Microcystin-LR induces intestinal injury and microbiota-derived metabolites dysbiosis in zebrafish (*Danio rerio*)

Shangwu Liu [a], Panliang Wang [a*]

[a] Henan International Joint Laboratory of Aquatic Toxicology and Health Protection, College of Life Sciences, Henan Normal University, Xinxiang, 453007, China

*Corresponding authors, E-mail: Henan Normal University, Xinxiang, 453007, P.R. China, E-mail: wangpl91@163.com

ABSTRACT: Microcystin-LR (MC-LR) is typically produced along with the occurrence of cyanobacterial blooms, potentially exerting deleterious effects on intestinal health in aquatic animals. To date, the underlying mechanism by which MC-LR affects intestinal health remains elusive. In this study, adult male zebrafish were exposed to MC-LR to assess its impact on intestinal health from the perspectives of histopathology, microbiome and metabolome. Histopathological and biochemical results indicated that MC-LR damaged intestinal villi and epithelial cell, induced intestinal barrier injury and inflammatory response in zebrafish. Metabolomics results indicated that MC-LR induced the dysbiosis in amino acid, carbohydrate, lipid, energy metabolisms, and specifically altered glycine, serine and threonine metabolism in amino acid metabolism. Metagenomics results demonstrated that MC-LR altered the composition of intestinal microbiota, perturbed the microbial functions associated with amino acid, lipid, carbohydrate and energy metabolisms, as well as barrier function and inflammatory response. Multiomics analyses further confirming MC-LR caused the dysfunction of glycine, serine and threonine metabolism, which was precisely regulated by dominant Proteobacteria, Firmicutes, Fusobacteriota and Bacteroidota. This study offers a novel perspective on the toxicity of microbiota and microbiota-derived metabolism in fish intestines induced by MC-LR and deepens our comprehension of the disruptive influence of MC-LR on intestinal homeostasis in organisms.

Keywords: Microcystin-LR; Zebrafish; Intestinal barrier; Microbiota; Amino acid metabolism