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MEETING ABSTRACTS

PHARMACOLOGICAL MODULATION OF M-TOR IN ANIMAL MODEL OF NAFLD/NASH

Mahak Arora [1], Nikolina Kutinová Canová [1], Zuzana Pavlíková [2]
Presenting author: Mahak Arora (Mahak.Arora@lf1.cuni.cz or mahakaroradr@gmail.com)

[1] Institute of Pharmacology, 1st Faculty of Medicine, Charles University in Prague, Albertov 4, 128 00 Prague 2, The Czech Republic.
[2] Institute of Histology and Embryology, 1st Faculty of Medicine, Charles University in Prague, Albertov 4, 128 00 Prague 2, The Czech Republic

Non-alcoholic Fatty Liver Disease (NAFLD) promotes to Non-alcoholic Steatosis Hepatitis (NASH), liver cirrhosis and cancer. However, there is no specific clinical treatment for NASH. Previously, we screened *in vitro* model for novel drug candidates towards NAFLD/NASH. The mTOR inhibitor was found to significantly alleviate palmitic acid-induced lipotoxicity in hepatocyte culture. Therefore, the aim of presented study was to investigate the effect of non-specific mTOR inhibitor (KU-0063794) when given orally in dietary model of NAFLD/NASH. To develop NAFLD and NASH *in vivo*, male mice C57Bl6J were fed with Atherogenic High Fat Diet (AHFD), and fructose/glucose in drinking water for 12 and 16 weeks, respectively. KU-0063794 treatment for 17 days displayed a trend towards decreasing serum glucose, inflammation (e.g. serum TNF-α), hepatocyte oxidative stress (e.g. conjugated DENES) and an improvement in expression of metabolic genes in liver homogenates. However, KU-0063794 had no effect on liver NASH morphology (e.g. NAS or fibrosis score). In conclusion, oral KU-0063794 treatment for an acute period displayed a trend to improve the highly progressed NASH with no signs of toxicity and therefore, chronic treatment should follow.

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Keywords: Atherogenic high fat diet; NAFLD/NASH; lipotoxicity; oxidative stress; mTOR inhibitor

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