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# Galectin-3 Plays an Important Pro-inflammatory Role in the Induction Phase of Acute Colitis by Promoting Activation of NLRP3 Inflammasome and Production of IL-1β in Macrophages

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## Abstract

**Background and Aims:** 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 acute colitis. The role of Gal-3 in pathogenesis of this disease was tested by evaluating disease development in Gal-3 deficient mice and administration of Gal-3 inhibitor. Disease was monitored by clinical, histological, histochemical, and immunophenotypic investigations. Adoptive transfer was used to detect cellular events in pathogenesis.
**Results:** Genetic deletion or pharmacological inhibition of Gal-3 significantly attenuate DSS-induced colitis. Gal-3 deletion suppresses production of pro-inflammatory cytokines in colonic macrophages and favours their alternative activation, as well as significantly reducing activation of NOD-like receptor family, pyrin domain containing 3 [NLRP3] inflammasome in macrophages. Peritoneal macrophages isolated from untreated Gal-3$^{-/-}$ mice and treated *in vitro* with bacterial lipopolysaccharide or DSS produce lower amounts of tumour necrosis factor alpha [TNF-α] and interleukin beta [IL-1β] when compared with wild type [WT] cells. Genetic deletion of Gal-3 did not directly affect total neutrophils, inflammatory dendritic cells [DCs] or natural killer [NK] T cells. However, the total number of CD11c+ CD80+ DCs which produce pro-inflammatory cytokines, as well as TNF-α and IL-1β producing CD45+ CD11c- Ly6G+ neutrophils were significantly lower in colons of Gal-3$^{-/-}$ DSS-treated mice. Adoptive transfer of WT macrophages significantly enhanced the severity of disease in Gal-3$^{-/-}$ mice.
**Conclusions:** Gal-3 expression promotes acute DSS-induced colitis and plays an important pro-inflammatory role in the induction phase of colitis by promoting the activation of NLRP3 inflammasome and production of IL-1β in macrophages.

**Keywords:** Gal-3; DSS colitis; NLRP3