Modeling and Experimental Characterization of IgE Receptor Signaling to Develop Drugs for Allergies

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Allergies are an important health issue in our community. We want to develop a drug to lower the effects of allergies by characterizing the IgE receptor in a mast cell. The mast cell is an immune cell with many receptors on its membrane. Our project focuses on an IgE receptor called FceR1, which plays a critical role in the allergy signal cascade within the mast cell. The FceR1 has three protein subunits: the alpha, beta, and gamma chain. In the gamma chain, there are two tyrosines (amino acid). The phosphorylation (transfer of a phosphate) of these tyrosines is known to be important for the initiation of signaling. However, the timeline and pattern of phosphorylation of each tyrosine is unknown. In our project, we will investigate these unidentified parameters using two independent methods: modeling and experimental biology. These two approaches allow us to gain independent results that will complement and verify each other. Using simulations, we calculated the rate of tyrosine phosphorylation. The experimental part of the project utilized viruses and yeast to select a specific antibody to the first phospho-tyrosine. We are currently investigating phosphorylation patterns of the gamma subunit using this antibody and the model. We will also use modeling to investigate whether single or double phosphorylation is required to start the signal cascade. These results will help us design a small molecule drug to arrest the signal cascade initiation in mast cell leading to new treatment options for allergy.

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