Summary: Antigen Discovery and Specification of Immunodominance Hierarchies for MHCII-restricted Epitopes (Graham et.al)

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For well over a decade, the world of immunology has been gaining traction as a core focus to better understand, and cure, many human diseases. The science and medical community alike have gained appreciation for the role of immunological processes in infectious diseases, autoimmune diseases, and cancer. As the prevalence of these conditions increases, there has never a more critical time for researchers to better understand the immune system and its potential for therapeutics.

Behind the development of new and exciting immunotherapy and pharmaceutical interventions is rigorous, basic science research that forms the foundation upon which we can develop these advanced treatments. We still have a lot to learn about how the human immune system functions, how it can both keep us healthy or lead to disease, and how we can best study these mechanisms. In the newly published paper by Graham, et.al. in *Nature Medicine*, immunologists and researchers take on the difficult task of identifying the key components of immunologic processes.

In their investigation, the authors developed a way to identify the T cell epitopes that play a dominant role in antigenicity. More specifically, they outline a unique approach to identifying and predicting the specific molecules that initiate clinically significant immune responses. They focused on epitopes associated with major histocompatibility complex II (MHCII), which are the key proteins that bind the T cell to activate immune mechanisms implicated in both health and disease. Using a broad, unbiased survey of proteins, they developed a model that predicts dominant MHCII epitopes on a genome-wide scale. This essentially provides researchers with the tool to take a collection of bacterial species, for example from the human gut microbiome, and create a map of the immunodominant epitopes. This is an important step in identifying the antigenic pathways that lead to development and propagation of disease (such as in Inflammatory Bowel Disease, in keeping with the microbiome example). When they put their model to the test, it accurately predicted novel T cell epitopes from both pathogenic and commensal bacteria.

Amidst a thirst for promising new immunotherapies to treat chronic and terminal disease, this paper is a powerful reminder of the role, and necessity, for developing new ways to study core immunologic mechanisms and pathways.