The Effect of Matrix Stiffness on Lipid Processing, Cell Function, and Morphology in HepG2 cells

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INTRODUCTION

- Disease progression to cirrhosis in Non-Alcoholic Steatohepatitis (NASH) leads to increased mechanical stiffness that affects liver parenchymal and non-parenchymal cells.
- Mechanical stiffness of the extracellular matrix (ECM) is sensed by cells through mechanotransduction, which influences cell function and metabolism.

AIM

To model how liver ECM stiffness affects liver specific HepG2 cell lipid processing, cell function and morphology.

MATERIALS AND METHODS

- Polyacrylamide gels of three different stiffnesses, 0.1 kPa, 1.3 kPa, and 35 kPa were cast and covered with Collagen I.
- HepG2 cells were treated with serum-free media or supplemented with 200 uM Oleic Acid (OA) for 24 hours on collagen laden gels.
- Cells were imaged using Bodipy neutral lipid stain, Hoechst nuclei stain, and Phalloidin stain for the actin cytoskeleton.
- Cell analysis was performed using ImageJ.
- Immunofluorescence assessed the nuclear transcription factors YAP1 and HNF4 expression, HLA-ABC, ATP8, MTATN3, and TLC2D (p<0.01).
- qPCR and RNAseq evaluated gene expression.

RESULTS

- Increased (Inc) Cell Spread (avg cell area: 146 uM and 277 uM in 0.1 and 35 kPa)
- Inc mitochondrial metabolic gene expression MT-ND1, MT-ND2, MT-CO2, MT-ATP8, MT-ATP6 (p<0.05).
- Inc mechanotransduction and membrane rigidity gene expression, HLA-F, MATN3, and TLC2D (p<0.01).

CONCLUSION

- Increasing matrix stiffness affects lipid processing, transcription factor gene expression, and cell morphology of HepG2 cells.
- This reflects the changes that cells experience throughout disease progression through fibrosis and cirrhosis, altering gene expression, structure, and function.

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REFERENCES


DISCLOSURES

Nothing to disclose

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