Evaluation of the Effects of the Clinical Escherichia coli NF73 Crisis in an Adult Type 1 Diabetes mellitus Patient Presenting with Diarrhea, Weight Loss and Hypoglycemic Attacks—A Rare Entity

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Background Gut microbiota plays critical roles in nonalcoholic fatty liver disease (NAFLD). We have previously isolated and identified one clinical Escherichia coli (E. coli) strain from the intestinal mucosa of a nonalcoholic steatohepatitis (NASH) patient, and named it as E. coli NF73-1. Our aim is to investigate the role of E. coli NF73-1 in the development of NAFLD in a high-fat diet (HFD) mice.

Methods Conventional (CV) mice, plus mice treated with antibiotics (AB) to deplete gut microbiota, were fed with HFD for 12 weeks. At the 10th week, mice were treated daily with oral gavage of LB, live-NF73-1, or pasteurized-NF73-1 (pas-NF73-1) for 2 weeks. AB mice were treated in drinking water containing 1 g/L ampicillin, 500 mg/L vancomycin, 1 g/L neomycin, and 1 g/L metronidazole for 4 weeks, starting at 6th week. In vivo bacterial translocation and transepithelial permeability assay was performed. Primary hepatocytes from NAFLD mice were cocultured with NF73-1 to evaluate inflammatory responses.

Results Live-NF73-1 group developed severer liver pathology than LB and pas-NF73-1 groups in both CV and AB mice, verified by increased NAFLD activity (NAS) score. Besides, intestinal permeability was higher in live-NF73-1 group than that in LB and pas-NF73-1 groups of both CV and AB mice, supported by decreased expression of ZO-1 and Occludin in the colon. In vitro bacterial translocation and transepithelial permeability assay indicated that HT-29 cells treated with live-NF73-1 developed a higher concentration of translocated bacteria and FITC fluorescein than LB and pas-NF73-1 groups. Interestingly, live-NF73-1 decreased mRNA levels of ZO-1, Occludin and Claudin2 in Caco2 cells, and downregulated mRNA expression of Claudin2 and E-cadherin in HT-29 cells compared with LB and pas-NF73-1 groups. NF73-1 also induced inflammatory responses of primary hepatocytes, supported by increased IL-6 expression.

Conclusions Clinical E. coli NF73-1 aggravates liver injury in NAFLD mice, through impaired intestinal integrity and inflammatory responses in hepatocytes. These findings provide new insights on management using specific bacterial strain.

Clinical Gastroenterology

Clinical Escherichia coli NF73-1 Isolated from a Patient with Nonalcoholic Steatohepatitis Induces Liver Injury Through Impairing Intestinal Barrier Function and Inducing Inflammatory Responses of Hepatocytes

Yang Song*, Zhe Wu, Jun Xu, Yujing Chi, Yifan Zhang, Yulan Liu. Peking University People’s Hospital, China

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