Clinical translatability of a diet-induced obese mouse model of non-alcoholic steatohepatitis

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INTRODUCTION AND AIM

The Amylin (AMLN) diet-induced obese (DIO) mouse model has become one of the preferred preclinical animal models of non-alcoholic steatohepatitis (NASH). The translatable value of preclinical data in this model is however still not properly validated. Our aim was to evaluate AMLN DIO-NASH mouse liver samples with the results from NASH patients.

METHODS

Liver samples were obtained from C57Bl/6J mice fed the AMLN diet (40% fat, 20% fructose, 2% cholesterol, AMLN, DIO-NASH mice), a 60% high-fat diet (DIO mice) or chow (lean mice) for at least 30 weeks, and compared to human samples collected from lean (BMI <25 kg/m²), obese (BMI > 30 kg/m²) and patients with histology-proven NASH (n=12). Histopathological assessment of NAFLD activity score (NAS) and fibrosis stage was performed, and quantitative histology was used to analyse steatosis (H&E staining), inflammation (galectin-3 immunohistochemistry), and fibrosis (Pico Sirius red staining).

STUDY DESIGN AND GROUPS

Our two study groups included lean mice, DIO-NASH mice, and patients with histology-proven NASH (n=12). All mice were fed a standard chow diet. Inflammation, fibrosis, and steatosis were assessed using histopathological methods.

RESULTS

Anthropomorphic characteristics and plasma markers

Liver histology

Histopathological scoring

CONCLUSION

- Liver histopathology is highly comparable between human and mice samples.
- Gene expression analysis showed similar regulation pattern in human and mice, albeit with a clearer separation between lean and NASH in mice.
- In conclusion, the AMLN DIO-NASH models show a liver phenotype highly similar to that of human NASH patients with moderate fibrosis.