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The Renaissance of Cancer Immunotherapy

The 7th International Cancer Vaccine Symposium

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ISSUE

The Renaissance of Cancer Immunotherapy

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ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *The Renaissance of Cancer Immunotherapy*

Cancer immunoediting: antigens, mechanisms, and implications to cancer immunotherapy

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Accumulated data from animal models and human cancer patients strongly support the concept that the immune system can identify and control nascent tumor cells in a process called cancer immunosurveillance. In addition, the immune system can also promote tumor progression through chronic inflammation, immunoselection of poorly immunogenic variants, and suppressing antitumor immunity. Together, the dual host-protective and tumor-promoting actions of immunity are referred to as cancer immunoediting. The current framework of cancer immunoediting is a dynamic process comprised of three distinct phases: elimination, equilibrium, and escape. Recently, we demonstrated that immunoselection by $CD8^+$ T cells of tumor variants lacking strong tumor-specific antigens represents one mechanism by which cancer cells escape tumor immunity and points toward the future of personalized cancer therapy.

Keywords: cancer immunoediting; immunosurveillance; tumor antigens; immunotherapy; tumor escape; cancer genome

Introduction

Cancer immunoediting

A plethora of evidence now provides strong support for cancer immunoediting, a process wherein immunity functions not only as an extrinsic tumor suppressor but also to shape tumor immunogenicity.[1] In its most complex form, cancer immunoediting occurs in three sequential phases: elimination, equilibrium, and escape. Elimination is a modern view of the older notion of cancer immunosurveillance, in which innate and adaptive immunity work together to detect and destroy transformed cells long before they become clinically apparent. However, sometimes tumor cell variants may not be completely eliminated but instead enter into an equilibrium phase in which the immune system controls net tumor cell outgrowth; in this phase, adaptive immunity constrains the growth of clinically undetectable occult tumor cells and edits tumor cell immunogenicity.[2] Finally, the functional dormancy of the tumor cell population may be broken, leading to progression of the cells into the escape phase, during which edited tumors of reduced immunogenicity begin to grow progressively in an immunologically unrestrained manner, establish an immunosuppressive tumor microenvironment, and eventually become clinically apparent.[3] Importantly, escape from immune control is now acknowledged to be one of the hallmarks of cancer.[4]

The antigens of unedited tumors

A central tenet of tumor immunology in general, and the cancer immunoediting process in particular, is that tumor cells express antigens that distinguish them from their nontransformed counterparts, thus permitting their recognition by T cells and their eventual destruction by immunological mechanisms. Although a deep understanding of human and mouse tumor antigens currently exists, it comes nearly entirely from analyses of tumor cells derived from immunocompetent hosts, which were likely subjected to the sculpting forces of cancer immunoediting during their development. Little is known about the antigens expressed in nascent tumor cells, for example, whether they are sufficient

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