Serum Proteomics Reveals Unique Association of CCL24 with Disease-related Pathways and Signatures in Primary Sclerosing Cholangitis

Ilan Vaknin

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Ilan Vaknin

- VP of Research and Development at Chemomab Therapeutics Ltd | Immunologist with 20 years' experience in academia and biotech | PhD in Immunology from the Hebrew University, Postdoctoral Graduate from the Weissman Institute in Neuroscience.

Disclosure and Forward-Looking Statements

- Presenter: Ilan Vaknin
- I disclose the following financial relationship(s) with a commercial interest:
- I work as VP R&D at Chemomab ltd, a Nasdaq traded company.

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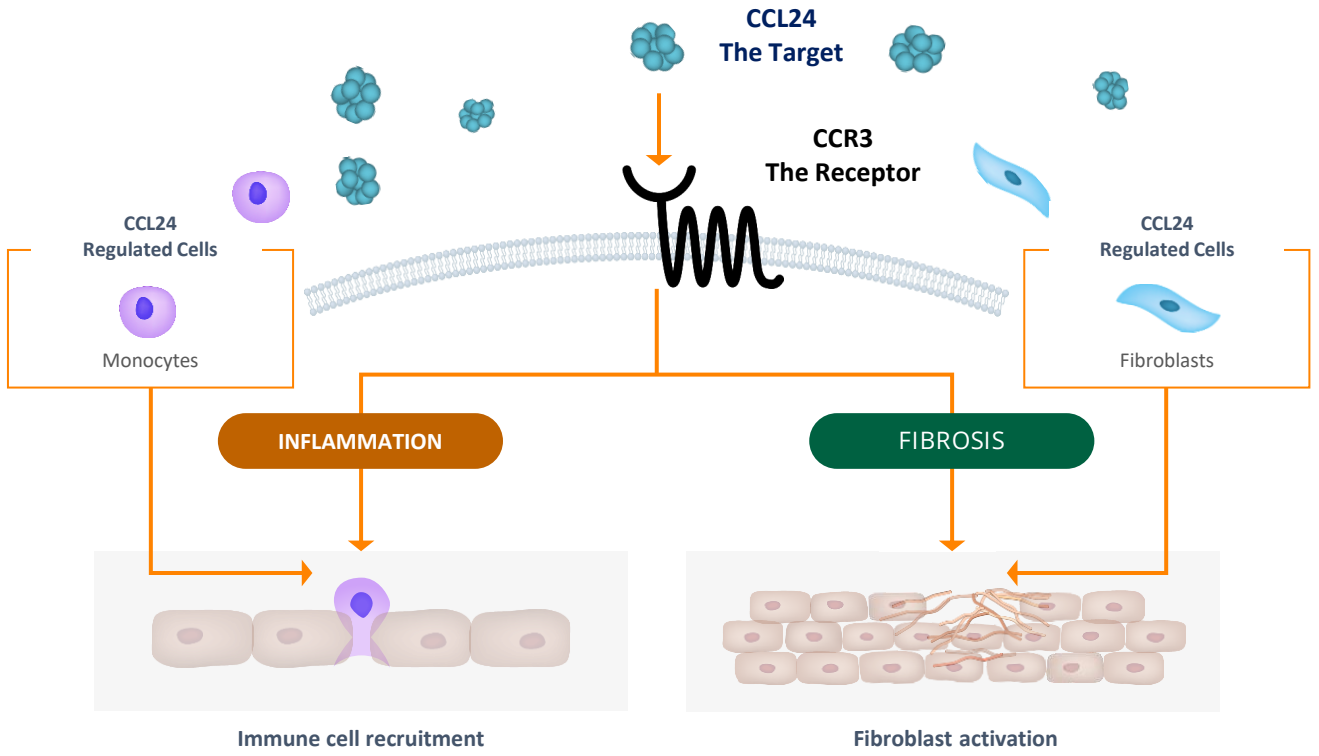
CCL24's Dual Role in Inflammation and Fibrosis-related Pathology



THE POWER OF CCL24

Dual Role in Promoting Fibrosis & Inflammation

Directly activates fibroblasts

Enhances local immune cell recruitment

Differentiated Activity

Data shows unique role vs. other chemokines

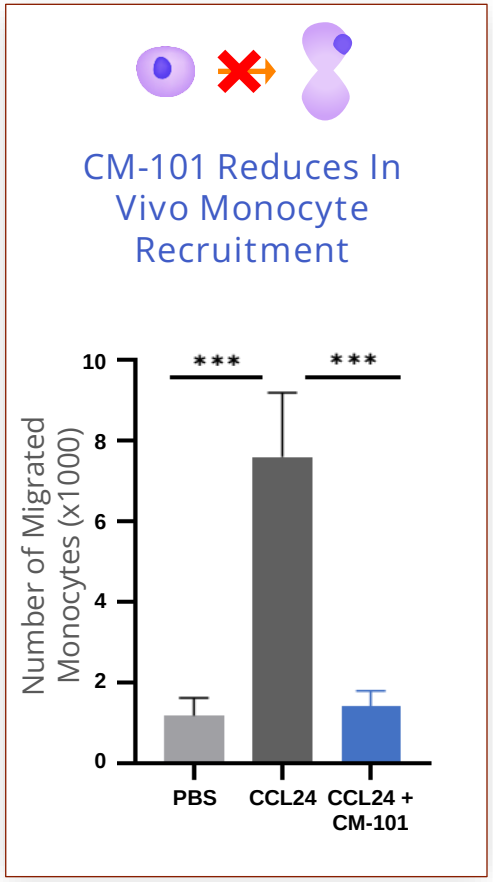
Correlates with fibrotic biomarkers and disease outcome

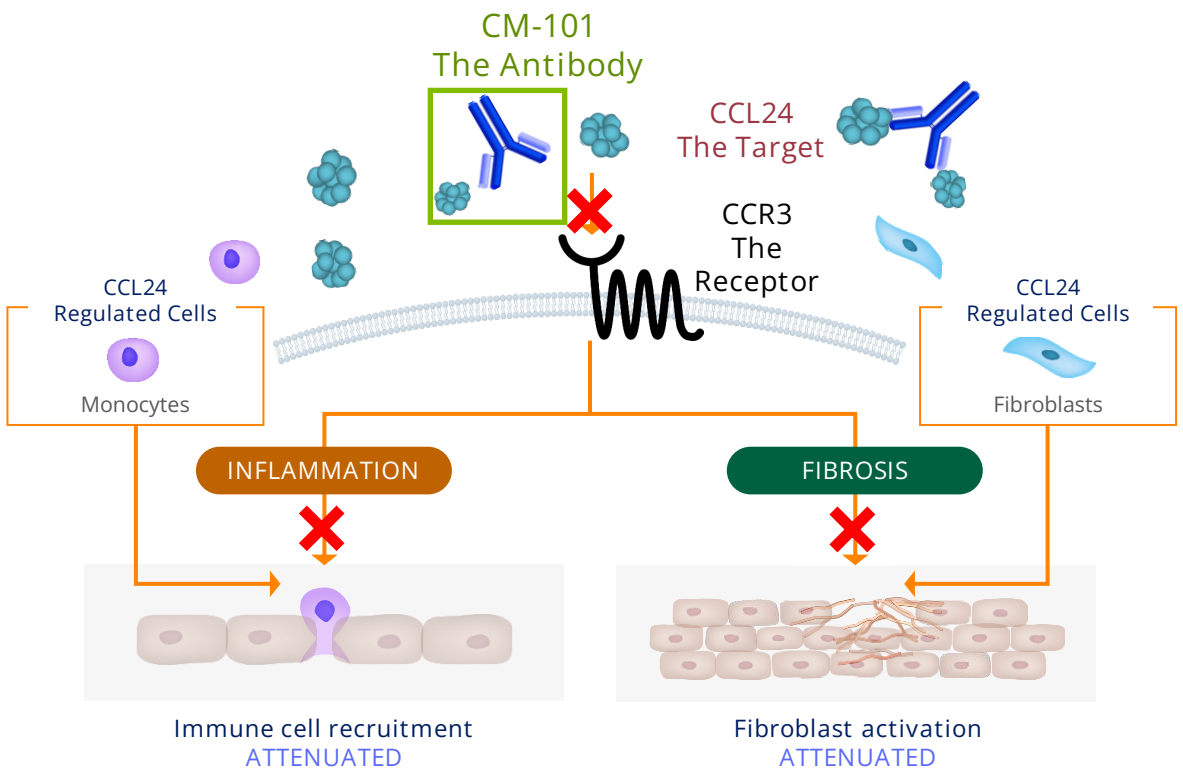
Low in Healthy Tissue; Elevated in Fibrotic Tissue

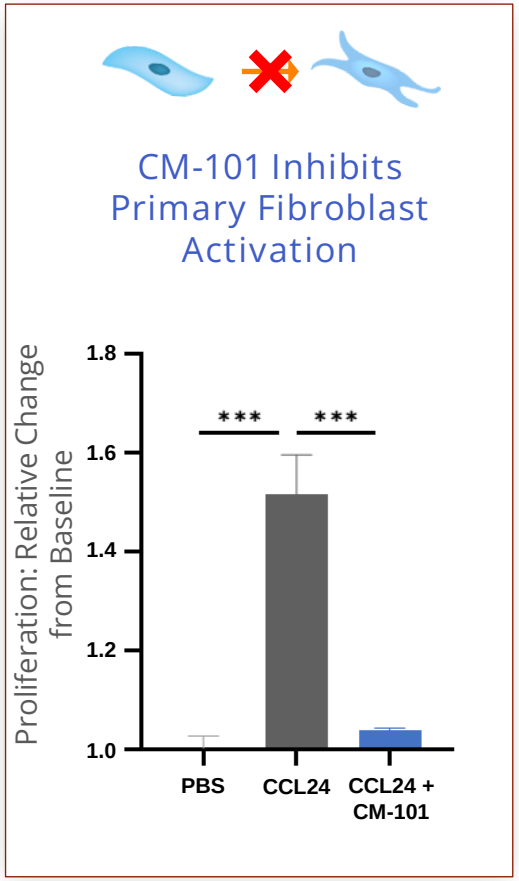
Liver, skin, lung, kidney, others

Wide therapeutic margin

CM-101 Neutralizes CCL24 and Reduces Inflammation and Fibrosis

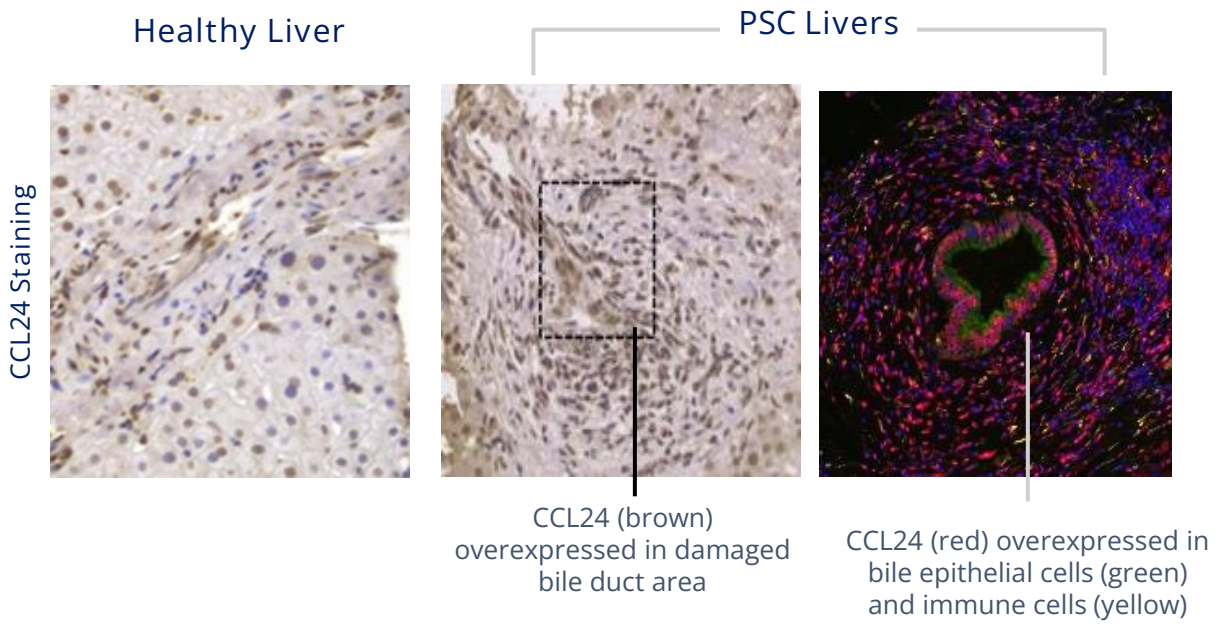




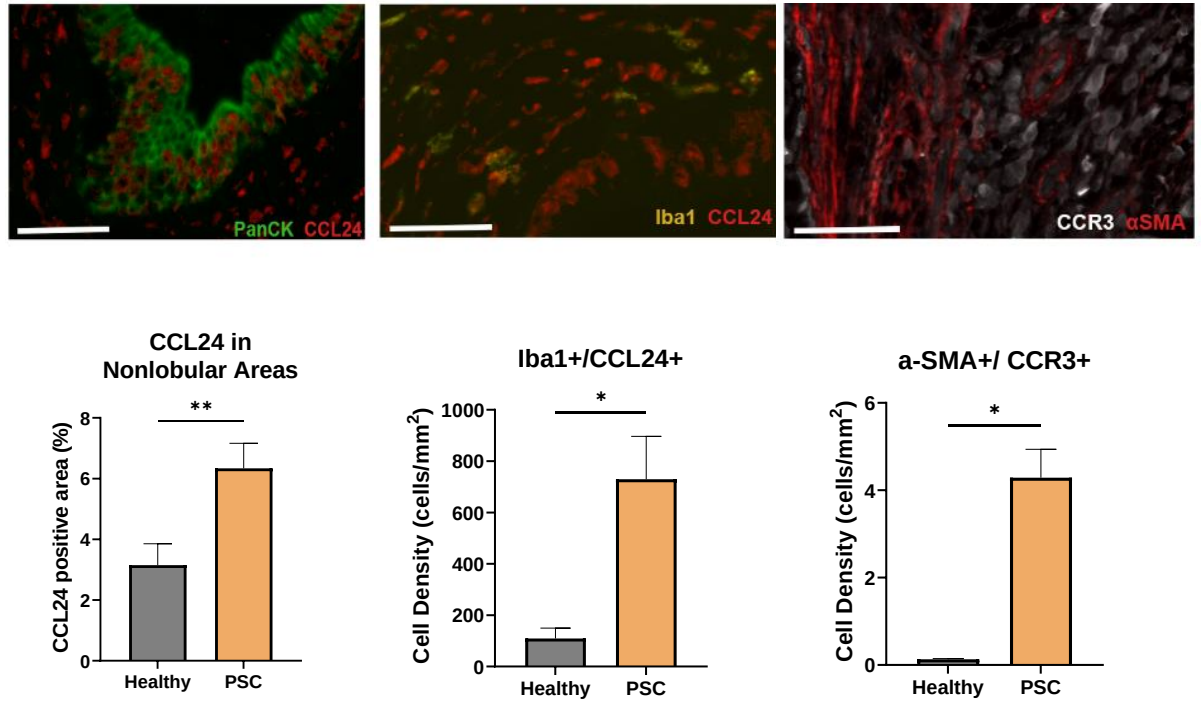


Clinical Relevance of CM-101 Supported by Elevated CCL24 Levels in PSC Patients

CCL24 LEVEL IN HEALTHY VS PSC PATIENT LIVER TISSUE

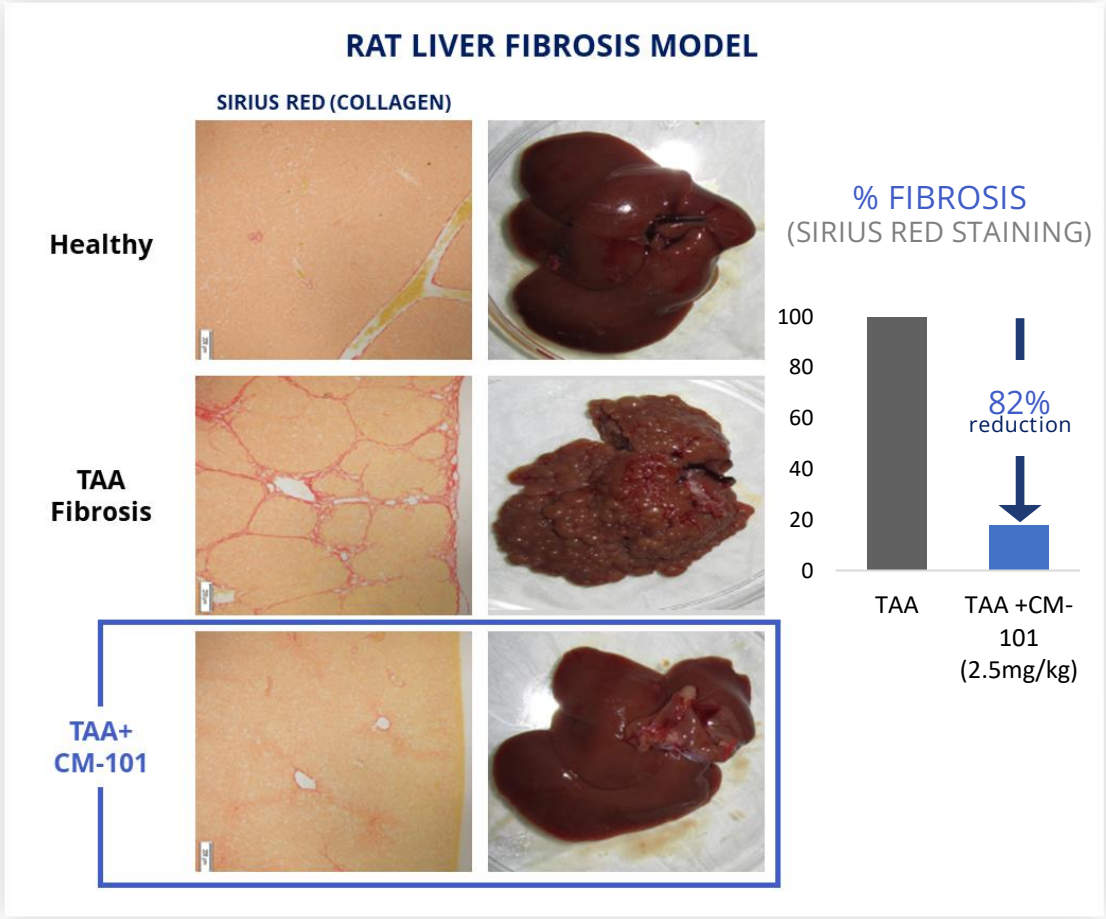


CCL24 AND CCR3 EXPRESSION IN PSC PATIENT LIVER TISSUE

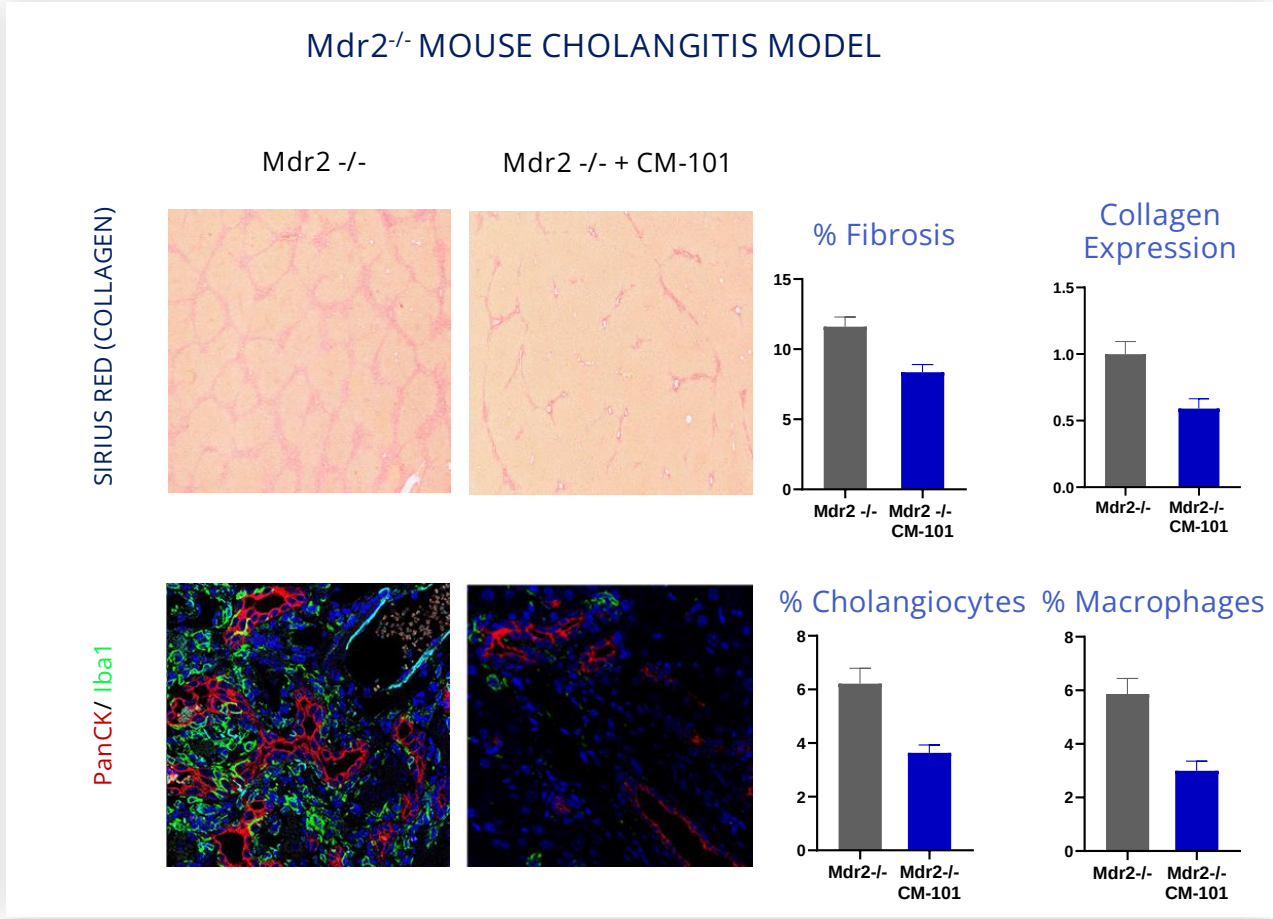


Greenman et al, JCI Insight 2023

CM-101 Reduces Liver Injury & Fibrosis in Multiple PSC Animal Models



Segal-Salto et al, JHEP reports 2020



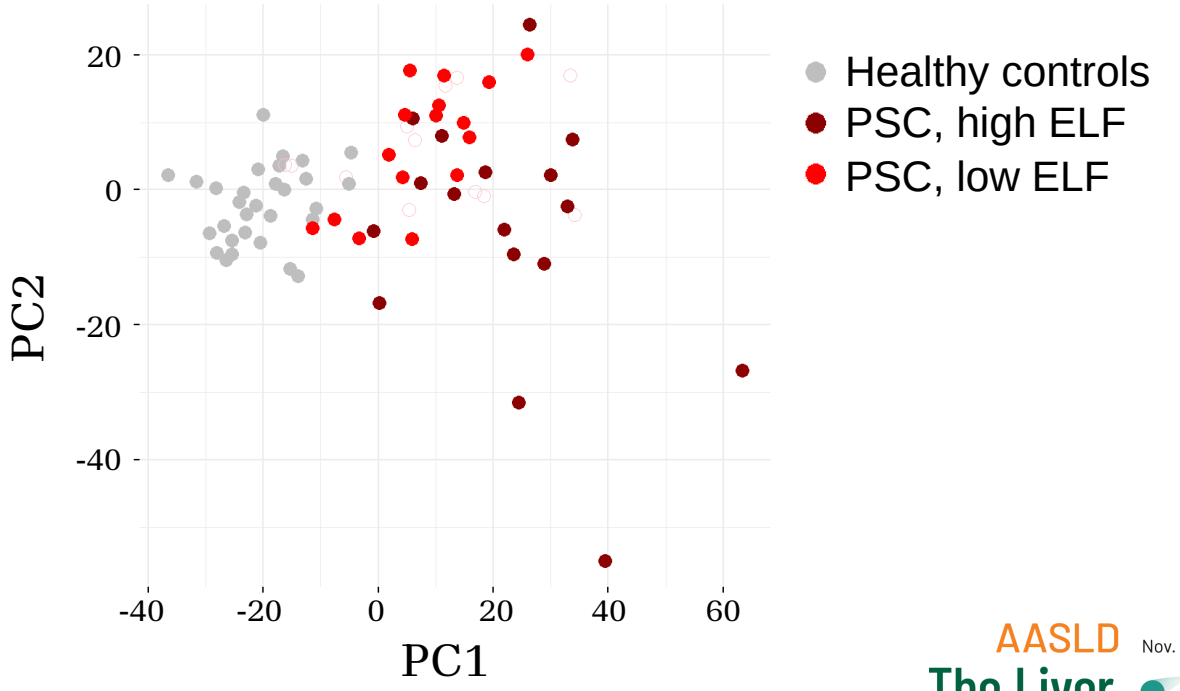
Greenman et al, JCI Insight 2023

Serum Proteomics to Reveal Disease-Related Pathways

- Canonical pathways
- Upstream regulators
- Liver-related toxicity functions

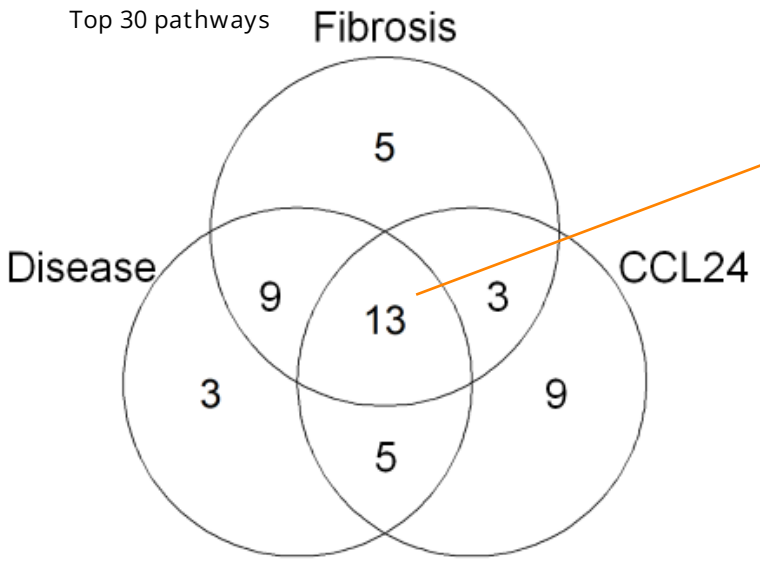
3 Comparison Groups:

- Disease (PSC vs HC)
- Fibrosis Severity (PSC: high vs low ELF score; 9.8 as cutoff)
- CCL24 Levels (PSC: high vs low CCL24; median as cutoff)

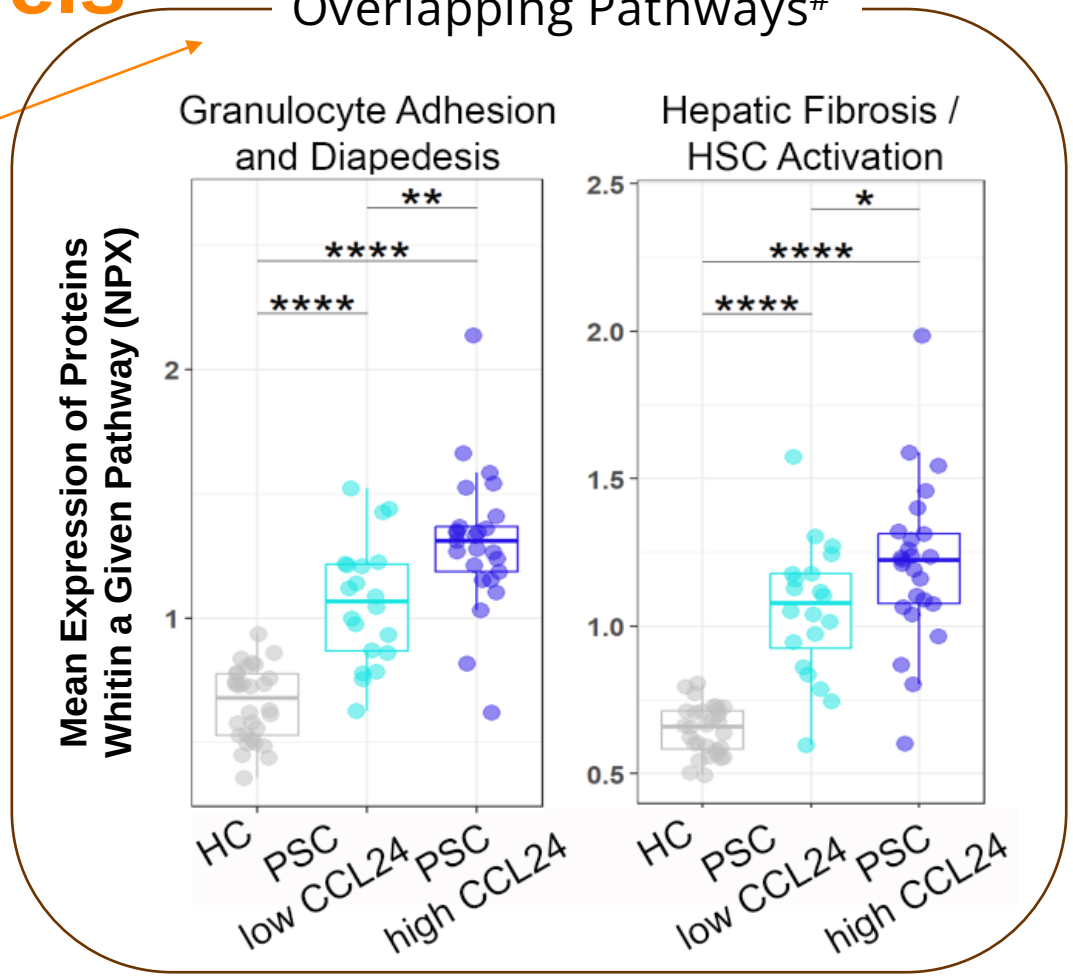


HC, Healthy Controls
ELF, Enhanced Liver Fibrosis

Disease-Related Canonical Pathways Are Elevated in Patients with High CCL24 Levels



Top Overlapping pathways:
[1] Pathogen Induced Cytokine Storm Signaling Pathway
[2] Granulocyte Adhesion and Diapedesis
[3] Agranulocyte Adhesion and Diapedesis
[4] Hepatic Fibrosis / Hepatic Stellate Cell Activation
[5] Wound Healing Signaling Pathway

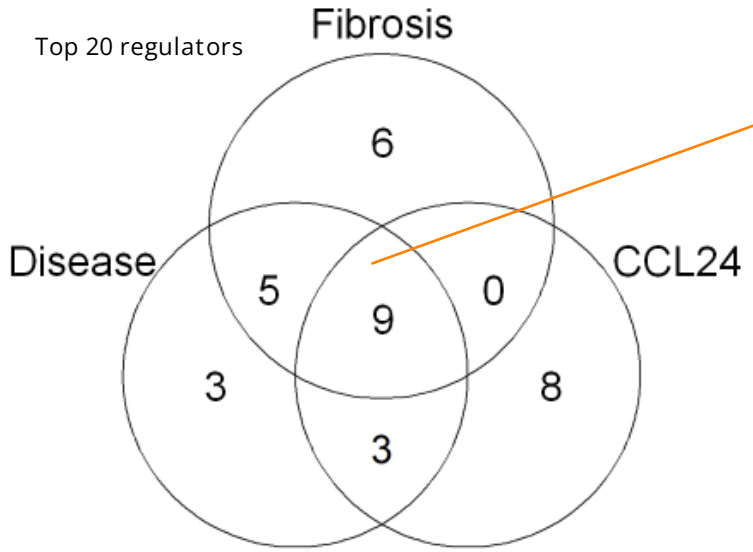


HC, Healthy Controls
HSC, Hepatic Stellate Cells

* p<0.05, **p<0.01, ***P<0.001,**** P<0.0001 Welch 2-sample t-test

* Similar effects in other overlapping canonical pathways, including fibrosis, chemotaxis and inflammation pathways

Disease-Related Upstream Regulators Are Elevated in Patients with High CCL24 Levels

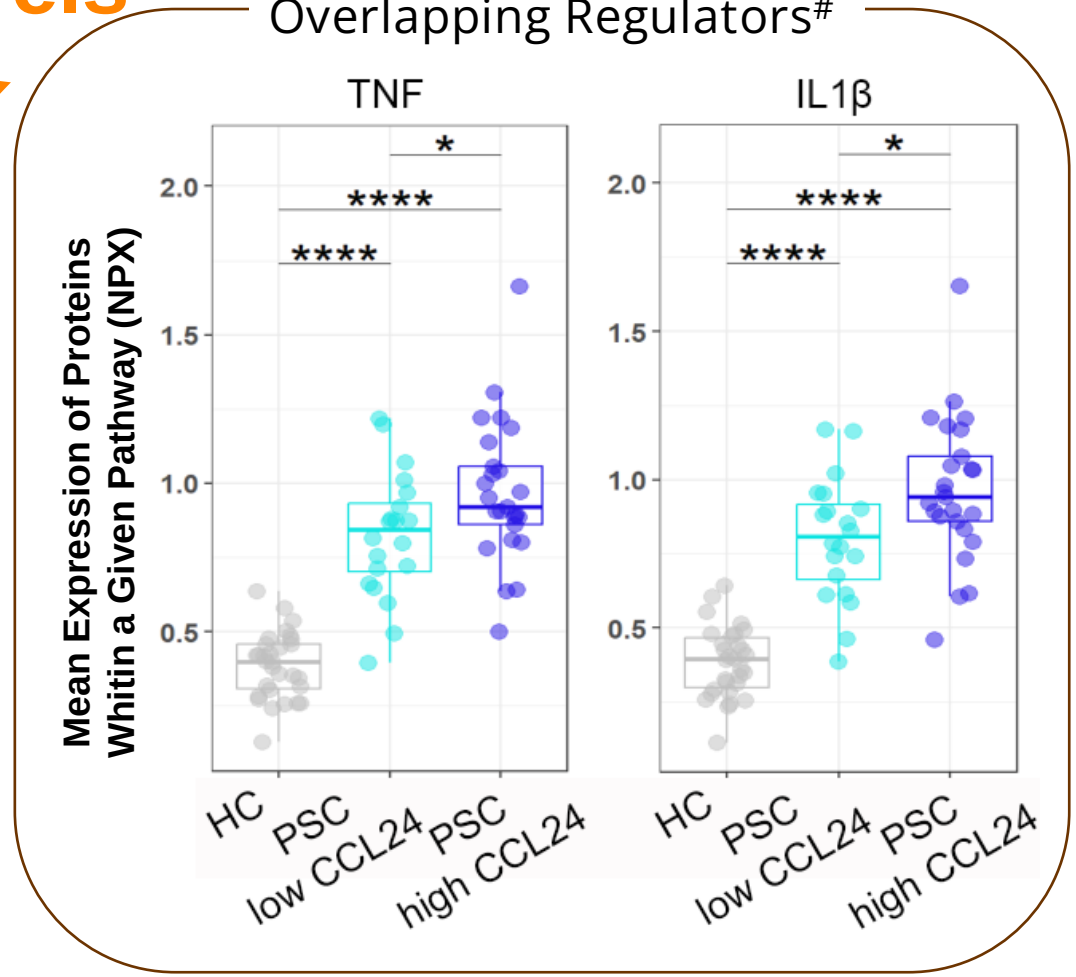


Overlapping regulators:

[1] TNF
[2] IFNG
[3] IL4
[4] TGFB1
[5] Immunoglobulin
[6] IL1B
[7] IL10
[8] IL6
[9] STAT3

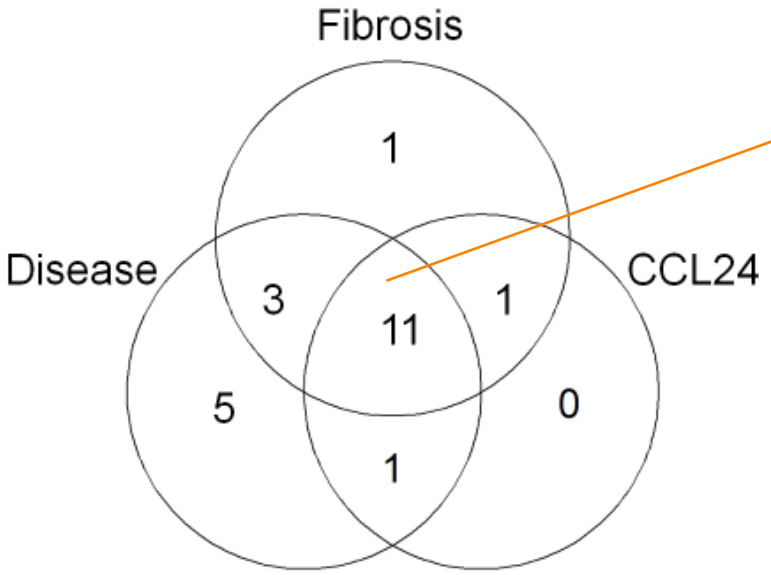
HC, Healthy Controls

* Similar effects in other overlapping upstream regulators, including fibrosis and inflammation regulators

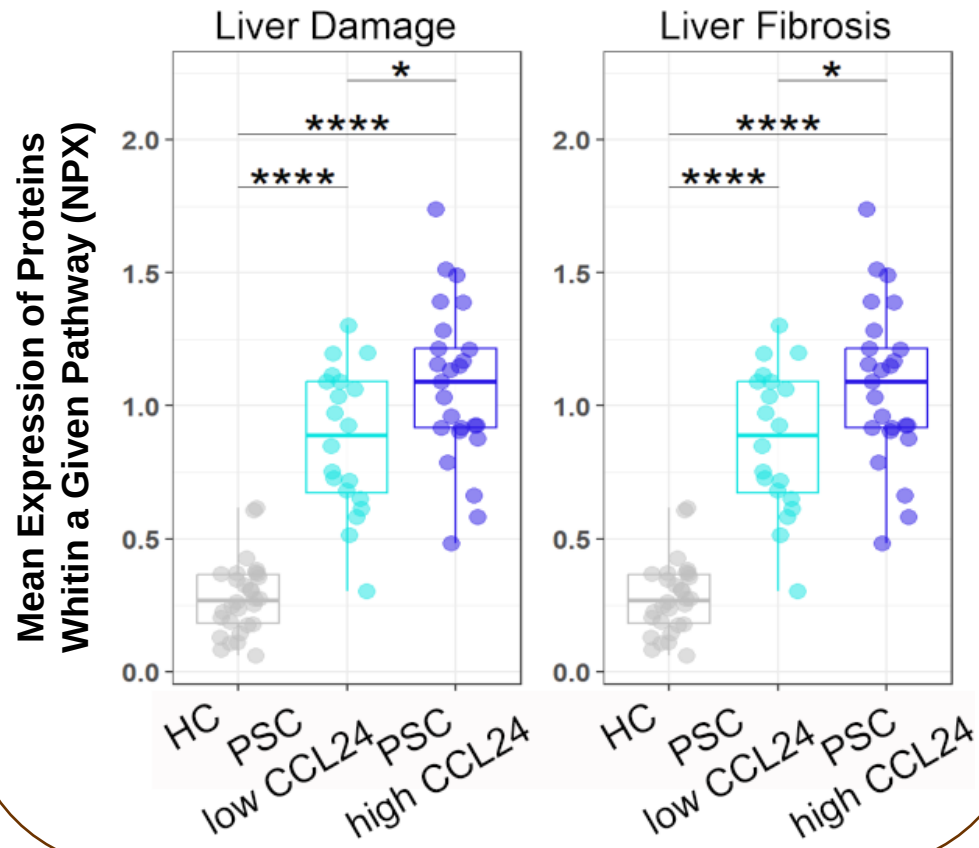


* p<0.05,**** P<0.0001 Welch 2-sample t-test

Disease-Related Toxicity-Functions Are Elevated in Patients with High CCL24 Levels



Overlapping Toxicities#



Overlapping toxicity functions:

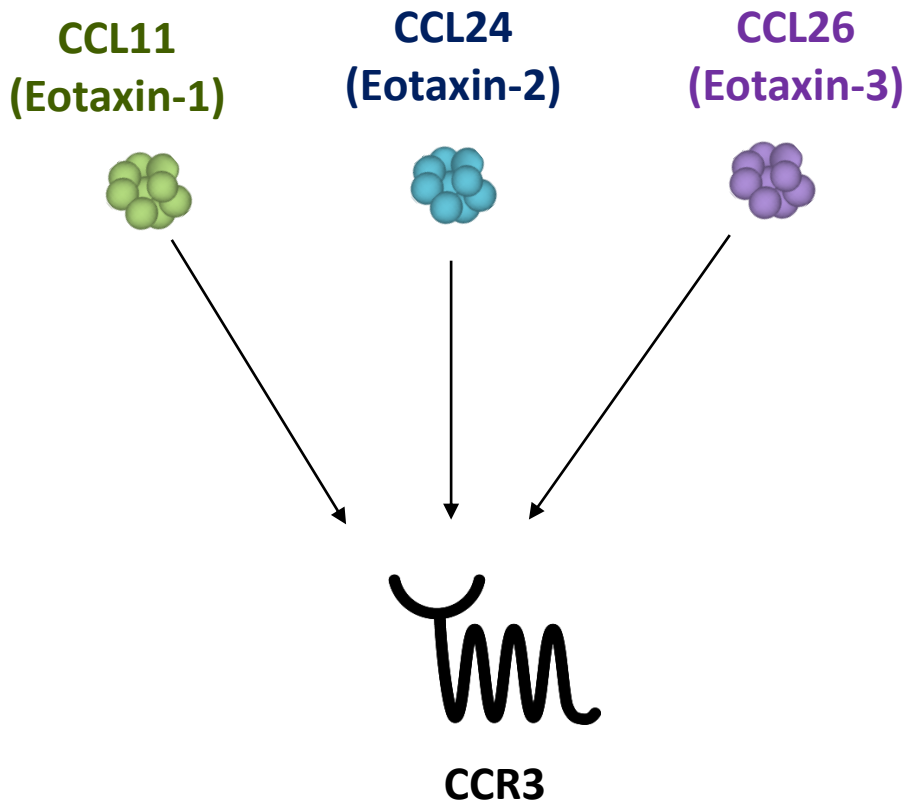
[1] Degeneration of liver
[2] Hepatocellular carcinoma
[3] Liver Cirrhosis
[4] Liver Damage
[5] Liver Enlargement
[6] Liver Fibrosis
[7] Liver Hyperplasia/Hyperproliferation
[8] Liver Inflammation/Hepatitis
[9] Liver Necrosis/Cell Death
[10] Liver Proliferation
[11] Liver Steatosis

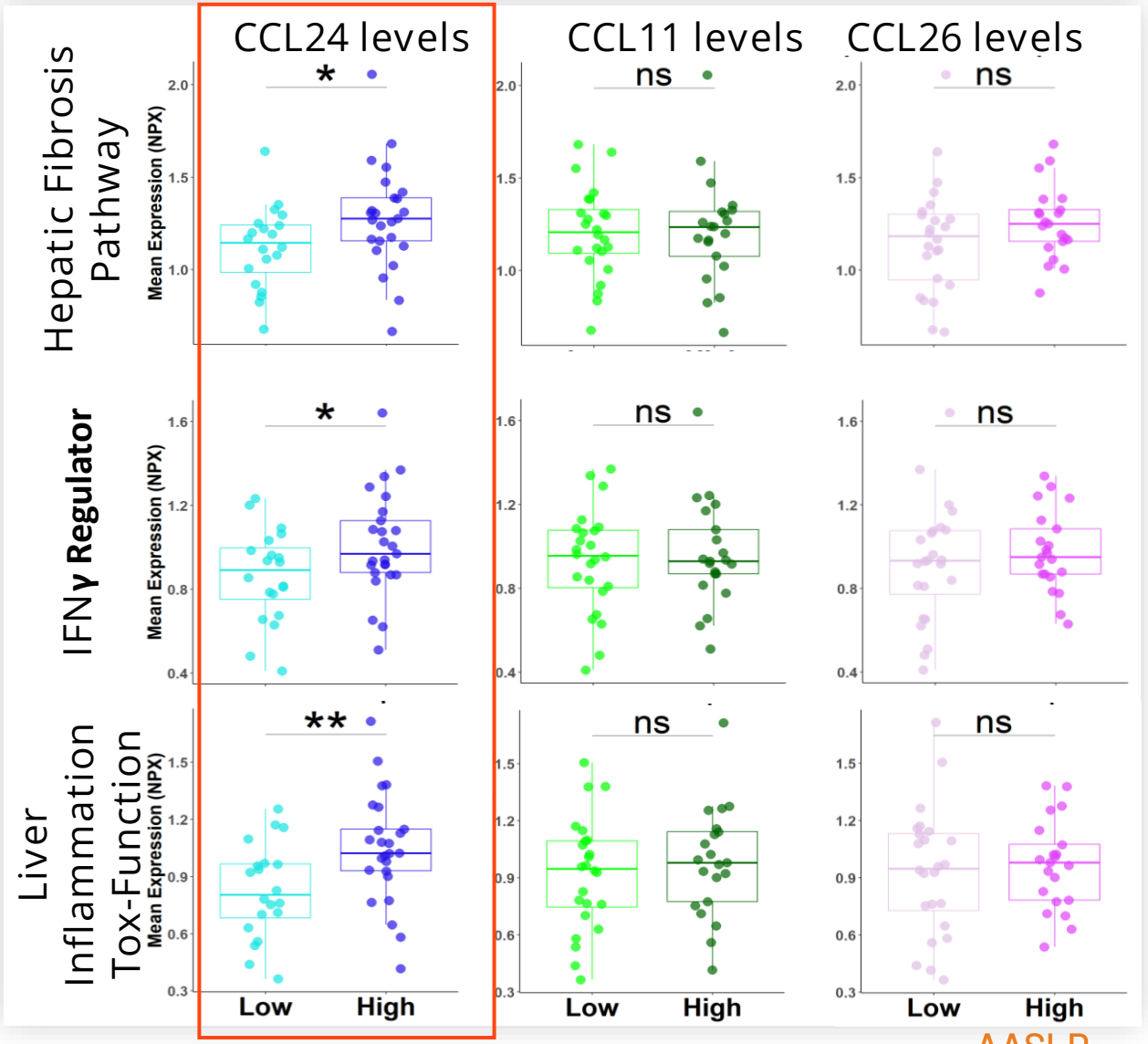
* p<0.05,**** P<0.0001 Welch 2-sample t-test

HC, Healthy Controls

Similar effects in other overlapping tox-functions, including liver inflammation, liver necrosis and liver proliferation

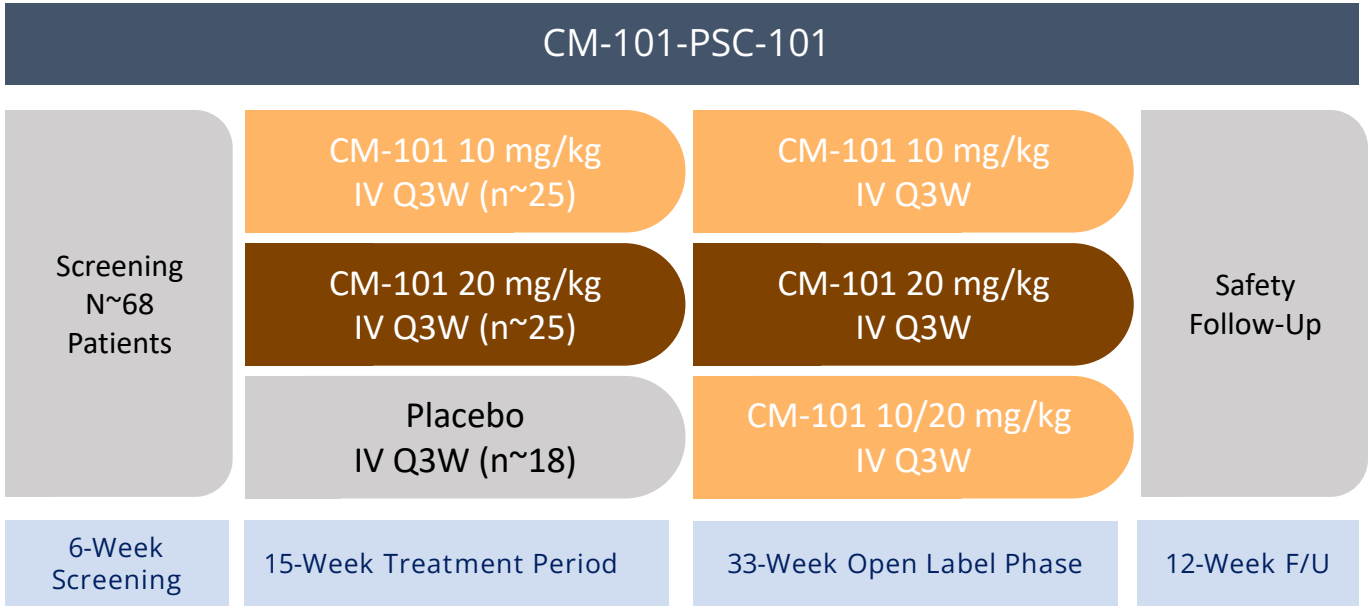
Unique Association of CCL24 with Key Disease-Related Pathways and Regulators





ns, nonsignificant, * p<0.05, **p<0.01; Welch 2-sample t-test

CM-101 Phase 2 Trial in Primary Sclerosing Cholangitis



Topline data expected in 2H 2024

Key Enrollment Criteria

PSC patients with large duct disease of >24 weeks duration
- ALP > 1.5 ULN
- Stable IBD allowed
- Stable UDCA treatment allowed

Outcome Measures

Primary – Safety and tolerability
Secondary - Change from baseline to Week15 in:
- Serum alkaline phosphatase
- ELF score
- FibroScan®
- Fibrotic biomarkers/liver enzymes (e.g., AST, ALT, Pro-C3, Pro-C5)
- Pharmacokinetics
- Pharmacodynamic parameters

Key Takeaways

- CM-101 Reduces Liver Injury & Fibrosis in Multiple PSC Animal Models
- Disease-related canonical pathways, upstream regulators and toxicity-functions are elevated in PSC patients with high CCL24 levels
- Unique Association of CCL24 but not other eotaxins with Key Disease-Related Pathways and Regulators

- CCL24 is associated with both inflammatory and fibrotic mechanisms
- Preclinical and patient derived serum proteomics data support further clinical investigation of an anti-CCL24 therapy in PSC

Royal Free London
NHS Foundation Trust

Dr . Francesca Saffioti
Prof. Douglas Thorburn
Prof. Massimo Pinzani
UCL Institute of Immunity & Transplantation, United Kingdom

Thank you!

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