Expression of the chemokine CCL24 and its receptor CCR3 in the sera and livers of patients with non-alcoholic fatty liver disease

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INTRODUCTION

- Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease.
- Inflammation and fibrosis are the key pathological processes involved in the progression of NAFLD to Non-alcoholic steatohepatitis (NASH).
- Chemokines play an important role in inducing inflammation and fibrosis and were found to play a key role in NASH progression.
- CCL24 (Eotaxin-2) was recently found to be involved in the progression of inflammatory and fibrotic diseases.
- ChemomAb is developing Anti-CCL24 monoclonal antibody for the treatment of NASH.

AIM

To study the levels of circulating CCL24 and its receptor-CCR3 in NAFLD patients' serum samples and liver biopsies and the association with disease stage.

METHOD

- Serum samples from NAFLD patients in different disease stages were analyzed for CCL24 levels using commercial ELISA kit.
- CCR3 expression in peripheral blood mononuclear cells were tested by flow cytometry.
- Immunohistochemistry staining was performed to evaluate CCL24 and CCR3 expression in liver biopsies.
- Fib4 score was used to divide the NAFLD population to subgroups according to disease severity.

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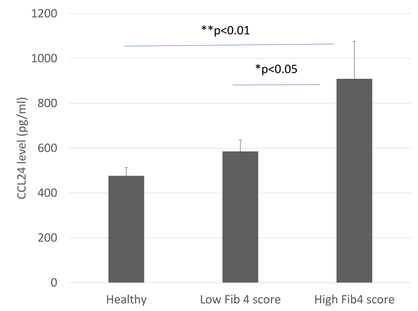
RESULTS

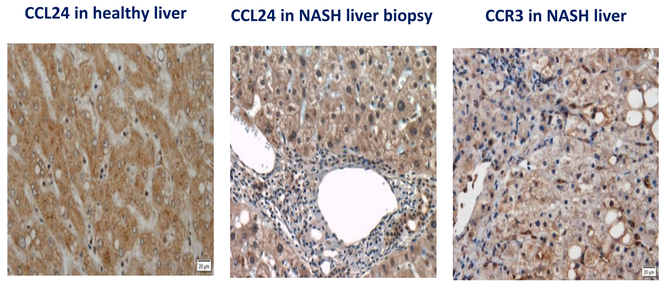
- In general, significant elevation of CCL24 serum levels in NAFLD patients compared to healthy volunteers was noted (718±78 pg/ml and 476±36 pg/ml, respectively, $p \leq 0.01$).
- CCL24 increased by ~2 fold in high NAFLD Fib4 score patients (Fib4 >1.5; n=23) compared to healthy volunteers (n=20) ($p \leq 0.01$) and by ~1.5 fold compared to low Fib4 score NAFLD patients (Fib4<1.5; n=28; $p \leq 0.05$).
- CCR3 was significantly overexpressed in mononuclear cells isolated from NAFLD patients' (n=35) compared to healthy volunteers (n=26) (3.81±0.16% and 0.98±0.361%, respectively, $p \leq 0.01$).
- Immunohistochemistry of NASH patients' liver biopsies with NAFLD Activity Score ≥5 versus normal livers demonstrated high expression of CCL24 and CCR3 ($p \leq 0.01$, $p \leq 0.05$, respectively).

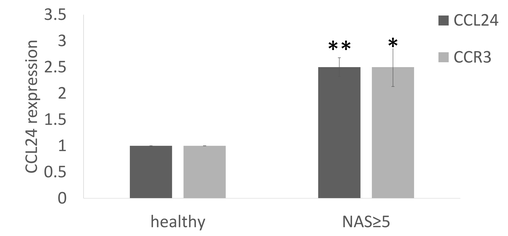
CCL24 circulating serum level increased in correlation with disease severity

Low Fib4 score (<1.5; n=28)
High Fib4 score (>1.5; n=23)
*Healthy volunteers (*n=20)



Representative immunohistochemistry staining of liver biopsies

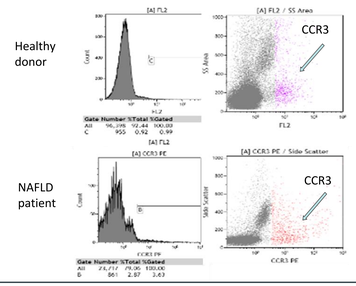


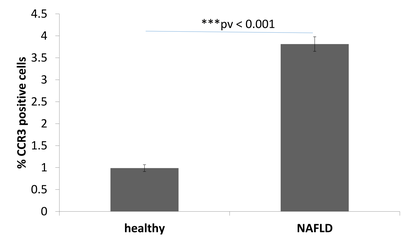


CCL24 / CCR-3 IHC evaluation score:
Grade 0: no CCL24 / CCR-3 reaction at all
Grade 1: Up to 10% of the cells (hepatocytes and fibroblasts) are CCL24 / CCR-3 positive
Grade 2: Between 10-50% of the cells (hepatocytes and fibroblasts) are CCL24 / CCR-3 positive
Grade 3: Between 50-75% of the cells (hepatocytes and fibroblasts) are CCL24 / CCR-3 positive
Grade 4: Between 75-90% of the cells (hepatocytes and fibroblasts) are CCL24 / CCR-3 positive
Grade 5: Between 90-100% of the cells (hepatocytes and fibroblasts) are CCL24 / CCR-3 positive

CCR3 expression on peripheral blood mononuclear cells is elevated in NAFLD patients

NAFLD patients (n=35)
Healthy volunteers (n=22)





CONCLUSIONS

- We present for the first time, evidence that the chemokine CCL24 and its cognate receptor, CCR3, are significantly increased in NAFLD patients both in the circulation and in the liver.
  Furthermore, CCL24 expression correlates with disease severity.
- These results may indicate a potential involvement of CCL24-CCR3 axis in the pathogenesis of NASH , thus suggesting that CCL24 may serve as a potential prognostic tool and a therapeutic target for the treatment of patients with NASH.

REFERENCES

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