International Conference on
Gastroenterology and Liver
July 18-19, 2022 | Amsterdam, Netherlands
Volume: 12

The HDAC Inhibitor, SAHA, Prevents Colonic Inflammation by Suppressing Pro-inflammatory Cytokines and Chemokines in DSS-induced Colitis

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Inflammatory bowel disease (IBD) is an inflammatory disorder of the gastrointestinal tract that is caused by multiple factors, including dysfunction of the immune system and genetic and epigenetic alterations. Aberrant epigenetic regulation, especially histone acetylation, was found in biopsies from IBD patients and mouse models of colitis, suggesting that an epigenetic treatment approach may be useful for IBD therapy. Therefore, we investigated the effects of the histone deacetylase (HDAC) inhibitor, suberoylanilide hydroxamic acid (SAHA), in a mouse model of dextran sulfate sodium (DSS)-induced colitis. C57BL/6 mice were treated with 1.5% DSS for 5 days and/or SAHA (25 mg/kg BW/day) for 26 days. Levels of mRNA for the pro-inflammatory cytokines, interleukin (IL)-6 and tumor necrosis factor (TNF)-α, and the chemokines, Ccl2, were examined by qRT-PCR. CD11b, a marker of dendritic cells, macrophages, and monocytes, as well as Ccl2 expression, were examined by immunohistochemistry. IL-6, TNF-α, and Ccl2 gene expression peaked on day 5 in DSS-treated mouse colon, whereas SAHA treatment significantly decreased pro-inflammatory gene expression. Ccl2 protein expression resembled Ccl2 gene expression results. Moreover, localization of CD11b showed that migratory inflammatory cells were dramatically decreased by SAHA treatment compared to DSS-treated mouse colon. Thus, we conclude that the HDAC inhibitor, SAHA, attenuates inflammatory changes in DSS-induced colitis by suppressing local secretion of pro-inflammatory cytokines and chemokines and also by suppressing mobilization and accumulation of inflammatory cells.

Keywords: Inflammatory bowel disease, histone deacetylase inhibitor, dextran sodium sulfate, pro-inflammatory cytokines and chemokines

Biography

Noor Ali was born in a religious family of Herat in 1984. He got his elementary and secondary education at Jamoriat High School of Shindad District at Herat in 2001. He started his higher education by joining Department of Veternary at Agriculture Faculty of Herat University in 2002. Accomplishing his bachelor's degree successfully, he became a faculty member in 2006. Noor Ali Mohmmand earned and completed his master's degree from University of Karnataka in Bangalore India in 2010. Then he got his doctorate form Univeristy of Mezaki in Japan in 2018. He published more than 14 academic and research-based papers in different journals. he became acting dean of Veternary Faculty in 2018.

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