1. INTRODUCTION

Dysfunctions in metabolism are a common finding in clinical medicine. We report the use of $^1$H-NMR-based full quantitative metabolomics liver profiling to assess the metabolic disarrangements in the progression of steatosis to Nonalcoholic Steatohepatitis (NASH).

2. GOALS

Using NMR based quantitative metabolomics, it was our goal in the present study (i) to establish and validate NMR based metabolic differences between LDLr$^{-/-}$ fed chow diet and LDLr$^{-/-}$ fed high fat diet supplemented with cholesterol (ii) to identify metabolic pathways related to progression of steatosis towards NASH.

3. EXPERIMENTAL DESIGN

We conducted all experiments in male (C57BL/6J) rendered hyperlipidemic by the ablation of LDL receptor (LDLr$^{-/-}$).

4. LIVER EXTRACTION/$^1$H-NMR / IDENTIFICATION & QUANTIFICATION

- SUPERNATANT: Aqueous extract: $N_2$/lyophilise Reconstitute in $D_2O$+TSP (0.01%)
- PELLET: Lipidic extract: $N_2$/lyophilise
  Reconstitute in $CD_3$Cl:$CD_3$OD (2/1) TMS (0.01%)

5. RESULTS

6. CONCLUSIONS

- The full quantitative profiling approach we report allows for the quantification of up to 54 different metabolic markers.
- Evaluation of water-soluble and lipid-soluble extract metabolites is performed simultaneously in the same analysis.
- This metabolomic analysis proved to be fast, simple, reproducible and informative, revealing a suggestive relationship of the occurrence of SAMe depletion at the early stages of NASH development and a causal role of impairment of hepatic transsulfuration reactions.
- Our data suggests an intensive role of dietary cholesterol as a risk factor to the progression to hepatic inflammation in diet-induced NASH.

REFERENCES

ACKNOWLEDGEMENTS

CIBER de Diabetes y Enfermedades Metabólicas (CIBERDEM) is an initiative of ISCIII (Ministerio de Ciencia e Innovación).