CCL24 CORRELATES WITH FIBROTIC MARKERS IN PSC. BLOCKING CCL24 WITH CM-101 ATTENEATTES FIBROSIS AND CHOLESTASIS

CCL24 modulates fibrosis development in Primary Sclerosing Cholangitis. Correlation of human serum CCL24 levels with fibrosis markers and data from the MDR2-/- mouse model

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1 Introduction

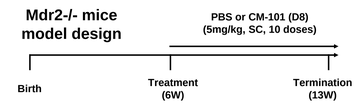
Primary sclerosing cholangitis (PSC) is a progressive cholestatic disease involving liver inflammation and fibrosis, with no effective medical treatment. CCL24, a chemokine that was shown to be involved in the development of liver inflammation and fibrosis is robustly expressed in liver biopsies of PSC patients. Blocking CCL24, was shown to attenuate liver fibroblast activation and reduce liver fibrosis in both NASH and PSC models[1].

2 Aim

- **To assess the effect of CCL24 blockage in the Mdr2-/- mouse PSC model**
- **To study the correlation between CCL24 and fibrotic biomarkers in PSC patients serum samples**

3 Method

- The effect of blocking CCL24, using the neutralizing monoclonal antibody CM-101 (D8), was evaluated in the Mdr2-/- PSC mouse model

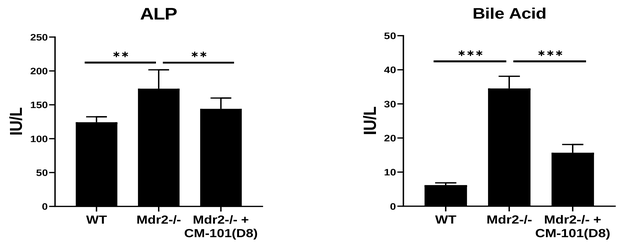


Evaluations included
- Serum liver enzymes
- Histology assessment of liver damage and fibrosis
- Fibrotic gene expression

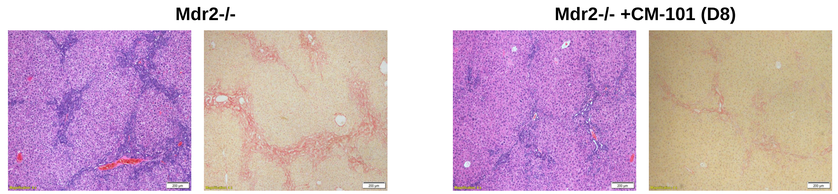
- CCL24 levels were quantified by ELISA in PSC patients serum samples and correlated with fibrotic biomarkers (TIMP-1 and ELF score)

4 Results

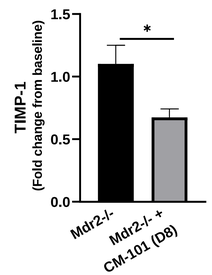
In Mdr2-/- mouse model blocking CCL24 using the mAb CM-101 (D8) ameliorated cholestatic injury and liver damage indicated by reduced serum ALP and bile acid levels



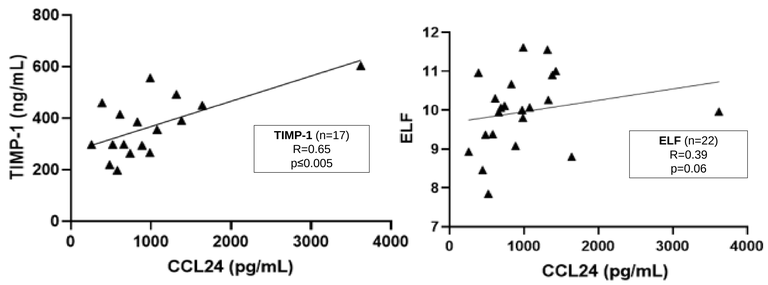
CM-101 (D8) treatment reduced liver fibrosis in Mdr2-/- mice, evaluated by H&E and Sirius Red staining



Expression of the fibrotic marker TIMP-1 was significantly reduced following 6 weeks of CM-101 (D8) treatment



In human PSC serum samples CCL24 correlated with the fibrotic markers ELF and TIMP-1, suggesting an association between CCL24 and PSC-related fibrosis



5 Conclusions

- **CCL24 levels in PSC patients serum positively correlates with TIMP-1 and ELF score, reflecting its role in fibrosis progression**
- **In the Mdr2-/- PSC mouse model treatment with CM-101, blocking CCL24, reduces cholestasis and hepatic fibrosis**
- **CCL24 was found to play a key role in PSC liver related pathologies. CM-101, a neutralizing CCL24 mAb, is currently being tested in a Phase IIa clinical trial as a potential treatment for PSC**

6 References

[1]**A Blocking Monoclonal Antibody to CCL24 Alleviates Liver Fibrosis and Inflammation in Experimental Models of Liver Damage.**
JHEP Rep. (2020) *Michal Segal-Salto , Neta Barashi, Avi Katav, Vicktoria Edelshtein , Arnon Aharon , Sharon Hashmueli , Jacob George , Yaakov Maor , Massimo Pinzani , Dan Haberman , Andrew Hall , Scott Friedman , Adi Mor*

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