

Deconstructing Cancer Immunoediting

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Cancer Immunoediting is the process by which the immune system controls and shapes cancer. We originally envisaged that cancer immunoediting would occur in three phases: Elimination (also known as cancer immunosurveillance, the host protective phase of the process), Equilibrium (the phase in which tumor cells that survive immune elimination remain under immunologic growth control resulting in a state of functional tumor dormancy) and Escape (the phase where clinically apparent tumors emerge because immune sculpting of the tumor cells has produced variants that display either reduced immunogenicity or enhanced immunosuppressive activity). Strong experimental data has now been obtained using mouse models of cancer to demonstrate the existence of each phase of the cancer immunoediting process and compelling clinical data suggests that a similar process may also occur during the evolution of certain types of human cancer. Our efforts now focus on elucidating the molecular and cellular mechanisms that underlie each phase of cancer immunoediting and identifying the critical checkpoints that regulate progression from one phase of the process to the next. This approach has helped identify the nature of antigens seen by immunity in nascent developing cancers and has further shown that immunoselection is a major mechanism of immunoediting. Moreover, we have found that edited tumors can still be controlled by the immune system if natural mechanisms that prevent autoimmunity are suspended. As reported by others, we have confirmed that inhibition of CTLA-4 induces ejection of edited MCA sarcomas. However, we have also found that inhibition of PD-L1 does the same, although by perhaps different mechanisms. These differences will be discussed.