NIH Award from the National Institute of Allergy and Infectious Diseases

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- Project: Genetic, Viral and Immunologic Studies in New England Mice
- Start Date: June 1, 2009
- Total Award Amount: $762,500

How the results of this project will benefit society:
Autoimmune inflammatory diseases, such as lupus, rheumatoid arthritis, multiple sclerosis, and insulin-dependent diabetes mellitus affect tens of millions of Americans, resulting in considerable morbidity (sickness), mortality (death), pain and suffering, and medical costs. This study will help in devising specific means to block the initial steps of tolerance breakdown in major autoimmune diseases.

The problem the project is trying to solve:
We have invented and developed a non-toxic, antigen-specific tolerance therapy targeted against autoimmune cells that would spare lupus patients from receiving mutagenic cytotoxic agents, corticosteroids and global immunosuppressants. The therapy also is aimed at maintaining lupus patients in remission, and preventing the initiation or progression of organ-damaging disease in patients at risk. In this application we will define how the therapy works to restore normal regulation of the immune system in lupus, and how it can be improved further.

How this project will work:
Our hypotheses and ensuing aims are focused on antigen presenting cells (APCs), to determine how novel APCs initiate breakdown of tolerance to nuclear antigens from apoptotic cells to induce pathogenic T-helper cell responses simultaneously in lupus and how this priming step can be blocked. We will also examine how other APCs, such as tolerogenic plasmacytoid dendritic cells can restore immunoregulation after antigen-specific tolerance therapy of lupus. A detailed understanding of the mechanisms would rapidly bring this therapy to patients in the clinic. The proposed studies will also provide a better definition of the disease pathogenesis initiated by a novel antigen-presenting cell inducing autoimmune response in not only lupus, but also other autoimmune diseases.

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