Title: Biomechanics of hepatic stellate cells

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Chronic tissue injury and inflammation produces liver fibrosis as a deregulation of normal healing process with upregulated secretion of extracellular matrix proteins. The transition of quiescent (fibroblast-like phenotype) to activated (myofibroblast-like phenotype) stellate cells is a marker for the onset of fibrosis that may appear for example in Hepatocellular Carcinoma (HCC). Stiff microenvironment provides tensional homeostasis needed for activated stellate cells to maintain their phenotype in a positive feedback loop. Tissue fibrosis can be tackled by breaking the quintessential mechanical response feedback loop - restoring extracellular matrix mechanics or pharmacological inhibition of cells ability to apply forces to the surrounding environment.

Project aims

Rigidity sensing has been shown to trigger numerous cellular process including carcinogenesis. The aim of this project is to investigate [by culturing cells on rigidities mimicking different liver
conditions (healthy and fibrotic)] alterations in: signalling pathways, involving changes in mutual inhibition and activation between RhoA-related pathway proteins (during cell migration towards fibrosis sites and the degree of matrix degradation by matrix metalloproteinases. This will lead to the identification of proteins taking part in different stages of fibrosis that we can target in future to efficiently inhibit or reverse fibrosis.

Key techniques: tissue culture, immunofluorescence, Western Blot, real-time qPCR, cell motility assays, gelatine zymography, Biophysical and cell biology techniques used in our group. http://biomechanicalregulation-lab.org/techoverview/

References:

Recent from the CMBL group:


Haining AWM, Rahikainen R, Cortes E, Lachowski D, Rice AJ, von Essen M, Hytönen VP, del Río Hernández A. **Mechanotransduction in talin through the interaction of the R8 domain with DLC1.** *PLoS Biology 2018*

Lachowski D, Cortes E, Robinson B, Rice AJ, Rombouts K, del Río Hernández A. **FAK controls the mechanical activation of YAP, a transcriptional regulator required for durotaxis.** *FASEB J 2017*

General references – Hepatic Stellate Cells