Published OnlineFirst November 3, 2011; DOI: 10.1158/2159-8290.CD-RW110311OL-14

Immunotherapy

Major finding: [^{18}F]FLT PET allows visualization of antigen-specific immune responses to DC therapy.

Impact: Responders can be discriminated from non-responders after anti-cancer vaccination.

Strategy: Proliferating immune cells selectively take up and retain [^{18}F]FLT to allow *in vivo* imaging.

A NEW IMAGING TECHNIQUE CAN DIRECTLY ASSESS TUMOR VACCINE RESPONSES

The goal of antigen-specific therapy is to elicit an immune response to tumor cells, either by vaccination with tumor-specific antigens or by *ex vivo* education of autologous dendritic cells (DC). However, a major impediment to improvement of these therapies is the inability to quickly and noninvasively determine whether an immune response is successfully induced. Aarntzen and colleagues address this problem by using positron emission tomography (PET) to visualize proliferating T and B cells in the vaccinated lymph nodes of melanoma patients treated with DC therapy. This approach is distinguished from previous attempts to detect immune responses *in vivo* because the authors trace activated lymphocytes using a nucleotide analog, [^{18}F]-labeled 3′fluoro-3′-deoxy-thymidine ([^{18}F]FLT), instead of [^{18}F]-labeled fluoro-2-deoxy-2-D-glucose ([^{18}F]FDG), the more widely used method to visualize metabolically active cells. Activated, proliferating immune cells should have an increased nucleoside demand and therefore selectively uptake [^{18}F]FLT only after a successful antigenic stimulation. Consistent with this hypothesis, the [^{18}F]FLT PET signal increased only in lymph nodes populated with antigen-loaded DCs, even when very low numbers of DCs were present, and persisted several days after intranodal DC injection. Importantly, this lymph node PET tracer retention correlated with evidence of antigen-specific T- and B-cell responses in the peripheral blood, indicating that the [^{18}F]FLT signal faithfully reflects immune activation in response to therapy. Further, activated T and B cells specifically retained [^{18}F]FLT, as [^{18}F]FDG did not correlate with a peripheral blood immune response. This approach establishes a framework to directly monitor *in vivo* immune responses shortly after cellular therapy that may be broadly applicable to multiple tumor types, and has important clinical implications for identifying which patients respond to antigen-specific immunotherapy.

Aarntzen EH, Srinivas M, De Wilt JH, Jacobs JF, Lesterhuis WJ, Windhorst AD, et al. Early identification of antigen-specific immune responses in vivo by [^{18}F]-labeled 3′-fluoro-3′-deoxy-thymidine ([^{18}F]FLT) PET imaging. Proc Natl Acad Sci U S A. 2011 Oct 24. [Epub ahead of print].

Cancer Discovery; Published OnlineFirst November 3, 2011; doi:10.1158/2159-8290.CD-RW110311OL-14

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CANCER DISCOVERY

A New Imaging Technique Can Directly Assess Tumor Vaccine Responses

Cancer Discovery 2011;1:OF1. Published OnlineFirst November 3, 2011.

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