Local and systemic tumor immune dynamics

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Tumor-associated antigens, stress proteins, and danger-associated molecular patterns are endogenous immune adjuvants that can both initiate and continually stimulate an immune response against a tumor. In retaliation, tumors can hijack intrinsic immune regulatory programs that are intended to prevent autoimmune disease, thereby facilitating continued growth despite the activated antitumor immune response. In metastatic disease, this ongoing tumor-immune battle occurs at each site. Adding an additional layer of complexity, T cells activated at one tumor site can cycle through the blood circulation system and extravasate in a different anatomic location to surveil a distant metastasis. We propose a mathematical modeling framework that incorporates the trafficking of activated T cells between metastatic sites. We extend an ordinary differential equation model of tumor-immune system interactions to multiple metastatic sites. Immune cells are activated in response to tumor burden and tumor cell death, and are recruited from tumor sites elsewhere in the body. A model of T cell trafficking throughout the circulatory system can inform the tumor-immune interaction model about the systemic distribution and arrival of T cells at specific tumor sites. Model simulations suggest that metastases not only contribute to immune surveillance, but also that this contribution varies between metastatic sites. Such information may ultimately help harness the synergy of focal therapy with the immune system to control metastatic disease.