Project Title

Innovative studies of B-lymphocytes: insights into understanding autoimmunity and discovery of a subversion strategy used by infectious agents

Distinguished Researcher

Institute: Institute National de la Sante et de La Recherche Medicale (INSERM)

Researcher:
Prof Moncef Zouali
Nationality: **France**

Abstract

Moncef Zouali, a Director of Research at the French Medical Council (Institute National de la Recherche et de la Sante` Medicale, INSERM, Paris), has been responsible for the creation of ground-breaking paradigm shifts in two main areas of research in autoimmune and infectious diseases. First, in systemic autoimmune diseases, he provided important clues to the origin of pathogenic autoantibodies (Nature Genetics, Proc Natl Acad Scie USA, EMBO J, FASEB J, Arthritis & Rheumatism). His work disclosed a high rate of somatic mutations within the VH genes of human lupus autoantibodies, indicative of somatic selection pressures that are responsible for the production of these auto antibodies. He also provided a novel mechanism of production of pathogenic autoantibodies in human lupus whereby a subset of B lymphocytes may be unable to extinguish their high-affinity for self-antigens by receptor editing. Such a molecular blockade in receptor editing would be either somatically acquired or genetically determined. These experiments led him to identify a crippled signaling pathway that includes the protein tyrosine kinase Lyn, the protein tyrosine phosphates SHP-1 and CD45, and the cell surface receptor CD22. These observations have been confirmed by other investigators. They offer potential immunointervetions strategies in systemic autoimmune diseases. Second, he has pioneered our understanding of the interactions of human B lymphocytes with superantigens produced by infections agents. In studies underpinned by papers in Proc Natl Acad Sci USA, FASEB J, J Immunol, Infect immun, he was the first to map the binding sites of superantigens to their B lymphocyte receptors. He also discovered a novel mechanism used by some infectious agents to subvert the innate-like functions of B lymphocytes. These obserbvations were rapidly confirmed by other investigators.