

Literature Watch

Implications for Transplantation

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CD45-immunoPET: A next-generation tool for imaging inflammation

By Anita Qualls,
Christopher Chang,
James M. Gardner

Inflammation is a hallmark of many debilitating chronic diseases including cancer, diabetes, and autoimmunity. Serum biomarkers of inflammation are noninvasive but generally nonspecific, and while biopsy can be diagnostic, its invasiveness and complexity often limit its utility in surveillance. Imaging modalities such as computed tomography can visualize edema and other indirect signs of inflammation but lack functional resolution. Positron emission tomography (PET) offers a noninvasive approach to visualize cellular processes in vivo, but existing PET probes for inflammation experience limited specificity. For example, the most widely used tracer, [^{18}F]-fluorodeoxyglucose

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(FDG), is taken up by all glucose-avid tissues, limiting diagnostic utility in metabolically active organs. Antibody-conjugated PET probes (immunoPET), such as CD11b-PET (specific for murine tumor-associated macrophages)¹ and CD206-PET (in clinical trials for solid tumors)² have shown promise but remain narrow in scope.

In a recent publication in *Nature*, Farid et al introduced a PET imaging strategy targeting CD45, a pan-leukocyte marker, to robustly visualize inflammation across diverse disease states (Fig. 1). The authors developed both mouse and human anti-CD45 probes using small antibody fragments (nanobodies) optimized for improved tissue penetration, affinity, and clearance. In preclinical mouse models of acute respiratory distress syndrome and inflammatory bowel disease, the nanobody CD45-PET probe strongly correlated with histologic and clinical measures of inflammation and outperformed other molecular imaging techniques, including FDG-PET and CD11b-PET. Notably, signal variation was observed by anatomical region in the inflammatory bowel disease model—PET signal in the large intestine tracked closely with disease activity, while rectal signal did not.

The team next evaluated their human-specific CD45 probe in a humanized mouse model. The probe reliably visualized engrafted human peripheral blood mononuclear cells (PBMCs) with minimal background signal in nonimmune tissues. Clearance was inferred to occur via hepatic and renal pathways based on probe uptake observed in the liver and kidneys. Control experiments confirmed that vascular leak alone did not drive nonspecific uptake. Finally, in a longitudinal model of graft-versus-host disease, CD45-PET detected immune activity over time, although signal variability across mice highlighted the need for further optimization in this context. Together, these findings suggest CD45-PET is a versatile and quantitative platform for tracking immune responses in vivo.

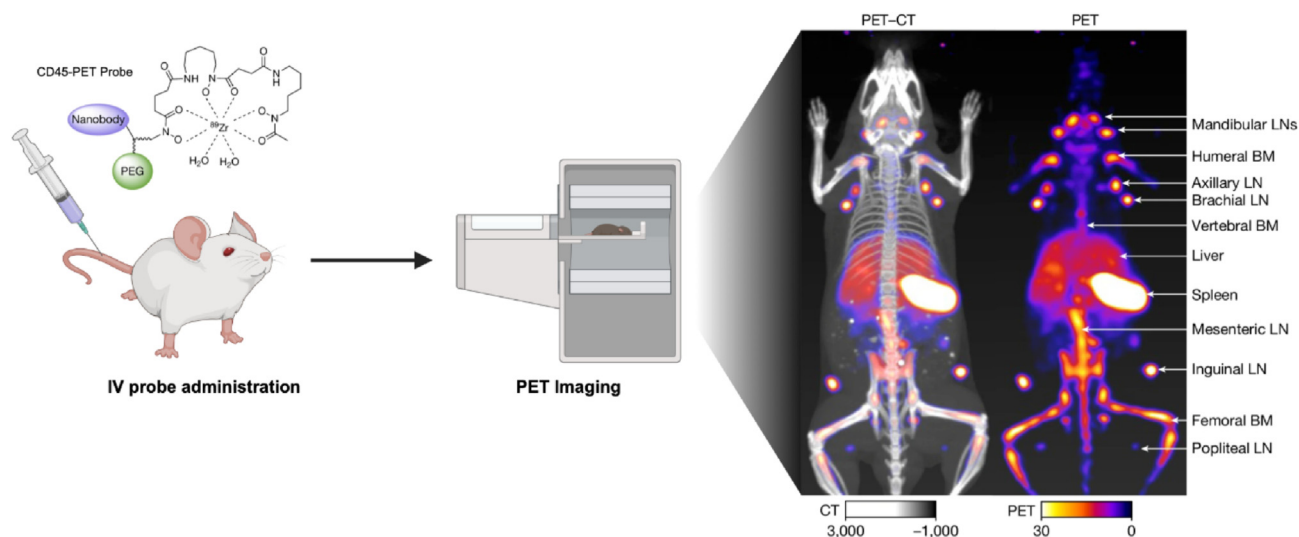


Figure 1. Intravenous administration of a CD45-PET probe (composed of a CD45-specific nanobody and deferoxamine chelator for radionuclide binding) enables the visualization of immune cell-rich organs in healthy C57BL/6 mice. This figure has been adapted from Farid et al, *Nature*. 2025. PET, positron emission tomography.

The authors propose its utility could extend to clinical monitoring of inflammatory conditions—including, potentially, solid-organ transplantation.

Biopsy is the current gold standard for diagnosing allograft rejection, but the invasiveness limits its use in routine monitoring. Extensive efforts have been made to develop alternative diagnostic technologies to monitor for early signs of transplant rejection. Organ-specific biomarkers (such as creatinine and troponin) have been used to track graft function for decades, but lack specificity. Donor-specific antibodies are also widely used to assess the risk of antibody-mediated rejection, but their utility in screening patients without other signs of organ rejection is limited, as is their ability to detect cellular rejection. Additionally, novel assays quantifying donor-derived cell-free DNA have shown promise in the early detection of both antibody-mediated and T cell-mediated rejection and are now being integrated into mainstream clinical practice.

Conventional computed tomography, ultrasound, and magnetic resonance imaging are commonly used to visualize allografts, but have limited value in the diagnosis of rejection. In contrast, PET and other molecular imaging techniques that capture immune cell migration and activity may enable early visualization of rejection. FDG-PET was recently used to assess cardiac allograft rejection in a small clinical trial,³ and intriguing preclinical studies suggest that immunoPET probes may outperform FDG-PET for rejection surveillance.⁴

Additional work is clearly needed to assess the value of CD45-PET in the context of allograft rejection—particularly given the complicating variable that these probes undergo both renal and hepatic clearance. Further, while targeting CD45 allows for broad labeling of all leukocyte populations, this technique could also be refined to track and quantify more specific immune subsets or activation states. Comparison of this CD45 nanobody approach with previously described immunoPET probes targeting dynamically expressed immune activation markers like OX40,⁴ for example, would be of significant interest. More broadly, ongoing improvements in binding domain design and screening techniques may accelerate the development of novel

molecular imaging probes and potentially provide unique windows to understand graft function and rejection.

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Anita Qualls is an MSTP student in the Department of Surgery and Diabetes Center at the University of California, San Francisco (UCSF).

Christopher Chang, PhD, is an MSTP student in the Parker Institute for Cancer Immunotherapy (PICI) at UCSF.

James M. Gardner, MD, PhD, is a transplant surgeon, assistant professor of surgery at UCSF, and an investigator in the Diabetes Center, the ImmunoX program, and PICI.