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Preface

Genetics of allergic and immunoregulatory disorders

Two recent issues of *Immunology and Allergy Clinics of North America* dealt with primary immunodeficiencies. In this issue, we attempt to review disorders in which the participating cells and molecules of host defense are dysregulated. In the first section, the genetic contributions to atopic and atopic-like diseases will be described. In the second section, disorders of host defense will be described.

Significant progress has been made in understanding the pathogenesis of many allergic disorders. Most if not all of these disorders are multi-factorial and polygenic. In spite of the tremendous complexity, dramatic progress in the past few years has led to an improved understanding of the genetic contributions to atopic and atopic-like disorders. For asthma, multiple potential genes have been identified using various methods including linkage disequilibrium and molecular and physical mapping. These studies in asthma have advanced to the identification of genotype–phenotype relationships and genetic contributions to varying responses to different medications. In atopic dermatitis, several candidate genes have been identified in the last year, while in the field of food allergies, the studies have just begun. The recent completion of the human genome project should speed this work and provide guidance for future therapies, identification of risk factors, risk stratification of patients, and understanding individual responses to therapy.

The disorders of host defense reviewed here often do not present with classic signs of immunodeficiency such as recurrent infection. Their main manifestations are often aberrant responses to infection. For example, in lymphocytic histiocytosis, X-linked lymphoproliferative disease, Chediak-Higashi disease, and one form of Griscelli disease, the life-threatening manifestation of the underlying disease is often an aberrant response to a herpes virus which leads to cytokine release and an aggressive, life-threatening inflammatory response. In two other diseases, immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX) and autoimmune lymphoproliferative syndrome (ALPS), the underlying defect results in an inability to turn off an ongoing immune response properly. These disorders represent a new field for clinical

immunologists. It is likely that future work will reveal more disorders of the regulation of the immune response.

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