**Title of the project:** Role of iron depletion and Mrp2 deficiency for development of estrogen-induced cholestasis

**Grant Agency:** Charles University  
**Project Number:** 5562/18

**Principal Investigator:** F. Alaei Faradonbeh

**Co-investigators:** S. Mičuda

**Starting date:** 13.03.2018  
**Duration (years):** 3

**Total funds allocated for project - Kč (thousands):** 270

**Summary of 2019 results**

**Title of the presentation:** Effect of cardiovascular drugs on the development of non-alcoholic steatohepatitis.

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Biliary secretion is essential pathway for elimination of lipophilic agents from the organism. This pathway is modified by numerous liver diseases, which may worsen accumulation of toxic compounds and predispose for further liver impairment. Nonalcoholic steatohepatitis (NASH) is a frequent disease associated with numerous metabolic and cardiovascular risks. Recent works demonstrated that bile acid homeostasis and bile formation markedly contributes to pathophysiology of NASH. It is therefore important to describe modulation of these mechanisms by all drugs regularly prescribed for therapy of NASH and accompanying risks. Primary aim of this project is to study in detail effects of drugs commonly used for these risks, carvedilol, metformin, and atorvastatin, and their combinations on the mechanisms of bile production and bile acid homeostasis using relevant mice model of NASH. During the second year of the project solution, we completed all in vivo studies based on continuous 24 week administration of high fat diet with glucose and fructose to induce NASH. Designed groups of animals received carvedilol, metformin, and atorvastatin or their combinations. The samples are currently analysed by analytical, histological, and molecular-biology methods. Preliminary data uncovered positive effects of metformin while carvedilol and atorvastatin neither improved nor worsened the course of NASH. The study will be finished during third year of the project.

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