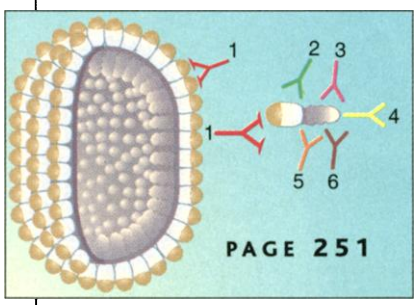
Immune Control, Memory, and Vaccines

A sweeping offensive to prevent infectious disease through vaccination remains a compelling goal in the movement toward improved public health in industrialized and developing societies. Expectations are high that vaccines will also soon be deployed in less conventional ways: to destroy tumors and prevent autoimmune diseases, for example. Yet the current range of vaccine targets remains remarkably narrow. How, then, will the scope and power of vaccination be improved?

The brisk pace of genome-related discoveries brings hope of revolutionary change for vaccine biology, as thousands of new targets and avenues for research emerge. But it will also be essential to maintain and renew investment in the exploration of basic immunology. This is reflected in this special issue, which visits some areas of immunity that are integral to vaccine research. Germain (p. 240) starts the ball rolling by discussing how the perspective of "systems engineer" might guide us toward an integrated view of the immune system. Ultimately, this may lead to new rationales in the design of vaccines and other forms of immune manipulation.

Vaccination relies on the immune system's memory of antigens that it encounters, yet our understanding of this fundamental characteristic remains limited. Sprent and Tough (p. 245) discuss current thinking on how memory T cells develop and the various factors that regulate their actions. Some new thoughts on how immune memory is maintained are also offered by Fearon and colleagues (p. 248), who reason that memory lymphocytes might be akin to self-renewing stem cells that are held in a state of arrested differentiation and perpetual readiness for encounters with antigens.

According to Zinkernagel and Hengartner (p. 251), the significance of balancing antigen in the immune equation is often underappreciated, as inherent features of antigen contribute significantly to the regulation of immune responses. Information about the pathogens from which antigens are derived is also important, and this is deciphered by dendritic cells, which guide T lymphocyte responses. As discussed by Pulendran *et al.* (p. 253), this is developing as a far-reaching paradigm in immunology and one that is increasingly applicable to vaccination strategies.



The News stories in this issue examine several ways in which new immunological tools are already being applied to vaccinemaking. A report on tuberculosis by Martin Enserink (p. 234) describes a fascinating conjunction of events that have led to trials of at least five new TB vaccines. Jon Cohen reports on a second area of technology (p. 236), focusing on a small biotech company's efforts to create antigens using a method called "DNA shuffling" to produce immune responses stronger than those generated by natural antigens. Finally, Giselle Weiss (p. 238) reviews the history—and uncertain future—of a renowned home for immunology in Europe: the Basel Institute of Immunology, now converted to a center for medical genomics.

This collection is full of contrasts: Immunology, which has been overshadowed in some ways by genome studies, is now using the tools of genomics to open exciting new avenues of basic and applied research. And although infectious diseases such as HIV and TB are on the rise, researchers are optimistic about their chances of developing new vaccines against these threats. The challenges for immunology and the possibilities for vaccine biology are enormous.

–STEPHEN SIMPSON AND ELIOT MARSHALL

CONTENTS

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