

## **Dimethyl fumarate reduces inflammatory responses in experimental colitis**

Fumaric acid esters have been proven to be effective for the systemic treatment of psoriasis and multiple sclerosis. We aimed to develop a new treatment for colitis. We investigated the effect of dimethylfumarate (DMF, 10-30-100 mg/kg) on an experimental model of colitis induced by DNBS. Compared with DNBS-injured mice, mice treated with DMF (100 mg/kg) and subjected to DNBS-induced colitis experienced a significantly lower rate in the extent and severity of the histological signs of colon injury. DNBS-treated mice experienced diarrhea and weight loss. Four days after administration of DNBS, the mucosa of the colon exhibited large areas of necrosis. Neutrophil infiltration was associated with an up-regulation of intercellular adhesion molecule ICAM-1. Immunohistochemistry for TNF- $\alpha$  showed an intense staining in the inflamed colon. On the contrary, the treatment with DMF significantly reduced the degree of hemorrhagic diarrhea and weight loss caused by administration of DNBS. DMF (30 and 100 mg/kg) also caused a substantial reduction in the degree of colon injury, in the rise in MPO activity, in the increase in TNF- $\alpha$  expression, as well as in the up-regulation of ICAM-1 caused by DNBS in the colon. Molecular studies demonstrated that DMF impaired NF- $\kappa$ B signaling via reduced p65 nuclear translocation. DMF induced a stronger antioxidant response as evidenced by a higher expression of Mn-superoxide dismutase. Moreover, DMF treatment reduces the degree of colitis caused by DNBS. We propose that DMF treatment may be useful in the treatment of inflammatory bowel disease.