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Preface

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The clinical outcome of a tumor results from a series of complex events which include the genotype and phenotype of tumor cells, their interactions with a diversified microenvironment as well as therapeutic interventions. Among elements which naturally interfere with tumor growth, invasion, and metastasis are cells and molecules of the immune system. Their role in controlling the fate of a cancer has been a long-debated issue, with pros and cons arguing harshly about, even the reality of tumor immunosurveillance against tumors of non-viral origin. Epidemiological studies showing a higher incidence of viral-induced cancers, although not only these, were used by the two camps to support their positions.

It is striking that the classical review of Hanahan and Weinberg defining the six hallmarks of cancer ignores immunity in 2000. At the same time, however, appeared the pioneering contributions by the groups of R.D. Schreiber and M.J. Smyth who analyzed deeply immunocompromised mice, deficient both for adaptive and innate immunities, which demonstrated that all mice eventually were diagnosed with tumors, of non-viral origin, even without experimental intervention. Moreover, they showed that dormant tumor cells remain for months in clinically free mice and that, due to their genetic plasticity, some malignant cells may eventually escape the immune control. These observations, confirmed in other experimental models, led R.D. Schreiber to propose the three Es hypothesis with, first, an Elimination phase, in which the immune reaction may prevent tumor proliferation, followed by an Equilibrium phase, in which the immune system keeps the tumor cells on hold for long periods, and eventually, an Escape phase, when some tumor cells evade the immune controls. In human, the higher incidence of cancer in immunodeficient individuals, the growth of tumors from donor origin in renal-transplanted patients, and the interplay between the favorable prognostic influence of immune cell infiltration and the acquisition of escape strategies by malignant cells witness the reality of the three Es hypothesis.

The knowledge that has developed from these basic studies is being used today to develop immune-based personalized medicine of cancer, leading to novel prognostic and predictive biomarkers and novel therapeutic approaches. Therapeutic monoclonal antibodies not only directed to kill tumor cells but also to modulate cancer immunity have proven efficacious to prolong patients' survival. A first therapeutic vaccine has been approved in 2010 on the basis of increased overall survival. The present volume discusses various aspects of immunity and tumor growth and metastasis by leading contributors to the field aimed to propose novel therapeutic ways to efficiently modulate the immune system in order to extend the equilibrium phase or prevent tumor escape and reach a good control of cancer evolution resulting in improved survival under good conditions for the patients.

The first four chapters by Mlenick et al., Sautès-Fridman et al., Chioda et al., and Khazaie et al. decipher the complex interactions between immunity and tumors and the role of adaptive, innate, and regulatory immune compartments.

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Three chapters by Kepp et al., Ma et al., and Tartour et al. analyze the immunomodulating effects of classical cancer treatments such as chemotherapy, radiotherapy, and targeted anti-angiogenic treatments. They propose new immune-associated biomarkers to predict and monitor therapeutic responses to these treatments. Chapters by Houot et al. and Abès and Teillaud focus on monoclonal antibodies and cytokines to modulate immune responses through unlocking checkpoints and inducing long-term anti-tumor adaptive immune control. Finally, Stewart and Smyth focus on reverting tumor-induced immunosuppression to prevent tumor escape.

Thus, the present volume is a reference to understand the flourishing new immunomodulatory therapeutics and the biology on what they are based. It provides knowledge and technical tools to foresee their future.