

Trilateral relationship: food-borne trematodes, microbiota, and experimental host

Pakharukova M.Y.^{1,2*}, Lishai E.^{1,2}, Zaparina O.¹, Sripa B.³, Hong S.-J.⁴, Mordvinov V.A.¹

¹ Institute of Cytology and Genetics, SB RAS, Novosibirsk, Russia

² Department of Natural Sciences, Novosibirsk State University, Novosibirsk, Russia

³ WHO Collaborating Centre for Research and Control of Opisthorchiasis (Southeast Asian Liver Fluke Disease), Tropical Disease Research Center, Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

⁴ Department of Medical Environmental Biology, Chung-Ang University College of Medicine, Seoul, Korea

* pmaria@yandex.ru

Key words: Food-borne trematodes, experimental model, parasite microbiome, *Helicobacter*

Background: Three epidemiologically significant food-borne trematodes (*Opisthorchis felineus*, *O. viverrini*, *Clonorchis sinensis*) have some similarities and differences. The definitive host are fish-eating mammals including humans. The flukes affect the hepatobiliary system inducing cholangitis, and bile duct neoplasia, and even cholangiocarcinoma among chronically infected individuals. Differences primarily concern the geographical range and main foci, where they are endemic to, and the carcinogenic potential to human. Two species, *O. viverrini* and *C. sinensis* are both recognized 1A group of biological carcinogens to human, whereas *O. felineus* is recognized to be potentially carcinogenic to animals. The mechanisms of carcinogenesis by the liver flukes are studied fragmentarily, the role of host and parasite microbiome is an unexplored aspect.

Methods and Algorithms: In order to characterize the microbial communities in adult parasites as well as in host bile and colon, the hamsters were infected with metacercariae of *C. sinensis* (South Korea), *O. viverrini* (Thailand) and *O. felineus* (Russia). We performed high-throughput sequencing (MiSeq, Illumina) of libraries constructed from V3 – V4 region of 16S ribosomal DNA isolated from adult worms and from colon faeces and bile from the hamsters. Furthermore, *ureA* and *cagA* genes of *Helicobacter pylori* were assessed by the real-time PCR method in the stomach, feces and bile of hamsters.

Results: As a result, 1,784,000 reads were assigned to 13,244 operational taxonomy units (OTUs) and, in turn, to 273 genera of Bacteria. Analysis revealed the significant phylogenetic diversity of the microbial communities among three liver flukes. Numerous bacterial species were identified in the bile of the infected animals, in particular, bile contains the same bacterial phyla as worms do. Prevalence of *H. pylori* and *ureA* gene copy number was significantly higher in the liver fluke-infected hamsters than in the uninfected ones.

Conclusion: The infection with any liver fluke significantly modified the bile and faecal microbiome, increasing the abundance of *H. pylori*. Mechanisms of host microbiome modification by the liver flukes are discussed.

Acknowledgements: This work was supported by the Russian Science Foundation (No. 22-24-20010).