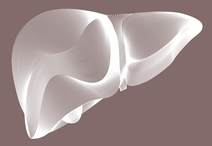

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Reading Between the Fibres: AI Reveals Hidden Patterns in MASLD

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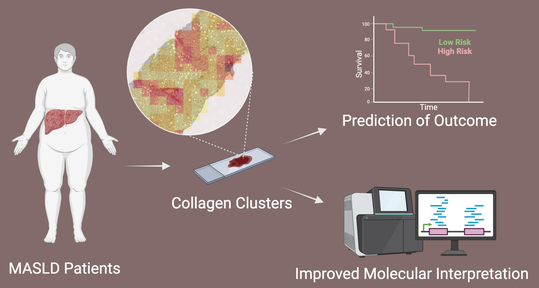
Objectives

We set out to provide a more granular assessment of liver fibrosis – one which overcomes the limitations of collagen proportionate area (CPA) and traditional fibrosis scoring.

- To identify patterns of fibrosis that can predict liver-related events.
- To assess if local morphology of the extracellular matrix (ECM) can be associated with established transcriptomic markers of fibrogenesis.



Our methods were developed and validated on a group of 187 MASLD patients and 15 healthy volunteers from the FLINC cohort.

Conclusions

Collagen phenotypes **bridge the gap between histology and transcriptomic profiling** allowing for a cost-effective analysis of retrospective cohorts of patients with MASLD. This approach can be used to develop histology-based biomarkers for disease progression.

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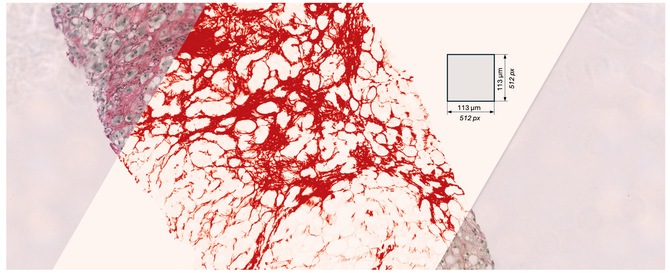
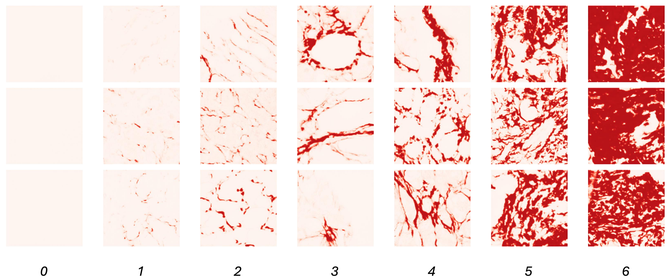
Online version

Methods

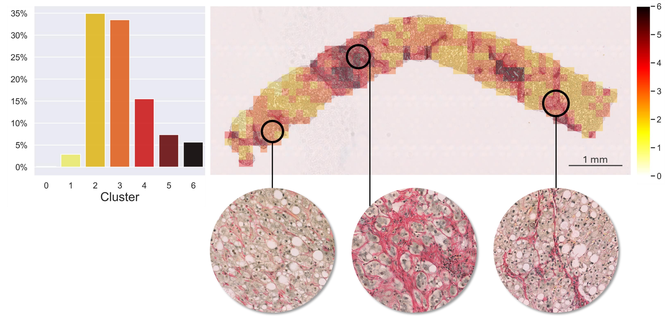
We've developed a **novel digital pathology pipeline for collagen analysis**.



Collagen fibres are identified from Picrosirius Red (PSR)-stained slides with high precision by a U-net deep learning network.

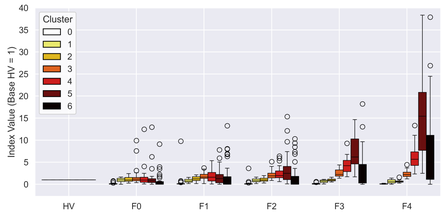


AI was leveraged to identify **7 clusters of ECM patterns**, ranging from no identifiable collagen *(0)*, through normal parenchymal ECM *(1)* to increasingly collagen-dense anatomical and pathological structures *(2-5)*, and scars *(6)*.



The trained AI model for collagen clusters allows to map spatial distribution of fibrosis and to **quantify the different components of ECM architecture**.

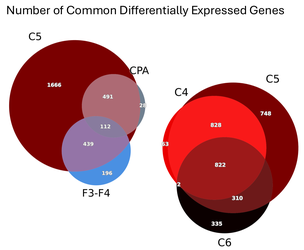
Results



Prediction of clinical outcome

C5 is an **independent predictor of liver-related events** on par with CPA and fibrosis score.

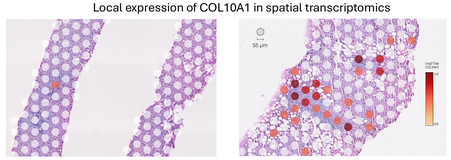
Further studies are needed to find evidence of improvement in risk stratification.



Biological discovery directly from clinical slides

Collagen clusters **are strongly associated with known biomarkers of fibrogenesis** (e.g. COL10A1) and link them with morphological features of the ECM.

Unlike CPA, collagen clusters offer a fine-grained description of **progression and regression** of fibrosis.

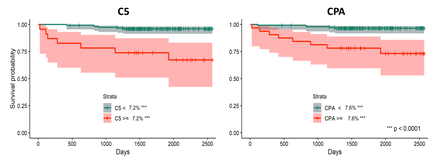


Alignment with fibrosis staging

Collagen clusters disentangle CPA into morphological subtypes of fibrosis.

Tissue proportions of collagen clusters C4, C5 and C6 increase significantly in advanced fibrosis.

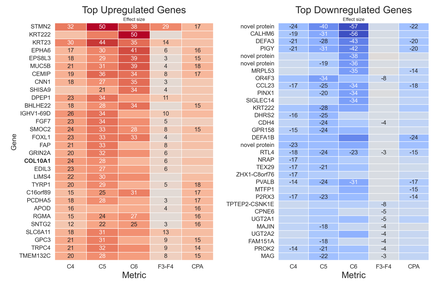
Cluster 5 (C5) is the strongest predictor of bridging fibrosis and cirrhosis.



Transcriptomic illumination

Collagen clusters C4-C6 are significantly **more sensitive transcriptomic markers** of fibrosis than histology score and CPA – allowing to screen for more molecules.

Proportion of C5 is significantly correlated with the highest number of differentially expressed genes, which indicates this cluster identifies areas most actively involved in fibrosis.



The values for C4, C5, C6 and CPA represent change associated with 1% increase in each respective metric. Values for F3-F4 represent fold increase vs. F0-F2. Only values meeting the statistical significance threshold of adjusted P < 0.05 or lower are displayed.

Power in numbers

Our modular method can be applied to **retrospective studies and large cohorts** – supplementing the local precision of spatial transcriptomics.

We are extending this approach to other features of liver disease.

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