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Targeted disruption of the galectin-3 gene results in decreased susceptibility to multiple low dose streptozotocin-induced diabetes in mice

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Abstract Galectin 3 (Gal-3) is an antiapoptotic and a proinflammatory lectin. We hypothesized that the proinflammatory properties of Gal-3 may influence disease induction in the multiple low doses of streptozotocin model of diabetes. Diabetes was induced in C57BL/6 Gal-$3^{+/+}$ and Gal-$3^{-/-}$ mice and disease monitored by blood glucose level, immuno-histology, insulin content of islets and expression of the proinflammatory cytokines, TNF-α, IFN-γ, IL-17, and iNOS in pancreatic lymph nodes. Gal-$3^{+/+}$ mice developed delayed and sustained hyperglycemia, mononuclear cellular infiltration and reduced insulin content of islets accompanied with expression of proinflammatory cytokines. Gal-$3^{-}/^{-}$ mice were relatively resistant to diabetogenesis as evaluated by glycemia, quantitative histology and insulin content. Further, we observed the weaker expression of IFN-γ and complete absence of TNF-α, and IL-17 in draining pancreatic lymph nodes. Macrophages, the first cells that infiltrate the islet in this model of diabetes, produce less TNF-α and NO in Gal-$3^{-/-}$ mice. Thus, Gal-3 is involved in immune mediated β cell damage and is required for diabetogenesis in this model of disease.

Abbreviations: EAE, experimental allergic encephalomyelitis; CFA, complete Freund's adjuvant; Gal, galectin; IFN-γ, interferon gamma; IL, interleukin; iNOS, inducible nitric oxide synthase; TNF-α, tumor necrosis factor-alpha; MLD-STZ, multiple low dose streptozotocin; LPS, lipopolysaccharide, mRNA, messenger ribonucleic acid; NO, nitric oxide; NFκB, nuclear factor-κB, RT-PCR, reverse transcriptase polymerase chain reaction.

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