



antibodies



Special Issue Reprint

The Role of Complement in Cancer Immunotherapy

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The dual role of complement in cancer development and treatment has been investigated extensively and is characterized by a substantial literature that documents conditions in which complement enhances tumor growth or promotes killing of malignant cells. Although direct *in vitro* complement-dependent cytotoxicity (CDC) of cancer cell lines by FDA-approved mAbs can be readily demonstrated, there are considerable challenges related to translation of these findings to the clinic. These approaches include: optimization of mAb dosing schedules; engineering Fc regions of mAbs to enhance complement activation; treatment with cocktails of mAbs that bind to different sites on targeted cells and therefore synergize in CDC promotion; and neutralizing complement control proteins on malignant cells to weaken their complement defenses. Target sites on malignant cells that have been successfully exploited for mAb-induced CDC include CD20, CD37, CD38, CD52 and Epidermal Growth Factor Receptors. MAbs specific for complement components have served as powerful analytical reagents to investigate detailed mechanisms of CDC, and they have been employed to document complement activation by cancer cells and to examine the role of complement proteins (C1q and fragments of C3 and C5) in supporting tumor growth. The use of polyclonal and mAb reagents has revealed a role for the intracellular complement system in cancer biology and strategies that focus on the interaction of complement with the tumor microenvironment, and examine the impact of the complement on the response to immunotherapy in cancer should lead to additional mAb-based therapies.



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