Melanoma-specific vaccines have minimal efficacy in patients with established disease but enhance survival when administered in the adjuvant setting. Therefore, we hypothesized that organs bearing metastatic-like melanoma may differentially produce T cell chemotactic proteins over the course of tumor development. Using an established model of metastatic-like melanoma in lungs, we assessed the production of specific cytokines and chemokines over a time-course of tumor growth, and we correlated chemokine production with chemokine receptor-specific T cell infiltration. CXCR3-cognate chemokines (CXCL9 and CXCL10) were significantly increased in lungs bearing minimal metastatic lesions, but chemokine was at or below basal levels in lungs with substantial disease. Chemokine production correlated with infiltration of the organ compartment by transferred CD8\(^+\) tumor antigen specific T cells in a CXCR3- and host IFN-\(\gamma\)-dependent manner. Adenosine signaling suppressed chemokine production and T cell infiltration in the advanced metastatic lesions, and suppression could be partially reversed by the adenosine receptor antagonist aminophylline. Collectively, our data demonstrate that CXCR3-cognate ligand expression is required for efficient T cell access of tumor-infiltrated lungs, and ligands are expressed in a temporally restricted pattern that is governed, in part, by adenosine. Thus, modulation of adenosine activity may impart therapeutic efficacy to immunogenic but clinically ineffective vaccines.

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