Modeling and Experimental Characterization of IgE Receptor Signaling, Year Two

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Allergies are an important health issue. We want to study the allergy signal cascade by characterizing IgE receptors in mast cells. Mast cells are immune cells. Our project focuses on an IgE receptor called FceR1, which plays a critical role in allergy signaling within mast cells. This research could potentially be used to develop drugs for allergies. The FceR1 has three protein subunits: the alpha, beta, and gamma. In the gamma chain, there are two tyrosines (amino acid). The phosphorylation (transfer of phosphate) of these tyrosines is important for mast cell signaling initiation. However, timeline and pattern of each tyrosine's phosphorylation is unknown. We are investigating these unidentified parameters using two methods: modeling and experimental biology. Both approaches allow us to gain independent results that complement and verify each other. The experimental part of the project utilized viruses and yeast to select a specific antibody to the first phosphotyrosine which detects phosphorylation one tyrosine. This antibody from year 1 was affinity matured. The new antibody detects constant phosphorylation of the first tyrosine, and double phosphorylation after 2 minutes of allergen stimulation in cells. The model is written in a programming language called BioNetGen. The advantages of writing a model are ease of manipulation of each component, studying the effects on the system, and simulating without paying for supplies and reagents which experimentation requires. Currently, the model reflects the experimental data. We will also use the model to predict the second phosphotyrosine phosphorylation which can be verified by experiments.

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