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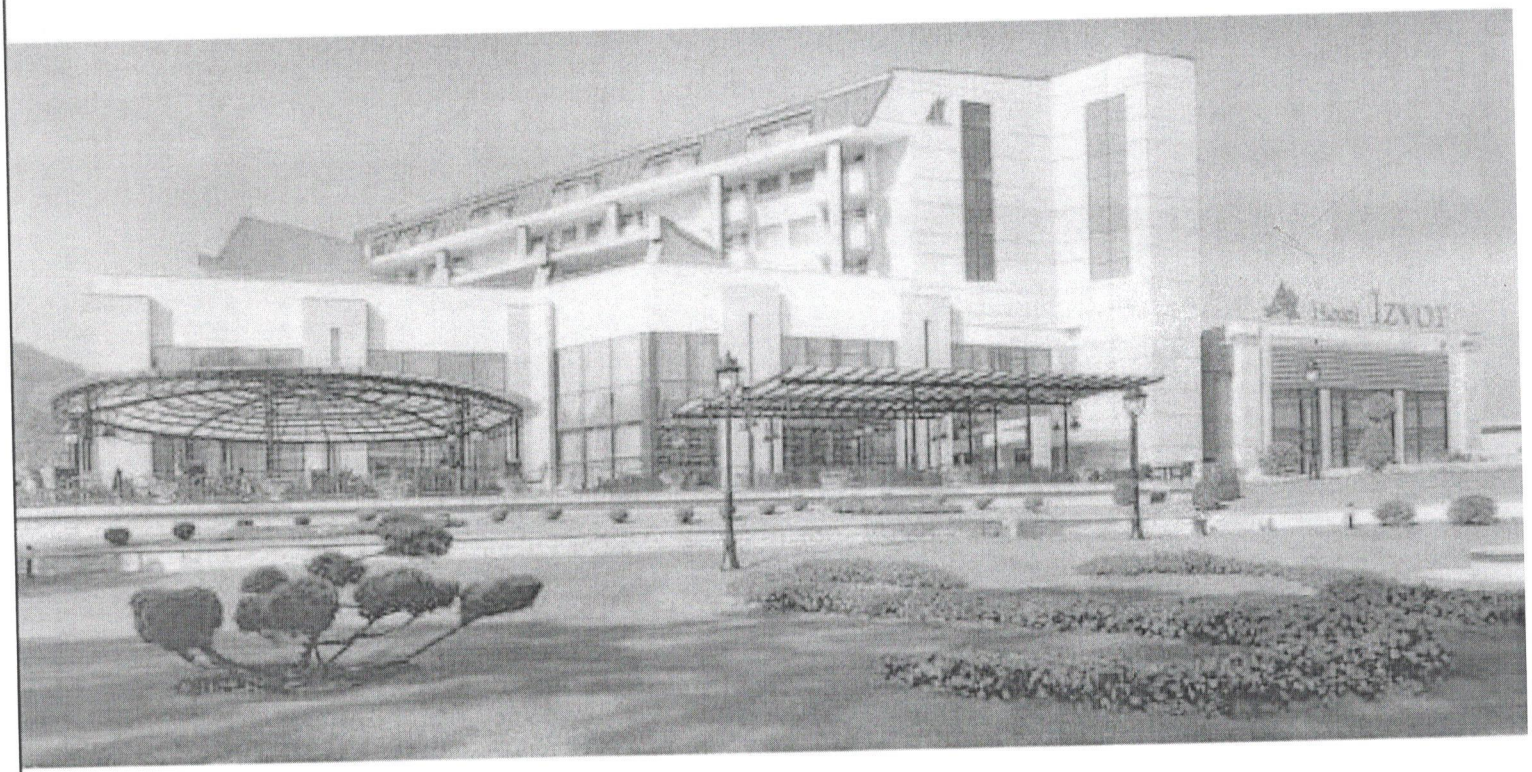

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PRESENTATION

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Genetic deletion of Galectin-3 attenuate dextran sodium sulphate colitis in mice

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Introduction. Galectin-3 (Gal-3) is an endogenous lectin with a broad spectrum of immunoregulatory effects: it plays an important role in autoimmune/inflammatory and malignant diseases, but the precise role of Gal-3 in pathogenesis of ulcerative colitis is still unknown.

Methods. We used a model of dextran sulphate sodium (DSS)-induced colitis, that has a high degree of uniformity and reproducibility to human colitis, to test susceptibility of wild-type C57BL/6 and Gal-3-deficient mice (Gal-3$^{-/-}$) to this disease. DSS (3%, molecular weight 40kDa) was dissolved in water and given to C57Bl/6 and Gal-3$^{-/-}$ mice in place of normal drinking water (ad libitum) for 7 days. Disease Activity Index (DAI: weight loss, stool consistency, visible blood in feces), was used to assess the clinical signs of colitis. The cellular make up of colon and phenotype of colon-infiltrated immune cells were determined by flow cytometry.

Results. Genetic deletion of Gal-3 significantly reduce the damage of colon tissue of DSS-treated mice. Level of pro-inflammatory cytokines (IL-1β, TNF-α и IL-6) were significantly lower in sera and colons of DSS-treated Gal-3$^{-/-}$ mice when compared to WT DSS-treated mice. The total number of CD11c+ inflammatory dendritic cells (DC) which expressed CD80 and I-A and produce pro-inflammatory cytokines (TNF-α and IL-6) as well as TNF-α and IL-1β producing CD45+CD11c-Ly6G+ neutrophils were significantly lower in colons of Gal-3$^{-/-}$ DSS-treated mice. In addition, the total number of inflammatory colonic (F4/80+CD11b+SiglecF-, F4/80+CD11b+I-A+, IL-1, IL-6 and IL-12 producing) macrophages were significantly lower in Gal-3$^{-/-}$ mice compared with WT DSS-treated mice. On contrary, there was significantly higher number of IL-10 producing regulatory DC and alternatively activated M2 macrophages in colon tissue of Gal3$^{-/-}$ DSS-treated mice. In vitro lipopolysaccharide (LPS) and DSS-stimulated peritoneal macrophages isolated from untreated Gal-3-/- mice produce lower amounts of TNF-α and IL-1β when compared to WT cells. Adoptive transfer of WT macrophages managed to significantly enhance the severity of DSS-induced colitis of Gal-3-/- mice. Antibiotic treatment did not affect differences between DSS-treated WT and Gal-3-/- mice.

Conclusion. Gal-3 expression promotes acute DSS-induced colitis. This effect is due to its pro-inflammatory role in particular on peritoneal macrophages rather than its role as a receptor for pathogens.

Keywords. DSS, colitis, Gal-3

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