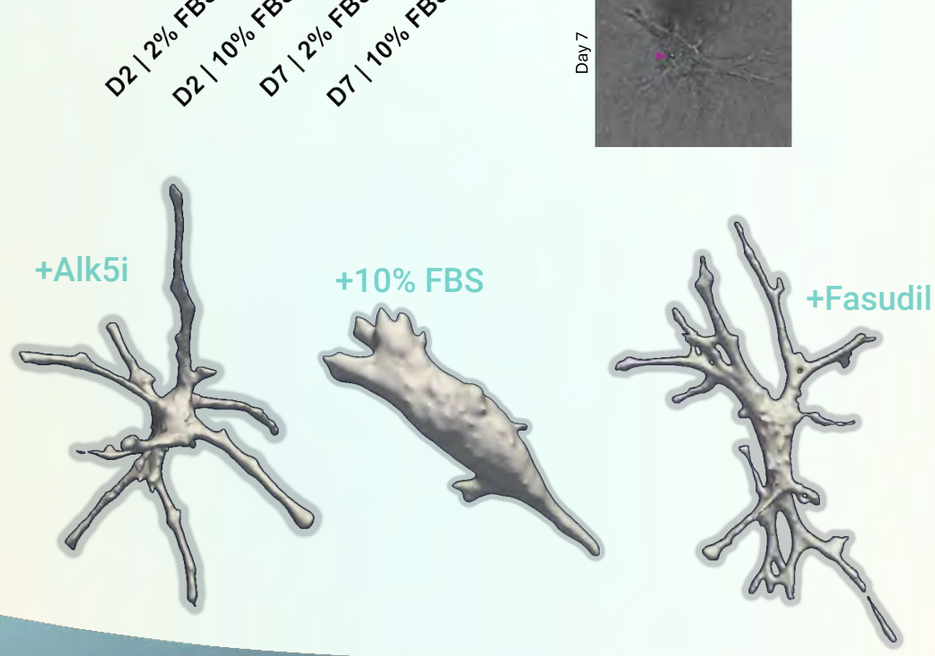


PDE5 inhibitor Sildenafil affects HSC contractility and morphology

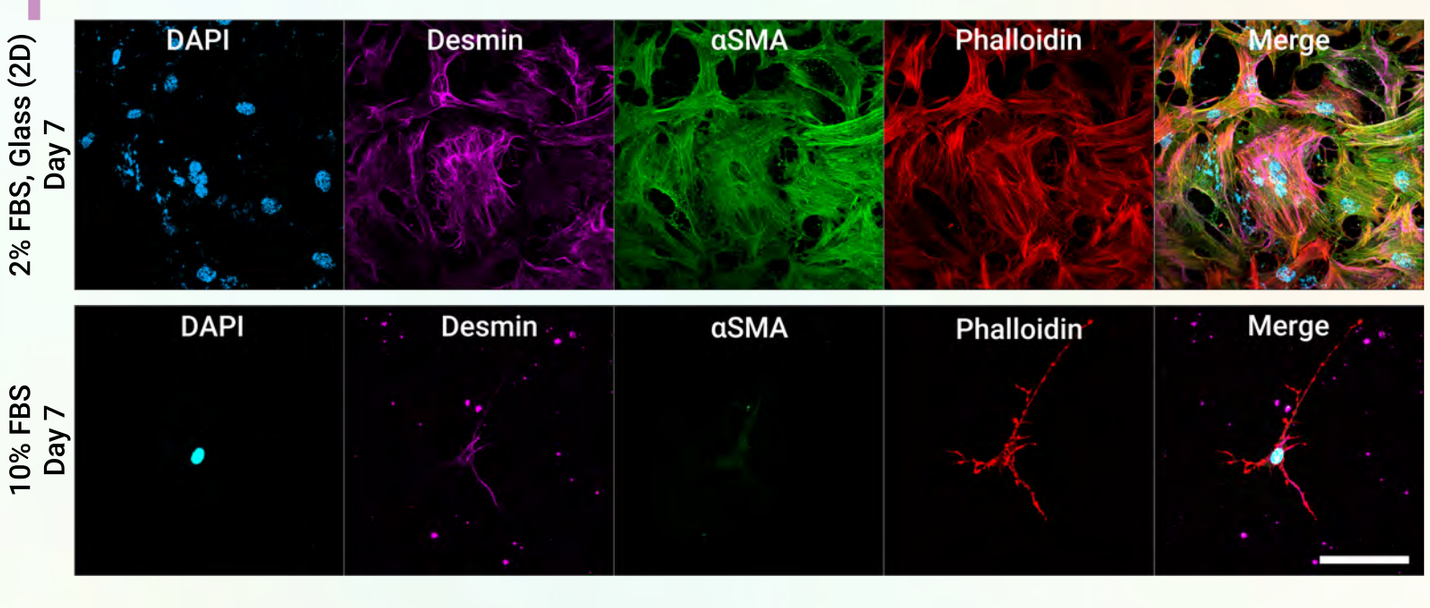


Lipid droplet loss increases by activation factors





Evaluation of αSMA expression as a marker for HSC activation



References

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[2] Troeger, Juliane S., et al. "Deactivation of hepatic stellate cells during liver fibrosis resolution in mice." Gastroenterology 143.4 (2012): 1073-1083.

[3] Iwakiri, Yasuko, and Jonel Trebicka. "Portal hypertension in cirrhosis: Pathophysiological mechanisms and therapy." JHEP reports 3.4 (2021): 100316.

[4] van Os, Elise Anne, et al. "Modelling fatty liver disease with mouse liver-derived multicellular spheroids." Biomaterials 290 (2022): 121817.

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