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EDITORIAL

The Elements of Immunity

Lymphocytes, which orchestrate the body's response to infectious agents, rank among the most studied and best understood of all cell types. For example, we have detailed knowledge about how an unlimited array of cell-surface receptors is generated by rearrangement of a limited number of genetic elements, and how these receptors trigger the elaborate ballet of interacting signal cascades that control a cell's response. But although our understanding of the molecular basis of immunological specificity has progressed to the point where "immunology has reached the end of its history,"* we are still far from a true understanding of immunity. To achieve it, we must attain the same degree of insight into each of the elements of immunity as we currently have for immunological specificity. We must also learn how these elements coordinate to counter infection while sparing the host. At present, too many of the essential elements—such as immune responsiveness and memory, nonspecific immunity, physiology and homeostasis, population biology, and host-parasite interactions—remain elusive. One way to move forward is to apply the molecular knowledge base to the study of these elements. The special section in this issue illustrates several key areas in which this approach is yielding major advances.

The first article provides a fundamental reconsideration of the role of innate, or nonspecific, mechanisms of defense. Previously, innate immunity was thought to work independently of specific immunity or to be manipulated by the products of lymphocytes. But Fearon and Locksley (p. 50) describe an emerging picture of a two-way interaction in which innate mechanisms have a major influence on specific immunity. This is a new level of integration and interdependence among the different types of immunity.

A topic of frequent, often passionate, discourse—immunological memory—is broached by Ahmed and Gray (p. 54). The phenomenon is not in dispute: Secondary exposure to an antigen clearly produces a response that is more vigorous than the initial reaction. But what are the underlying mechanisms? What are the roles of antigen persistence, bystander activation, cellular life-span, and organism aging in B and T cell memory?

In terms of cell number, the immune system ranks alongside the brain and the liver as one of the three largest organs. Butcher and Picker (p. 60) consider the logistics of the immune system as an organ, focusing on how the recirculation of lymphocytes through the lymphatics, tissues, and bloodstream influences cell fate and the dynamics of lymphocyte homeostasis.

Field studies are difficult and perhaps unglamorous, but are crucial to the overall goal of understanding immunity. Parham and Ohta (p. 67) describe the population biology of the best-studied molecules of the human immune system, the polymorphic class I major histocompatibility complex (MHC) molecules. The convergence of molecular genetics and population immunology has improved understanding of the long-term dynamics of the MHC system and offers insight into evolutionary biology, medicine, and anthropology.

Mathematical biologists have long been fascinated by the dynamics of the immune system. The goal in building mathematical descriptions of the immune system is often misunderstood. It is not to provide some formulaic "answer" to the mechanisms of immunity, but to give a useful approximation of interactions, which might reveal new relations and suggest novel avenues of experimentation. In the final article, Nowak and Bangham (p. 74) use molecular details to model the generic immune system–virus interaction and then generate explanations for some characteristic findings in different viral infections.

In all of the above cases, molecular knowledge is a great catalyst for progress toward grasping the bigger picture. But what about applied immunology? A news story by Williams (p. 28) examines the current status of the transfer of new knowledge into practice. We also use *Science*'s World Wide Web site at http://science-mag.aaas.org/science/ to consider future advances. For this we need your help. Please complete the questionnaire on the Web; we will collate the responses and post an analysis of where the field thinks it is headed. It will be intriguing to find out if that assessment coincides with our view that there are exciting times ahead, both for the understanding of immunity and for its application.

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*F. S. Rosen, *Nature* **379**, 36 (1996).