Inflammation and cancer

Inflammation and Cancer: New Targets for Therapy in Cancer

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The concept that leukocytes are critical components of solid tumors is now generally accepted, however, their role(s) in regulating aspects of neoplastic progression, and/or response to cytotoxic, targeted and/or immune therapy is only beginning to be understood. Utilizing de novo mouse models of organ-specific solid tumor development (mammary, cutaneous, and pancreas carcinomas and mesothelioma), we now appreciate that adaptive leukocytes differentially regulate myeloid cell recruitment, activation and effector function, and in turn, activated tumor-infiltrating myeloid cells engage tissue-based programs to foster malignancy, and repress anti-tumor immunity by a diversity of mechanisms. Treatment of tumor-bearing mice with therapeutic agents that disrupt lymphocyte-myeloid cell interaction, myeloid cell activation, or myeloid cell functionality generally slow primary tumor growth kinetics when combined with cytotoxic therapy; however, their impact on metastases is variable. Similar to organ-specific regulatory programs co-opted to foster primary tumor growth, regulation of metastatic seeding and outgrowth is also regulated by tissue- and organ-specific mechanisms. Based on this, it stands to reason that therapeutic strategies may not be efficacious in both primary and metastatic locations. To be presented will be our recent insights into organ and tissue-specific regulation of primary and metastatic cancer development by adaptive and innate immune cells, how systemic regulation of humoral immunity and complement-mediated pathways regulate pro- versus anti-tumor immune responses, and new studies evaluating how attenuating protumor properties of select lymphoid and myeloid cells can be exploited to enhance therapeutic responses to cytotoxic and immune-based therapy.

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