

Visualization of a Primary Anti-tumor Immune Response by Positron Emission Tomography

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Current methodologies that monitor immune responses rely on invasive techniques that sample tissues at a given point in time. New technologies are needed to elucidate the temporal patterns of immune responses and the spatial distribution of immune cells on a whole body scale. We describe a noninvasive, quantitative and tomographic approach to visualize a primary anti-tumor immune response using positron emission tomography (PET). Bone marrow chimeric mice were generated by engraftment of hematopoietic stem and progenitor cells transduced with a trifusion reporter gene encoding synthetic Renilla luciferase (hRluc), enhanced green fluorescent protein (eGFP), and Herpes virus thymidine kinase (sr39TK). Mice were challenged with the Moloney murine sarcoma and leukemia virus complex (M-MSV/M-MuLV) and the induced immune response was monitored using PET. Hematopoietic cells were visualized using 9-[4-[¹⁸F]fluoro-3-(hydroxymethyl)butyl]guanine ([¹⁸F]FHBG), a radioactive substrate specific for the sr39TK PET reporter protein. Immune cell localization and expansion were seen at the tumor and draining lymph nodes (DLNs). 2-[¹⁸F]fluoro-2-deoxy-D-glucose ([¹⁸F]FDG), which is sequestered in metabolically active cells, was used to follow tumor growth and regression. Elevated glucose metabolism was also seen in activated lymphocytes in the DLNs using the [¹⁸F]FDG probe. When M-MSV/M-MuLV-challenged mice were treated with the immunosuppressive drug, dexamethasone, activation and expansion of immune cell populations in the DLNs could no longer be detected with PET imaging. The method we describe can be used to kinetically measure the induction and therapeutic modulations of cell-mediated immune responses.