

## 論 文 要 旨

〔 A high-fructose diet induces epithelial barrier dysfunction and exacerbates the severity of dextran sulfate sodium-induced colitis 〕

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【Introduction】 Epidemiological and clinical evidence has shown an association between IBD and several environmental factors, antibiotic use, modern lifestyle and diet. Excessive fructose intake is one of the risk factor for gut symptoms in patients with inflammatory bowel disease, however, its effect on the intestinal tract has not been evaluated previously. The present study investigated the impact of a high-fructose diet (HFD) on intestinal barrier function in mice with experimental colitis.

【Methods】 Six-week-old male C57/BL6 mice were randomly allocated into four experimental groups: either a HFD or control diet and either plain drinking water or water containing 1% dextran sulfate sodium (DSS) for 2 weeks. The body weight and colon length, the disease activity index (DAI), pathological scores, expression of inflammatory cytokines and the tight junction proteins were compared among the groups, and the proportions of fecal bacteria in the colon were analyzed. And we used the human HT-29 colon cancer cell line to examine the paracellular permeability and the cytotoxicity of fructose.

【Results】 The body weight and colon length were significantly decreased, and the DAI and pathological scores were significantly increased in the DSS/HFD-treated mice compared with the non-DSS-treated and control diet mice. Regarding the expression of inflammatory cytokines, the levels of interleukin (IL)-6, IL-1 $\beta$  and tumor necrosis factor- $\alpha$  were significantly increased, and the expression of the tight junction protein occludin was significantly decreased in the DSS/HFD-treated mice. The total bacterial count was increased in the HFD mice. In particular, the ratio of the *Bacteroides-Prevotella* group was elevated. And fructose enhanced the paracellular permeability of the cells and injured epithelial cells in a concentration- and time-dependent manner.

【Conclusions】 These results indicate that fructose increased paracellular permeability and was involved in the overgrowth of intestinal bacteria, thereby inducing intestinal inflammation. The excessive intake of fructose caused leaky gut syndrome, exacerbated enteric inflammation, and was considered to result in the symptoms of IBD.