

The evasion of immunologic detection and clearance of neoplastic cells and prevention of the host immune system's resolution of pro-neoplastic micro-environmental conditions are among the hallmark features of cancer. Like other hallmarks (unchecked proliferation, angiogenesis, replicative immortality, etc.), the origin of these characteristics lie within the genetic and epigenetic instability of transforming cells, which then undergo an intense biologic selection process. To better understand these immunologic changes is to better fundamentally understand cancer.

Radiotherapy has a greater than 100-year track record of efficacy against nearly all forms of malignancy. Yet, even in this modern era, not all of the mechanisms that foster this efficacy have been fully elucidated. The comprehensive immunogenic effects of radiation treatment are still largely unknown. The abscopal effects of radiotherapy have been observed and reported for decades and more recent biologic investigations have revealed that radiotherapy has a profound impact on the immunologic characteristics of neoplastic cells and the host response. To better understand these radiation-induced changes is to better understand radiotherapy itself.

Therefore, a tremendous opportunity stands before the field today; to improve the therapeutic index of radiotherapy by the modulation of post-radiation tumor immunology. As mechanisms of immunologic changes are further characterized, targeted therapeutic agents and treatment strategies can be developed to augment the response of tumor cells to radiotherapy – both locally and systemically.

With this goal in mind, The AME Publishing Company has teamed with over 40 researchers, editors, and leaders in the radio-immunologic field from around the world to bring about this book, *Radiotherapy with Immuno-Targeted Therapies*. It puts the latest work and thought processes into one convenient source. The book is organized into two principle sections: The first provides an overview of some of the basic observations pertaining to the impact of radiotherapy on cellular immunology. Discussed are the molecular events within the innate and adaptive immune systems that occur after exposure to ionizing radiation. Central to these events being tumor antigen presentation via major histocompatibility complex (MHC) classes I and II and the elaboration of the myriad cytokines which can either enhance or diminish the tumor clearance capability of these systems. The second section highlights the disease-specific translational and clinical efforts that are ongoing. Emphasis is placed upon the different immunologic effects of ablative versus fractionated radiotherapy, mechanisms of the abscopal effect, the immunologically complicated tumors arising in brain parenchyma (primary and metastatic), and the role of EGFR in head and neck cancers.

We hope this book not only informs the reader, but inspires new questions and lines of investigation that will be incorporated into their future work.

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