Antigen Coupled with Lewis-x Trisaccharides Elicits Potent Immune Response in mice

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摘要

Abstract

Background: Glycoproteins containing Lewis-x (Lex) trisaccharides are often associated with the host's adaptive TH2-type immunity, but the mechanisms underlying the TH2-biased response are at present unclear. Objective: The modulatory effect of Lex or its glycoconjugates on IgE/TH2 responses was investigated. Methods: The levels of serum antibodies and cytokines were analyzed by means of ELISA, RT-PCR, or both. Results: In C3H mice Lex coupled with BSA (Lex-BSA) elicited higher levels of specific IgE and IgG1, but not IgG2a, which were associated with increased levels of splenic TH2 cytokines when compared with those seen in BSA-sensitized mice. In BALB/c mice sensitized with Lex-BSA or Lex mixed with ovalbumin, significantly increased levels of specific IgE and IgG2a antibodies were found concomitant with reduced levels of serum IL-12p70. These effects were attenuated in IL-12-deficient BALB/c mice. Lex and an isomer, Ley, but not other isomers, inhibited the production of LPS-induced IL-12p70, associated with a significant reduction of nuclear NF-κB, in bone marrow-derived dendritic cells from BALB/c mice, suggesting that Lex-induced suppression of IL-12p70 results in an enhanced TH2 response. The addition of mannan, a known ligand for dendritic cell-specific intercellular adhesion molecule 3-grabbing nonintegrin, abrogated the suppressive effect of Lex trisaccharides. Conclusion: These results provide evidence for a potential role of Lex trisaccharides in shaping the immune responses through, at least in part, its suppressive effect on IL-12p70 production. Considering the relative ubiquity of glycoproteins with Lex or similar oligosaccharides, including plant-derived (or food-derived) allergens, these findings might have a broad implication. Clinical implications: The adjuvant activity of Lex trisaccharides might aid in vaccine design and might be important in determining the allergenicity of proteins containing this or other similar structures