RESEARCH PAPER AMALYSIS

CAN ANTIBODIES TO IGE ACT AS ANTI-ALLERGICS?

Immunoglobulin E (IgE)-an otherwise minor component of the immunoglobulin repertoire-mediates most forms of immediate-type hypersensitivity, including asthma, by binding to the Fce receptors on the surfaces of basophils and mast cells. Cross-linking of this IgE by an allergen leads to aggregation of the underlying receptors, and the subsequent release of histamine and the other chemical modulators of an allergic response. Except for a possible role in potentiating immunity to parasite antigens, IgE appears to be completely dispensible: Normal adults have less than one milligram. Consequently, most strategies for allergy prevention have focused on ways of depleting or eliminating it.

To date, approaches involving IgE-binding factors and interleukin-4 (IL-4)—both T cell products—have received the most attention. Binding factors suppress IgE synthesis in vitro, and inhibitors of IL-4—which can switch B cells from IgG to IgE production—are being actively sought. Researchers have not seriously considered using antibodies directed

against IgE because such antibodies efficiently cross-link surface IgE and so are potent pseudo-allergens.

IgE associates with cells in at least two additional ways, as well. It binds to low-affinity (FCeRII) receptors on some B cells, T cells, and monocytes. And the B cell sub-population that secretes IgE bears it as a surface marker. These various modes of association suggested to Tse Wen Chang and his colleagues at Tanox Biosystems (Houston, TX) and Johns Hopkins School of Medicine (Baltimore, MD) the existence of epitopes on free IgE, and IgE at the surface of B cells, that were not accessible when the immunoglobulin was complexed to its receptors. They reasoned that antibodies directed at such epitopes would not interact with receptorbound IgE and thus would neither cross-link the molecule nor stimulate histamine release. As they report in this month's Bio/Technology, both suppositions are correct.

After immunizing mice with polyclonal human IgE, the researchers prepared and screened several thousand hybridomas for those producing

high-affinity anti-IgE monoclonal antibodies (MAbs). Among these were several IgE-specific antibodies that were unable to stimulate histamine release from IgE-primed basophils even under extremely permissive conditions. These same antibodies were also unable to bind to a lymphoblastoid human cell line—characterized by high expression of the low-affinity receptor—in the presence of IgE. The antibodies did, however, bind strongly to IgE-secreting B cells.

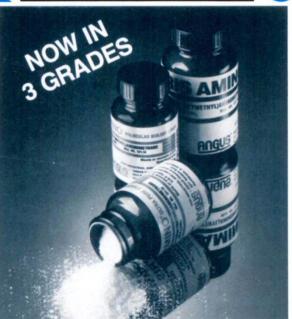
As research tools, these MAbs will be useful reagents with which to purify IgE-secreting B cells, and for peptide mapping studies. But their therapeutic potential may be even more important. The scientists envisage two ways in which these MAbs might be used to reduce the amounts of IgE in allergic patients. One way involves removing IgE from the circulation by using the antibody as a binding factor. The second relies on the ability of many lymphocyte-specific MAbs to destroy target cells in vivo by mediating antibody- and complement-dependent cytolysis. -Harvey Bialy

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