

Induction of resistin-like molecule beta (RELM β) by respiratory allergen, IL-4, IL-13, and STAT6 in experimental asthma.

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Rationale:

Prompted by the current rising incidence and severity of asthma despite intense ongoing research efforts, we utilized an unbiased, empiric approach involving transcript profiling of asthmatic lung RNA.

Methods:

Lung RNA from asthmatic and control mice were subjected to transcript profile analysis using Affymetrix microarrays that contained the largest commercially available collection of murine genes. The data obtained from these experiments demonstrated a strong induction of RELM β in the lungs of asthmatic mice. RELM β is a member of the resistin family of proteins, a structurally related group of cytokines that have been associated with resistance to insulin (obesity). In order to more fully characterize the activity of this cytokine during allergen induced asthma, northern blot analysis of wild type, allergen induced and cytokine over expressing gene targeted mice was performed.

Results:

Employing asthma models induced by different allergens and protocols, we found strong induction of the mRNA for RELM β . RELM β mRNA was not detectable in control lungs, but was markedly increased following the development of OVA (ovalbumin) and *Aspergillus fumigatus* antigen-induced experimental asthma. A time and dose dependent expression of RELM β in OVA challenged mice was demonstrated. RELM β was also induced in the lungs of IL-4 transgenic mice and by intratracheal treatment with recombinant IL-13. Using mice deficient in signal-transducer-and-activator-of-transcription (STAT)6, allergen and IL-4/IL-13-induced RELM β expression was demonstrated to be dependent upon this transcription factor. In contrast, IL-5 deficient mice had normal induction of RELM β compared with wild type mice.

Conclusion:

RELM β is induced by allergen, IL-4, and IL-13 by a STAT-6 dependent mechanism in the asthmatic lung. These results provide a mechanistic link between the pathogenesis of insulin resistance (obesity) and asthma.