INTRODUCTION

- HCC is the 2nd most common cause of cancer related death mortality world wide.
- HCC is mainly associated with liver fibrosis/cirrhosis which is regarded as a crucial factor in hepatocarcinogenesis.
- Fibrosis/cirrhosis modifies liver vascularization, extracellular matrix composition, and drug metabolism.
- Besides, immune system of the liver contributes to the establishment of the fibrosis, cirrhosis and to the disease progression towards HCC.
- Inhibitory immune-check point Cytotoxic T-Lymphocytes protein 4 (CTLA-4), contributes to impaired anti tumor immune surveillance.
- Newly developed therapies should be pre-clinically tested in an appropriate animal model to recapitulate above features.
- Diethylnitrosamine induced rat (DEN) model faithfully reproduces human scenario of advanced HCC.

AIM

- Deeply characterize DEN-induced HCC rat model during development of cirrhosis and HCC with special focus on liver inflammatory micro-environment.

RESULTS

CONCLUSIONS

- DEN administration induced tumor development (tumor number, size and hepatocyte proliferation) and liver fibrosis/cirrhosis.
- DEN-induced HCC is associated with impaired intrahepatic immune response (T-cells, CTLA-4 and macrophage modulations).
- Thus, DEN-induced rat model faithfully mimics multiple features of human advanced HCC and can be used for preclinical studies of new therapies, including immunotherapies.