Understanding the Origins of Autoantibodies

Professor Betty Diamond
Center for Autoimmune and Musculoskeletal Diseases,
The Feinstein Institute for Medical Research &
Hofstra Northwell School of Medicine

Abstract
Many therapeutic interventions that are effective in murine lupus have failed in clinical trials in patients. We believe this is because mouse models phenocopy only some patients, and because there is patient heterogeneity that reflects genetic risk. We have developed a mouse model which phenocopies the Blimp-1 SLE risk allele, with enhanced activation of dendritic cells (DCs) of female mice. The autoantibodies in this mouse are generated by somatic mutation in a germinal center response, secondary to an altered T follicular help cell compartment. This model allows us to explore new therapies targeted to a specific subset of patients.

About Our Speaker
Dr. Betty Diamond is a rheumatologist and scientist by training. She graduated with a BA from Harvard University and an MD from Harvard Medical School. She performed a residency in internal medicine at Columbia Presbyterian Medical Center and received postdoctoral training in immunology at the Albert Einstein College of Medicine.

Dr. Diamond has headed the rheumatology divisions at Albert Einstein School of Medicine and at Columbia University Medical Center. She also directed the Medical Scientist Training Program at Albert Einstein School of Medicine for many years. A former president of the American Association of Immunology, Dr. Diamond has also served on the board of directors of the American College of Rheumatology (ACR) and the Scientific Council of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). She is currently Professor and Head of the Center for Autoimmune and Musculoskeletal Diseases at The Feinstein Institute for Medical Research and director of the PhD and MD/PhD programs at the Hofstra Northwell School of Medicine. Dr. Diamond is a fellow of the American Association for the Advancement of Science (AAAS), a member of the Institute of Medicine and an ACR Master.

Dr. Diamond's primary interests are in the mechanisms of central and peripheral tolerance of autoreactive B cells and the defects in these mechanisms that are present in autoimmune disease, as well as the role of antibodies in brain disease. She first discovered that a peptide that binds to anti-dsDNA antibodies in mice and systemic lupus erythematosus (SLE) patients represents an epitope on N-methyl-D-aspartate (NMDA) receptors of the brain. Antibodies against this epitope are present in the blood, cerebrospinal fluid and brain tissue of patients with neuropsychiatric lupus. These anti-NMDA receptor antibodies alter function in the adult brain following a breach in the blood-brain barrier and alter fetal brain development as a consequence of in utero exposure to maternal antibodies. Her work provided a mechanism for aspects of neuropsychiatric lupus and has been hypothesized that these antibodies may contribute to acquired changes in cognition or behavior. Dr. Diamond’s laboratory has recently extended their studies of anti-brain antibodies to ask whether these might account for some cases of autism and post-traumatic stress disorder.