

might actually be an anti-prophyllin one. The presence of different epitopes might also lead to each of them being able to induce the generation of its own specific IgE; as the RAST/CAP might not be able to differentiate them, they would be identified as a single comprehensive antibody.

Which should then be our attitude regarding this complex problem? We suggest incorporating the skin prick tests with latex into the routine studies in the following cases: children with atopic dermatitis, urticaria and angioedema; children at high risk (myelomeningocele, urogenital malformations, transplantation surgery, haemodialysis), and in all atopic children undergoing a second surgical intervention.

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New perspectives in the treatment of allergic sensitization

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The best therapy for allergic disease is its prevention: a good prophylaxis begins with allergen avoidance, and for this purpose measures should be taken which help in changing the Th2 environment towards a Th1 one¹⁻³, particularly in the case of the newborn and in children prone to this type of disease.

The atopic mother should avoid environments with a sensitizing risk during pregnancy. Warner et al⁴ demonstrated a good correlation between the IgE levels in amniotic fluid and those in maternal blood, suggesting a passage of IgE from the mother to the foetus through pathways different from the transplacental ones. The foetus may ingest and inhale immune complexes contained in the amniotic fluid comprising IgE from the mother and the corresponding allergens. As the foetal ileum expresses Class II molecules of the major histocompatibility complex by the age of twelve weeks, the hypothesis may be put forward that antigen presentation might occur already during pregnancy, turning the foetus into a potentially allergic patient⁵⁻⁷.

The cytokine environment in which the foetus is immersed is a fundamentally Th2 one, as a Th1 predominance is harmful for gestation⁸. Therefore, when birth occurs, the bias of the T cells must be changed to a Th1 one, thus preventing the contact with allergenic substances from inducing the generation of IgE antibodies⁹.

In the context of this change in the cytokine environment, there are environmental factors that have an influence on this trend towards a Th1 or Th2 environment. In a recent study by the group of Hopkin¹⁰, an inverse correlation was demonstrated between positive response to tuberculin and the apparition of atopic diseases. Other studies^{11,12} have also found an inverse correlation between allergic diseases and certain viral infections.

DNA THERAPY

This is the most promising therapeutic modality: it complements immunotherapy and considerably improves it, it is cheap, and it is applicable to a large nucleus of the population¹³. In a highly interesting report by Kline et al¹⁴, microorganism-derived oligodeoxynucleotides are described which induce Th1 responses through stimulation of the interleukin (IL) 12 synthesis. Furthermore, in a murine asthma model the administration of the antigen together with these sequences prevents the development of asthma or airway inflammation, bronchial hyperreactivity and eosinophilia, and an improvement of the symptoms was observed even in the model with already-established asthma.

Table I. Effect of galectin 3 on the CD32 expression in various cell types

Cells	CD32 expression		Inhibition (%)
	Control (%)	+ Galectin 3 (%)	
Allergic patients			
T ^a	21 ^b	7.6	63.8
B	8.7	1.8	80
Monocytes	9.5	4.5	53
Control			
T	29.3	28.1	4
B	11.3	8.3	26
Human Eosinophils	49.5	36	27
EoL-3 cell line	52	8.5	83.6

^a The cells were incubated with galectin-3 (10 µg/ml) at 37 °C for one hour and the monoclonal anti-CD32 antibody was then added (30 min at 4°C); the cells were then analysed by flow cytometry.

^b Per cent proportion of cells positively stained with PE-anti CD32. 10,000 cells were analysed in each experiment.

Not all are benefits, however: in the experimental context, and prior to progressing to the clinical studies level, the assurance must be achieved that the risk of inducing autoimmune diseases has been avoided, as certain microbial products might induce such diseases through a mechanism which is also IL12-dependent.

IMMUNOMODULATORS

As eosinophilic inflammation represents a fundamental factor in the development of allergic disease, particularly in the late reactions, studies have been carried out with a lectin of animal origin¹⁵ that may modulate the development of inflammation by inhibiting the gene coding for IL5.

Galectin 3 is an animal lectin which was previously designated "Mac-2"; it contains a domain which allows linkage to b-galactosides and thus to IgE and to the low-affinity IgE receptors. In order to link to the cell surface, galectin 3 requires an appropriate ligand in the cell membrane. This particular ligand is constituted by glycoproteins present in the lymphocytes, endothelial cells, eosinophils and macrophages.

We have described the ability of this lectin to inhibit the IL5 gene in cells which are important in inflammatory reactions, such as human eosinophils, antigen-dependent T cell lines¹⁶ and lymphocytes from allergic patients. Galectin 3 not only selectively inhibits the IL5 gene, but the corresponding protein is not synthesised in the supernatant of Th2 cells stimulated with their specific antigen.

This lectin might be defined as an immunomodulator for eosinophilic inflammation, according to the studies carried out *in vitro*, but this still awaits confirmation *in vivo* in an experimental murine asthma model; the appropriate studies are currently underway in our laboratory.

We have investigated the possible mechanism for the linkage of galectin 3 to the cell surface. Eosinophils, as well as the eosinophilic cell line EoL-3 express CD32 (receptors for Fc γ RII) more intensely than CD23. For this reason, and because of a certain structural analogy between the two receptors, we consider CD32 to be a good candidate for this interaction between galectin 3 and the eosinophils.

Flow cytometry has been used for studying the interaction of this lectin with the cell membrane; the results are summarised in Table I. A reduction of the expression of the CD32 Fc γ receptor is observed in different cell types after incubation of the cells with galectin 3. This inhibition was as high as 80% in several experiments. However, this type of experiment represents only an indirect indication of the linkage of galectin 3 to the cells. For this reason, we are currently carrying out experiments with fusion proteins of the GST-galectin type, which could provide direct corroboration of the cytometry experiments.

A further compound which might be of interest in the modulation of the eosinophilic inflammatory reaction is the transforming growth factor β (TGF- β)¹⁷.

TGF- β is an important cytokine which inhibits inflammation, reduces eosinophil viability, exerts inhibitory effects on IL4 and stimulates the release of fibronectin. Eosinophils and fibroblasts of the bronchial submucosa and epithelium are the main producers of TGF- β .

This cytokine is detected in high concentrations in the bronchoalveolar lavage fluid from asthmatic and chronic bronchitic patients, and it is consi-

dered to have a fibrogenic action in the remodelling of the airways and in the subepithelial fibrosis¹⁸⁻²⁰.

We are currently investigating the role of this cytokine in an experimental murine asthma model²¹ by blocking its action with specific monoclonal antibodies during the induction of a challenge-induced asthmatic reaction. In ovalbumin-sensitized mice, and after the induction of an eosinophilic inflammatory reaction in the airways through inhalation of the antigen, a cell infiltrate appears which is similar to the one observed in the course of the delayed reaction. Therapy with inhaled TGF- β blocks the local synthesis of this cytokine.

The repeated administration of antigens induces an accumulation of macrophages and CD8+ cells and a fall in the number of B-lymphocytes, together with an inhibition of the IL4 and IL5 transcripts.

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