

Preface

The recent FDA approval of Provenge[®] as the first therapeutic cancer vaccine together with the recent demonstration that Ipilimumab[®], a monoclonal antibody that blocks a negative immune checkpoint called cytotoxic T lymphocyte-associated antigen-4 (CTLA-4), prolongs patient survival are major achievements that usher in a new era of cancer immunotherapy (Hodi et al. 2010; Kantoff et al. 2010). These “first-into-class” treatments reflect the substantive progress that basic and translational scientists have made toward understanding the mechanisms underlying protective tumor immunity in cancer patients.

Immunotherapies were first explored at the turn of the twentieth century, but the crafting of potent treatments required more detailed knowledge of how the immune system responds to cancer. Advances in genetic, cellular, and biochemical technologies have begun to yield this critical information, which has stimulated the development and widespread application of monoclonal antibodies and bone marrow transplantation as highly beneficial therapies for many solid and hematologic malignancies. Moreover, recognition of the pathogenic involvement of microbial agents in cancer resulted in the generation of effective preventive vaccines against hepatitis B virus and human papilloma virus, which have and will significantly reduce the incidence of liver and cervical cancer, respectively.

The success of Provenge[®], Ipilimumab[®], and likely other cancer immunotherapies in the near future derives from a richer characterization of the processes of immune recognition and immune regulation. Dendritic cells are specialized to present cancer antigens to effector lymphocytes through a pathway that involves both positive and negative signals. In turn, the activities of effector lymphocytes are modified in the tumor microenvironment through mechanisms that normally contribute to the maintenance of self-tolerance. Moreover, in the context of an ineffectual host response, tumors evolve to exploit factors present in the microenvironment that facilitate disease progression. Thus, therapeutic manipulation of immune recognition, immune regulation, and tumor-promoting inflammation should prove decisive in triggering immune-mediated tumor destruction.

This volume brings together 13 groups that have made major contributions to the study of endogenous and therapeutic tumor immunity in model systems and patients. Collectively, these investigations have generated remarkable insights into the complex cross-talk between the tumor and host. This knowledge should render possible the identification of specific molecular mechanisms that restrain protective immunity in individual patients; this information will thereby guide the administration of appropriate immunotherapeutics to overcome these limitations and markedly impact patient outcome. It is likely that a combination of immune approaches that address complementary defects will prove most potent, and that immune treatments will be effectively integrated with other strategies for cancer therapy.

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<http://www.springer.com/978-3-642-14135-5>

Cancer Immunology and Immunotherapy

Dranoff, G. (Ed.)

2011, XIV, 306 p., Hardcover

ISBN: 978-3-642-14135-5