PROGRESS REPORT for Mizutani Foundation Research Grant

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Principal Investigator: Robert M. Anthony, Ph.D.
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Progress Report:

(a) Abstract: (within 1 page)

Immunoglobulin ε (IgE) antibodies are the primary mediators of allergic diseases, which affect more than one in ten individuals worldwide. IgE specific for innocuous environmental antigens, or allergens, binds and sensitizes tissue resident mast cells expressing the high affinity IgE receptor, FcεRI. Subsequent allergen exposure crosslinks mast cell-bound IgE, resulting in the release of inflammatory mediators, and initiation of the allergic cascade. It is well established that precise glycosylation patterns exert profound effects on the biology activity of IgG. However, the contribution of glycosylation to IgE biology is less clear. Here, we demonstrate an absolute requirement for IgE glycosylation in allergic reactions. The obligatory glycan was mapped to a single N-linked oligomannose structure in the constant domain 3 (Cε3) of IgE, at asparagine-394 (N394) in human IgE, and N384 in mouse. Genetic disruption of the site, or enzymatic removal of the oligomannose glycan altered IgE secondary structure and abrogated IgE binding to FcεRI, rendering IgE incapable of eliciting mast cell degranulation thereby preventing anaphylaxis. These results underscore an unappreciated and essential requirement of glycosylation in IgE biology.