IN THE MORE THAN 100 YEARS SINCE PAUL EHRlich COINED THE PHRASE “magische Kugel,” or “magic bullet,” scientists have been striving to develop targeted therapies for diseases ranging from cancer to Crohn’s disease. Although for many years the path toward this goal appeared to be pharmacologic in nature, four decades ago an important deviation was made: the advent of hybridoma technology. This allowed for the production of large quantities of antibodies specific for a single target: monoclonal antibodies. Now, the same molecules that were known to provide long-lasting protection against many infectious diseases had the potential to be harnessed for the treatment of many different diseases.

Although it took another decade for the first such therapy to be realized (muramab, used to prevent transplant rejection), the floodgates have been opened. More than 30 monoclonal antibodies have been approved by the U.S. Food and Drug Administration, and many more candidates are in clinical trials. Antibody therapeutics are now a multibillion-dollar industry. Śliwkowski and Mellman (p. 1192) review several of the monoclonal antibodies now approved to treat cancer and their mechanisms of action. They also make the point that antibody therapies are not limited to monoclonal antibodies alone anymore; antibodies specific for more than one target (bispecific antibodies) and antibody-drug conjugates, among other strategies, are being pursued to generate therapeutics that are more specific, more stable, and more effective.

Monoclonal antibodies are also taking a front seat in the difficult task of developing vaccines against chronic infections such as HIV. Recent advances in the isolation of monoclonal antibodies from infected patients have allowed for the discovery of several very potent broadly neutralizing antibodies that target HIV. Klein et al. (p. 1199) discuss these antibodies and how they can inform HIV vaccine design and perhaps also be used therapeutically to treat infected individuals. A related News Focus (p. 1168) recounts how it took more than two decades for these broadly neutralizing antibodies to rise to the fore in HIV vaccine research, and how they have spawned provocative new strategies that have reinvigorated the field. How to generate protective antibodies through vaccination is a major hurdle, however, for treating HIV and many other infectious agents. Part of the reason for this is an incomplete understanding of the cells that make such protective antibodies, so-called memory B cells. Tarlinton and Good-Jacobson (p. 1205) discuss recent advances in this area, including the various types of memory B cells, how they are generated during an immune response, and how some of these processes could be shaped to our advantage during vaccination.

This special section highlights the great success of these “magic bullets,” but it also shows that we have much to learn. The future of antibody-driven vaccine design and therapy is just now being glimpsed.

– KRISTEN L. MUELLER

Antibodies

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Editor's Summary

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