

Guiding translational medicine with immunotargeted probes for PET imaging of the cancer biomarker TEM1/Endosialin

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Tumor endothelial marker 1 (TEM1)/Endosialin/CD248 is a robust tumor vascular marker in over 20 human cancer subtypes, and its high expression levels correlate with high tumor grade and aggressive tumor behavior. With its expression concentrated on the tumor vasculature and limited expression in normal adult tissue, TEM1 is an ideal biomarker to which we can develop targeted agents for both early cancer detection and therapy. Positron Emission Tomography (PET) is becoming the method of choice for non-invasively imaging *in vivo* biomarker expression, due to its very high sensitivity, resolution, and unique potential to quantify radiotracer concentrations in a 3D volume.

In collaboration with the Penn Center for Ovarian Cancer Research, we have developed a series of TEM1-directed antibody constructs of variable size and valency as immunotargeted probes for PET detection of TEM1-positive tumor burden. Following protein labeling with the positron emitting isotope iodine-124 (¹²⁴I), we have assessed the targeting specificity *in vitro* and have fully evaluated the pharmacokinetic profile of these novel agents in mice. We have chosen a lead candidate to further assess targeting potential in a humanized tumor vascular mouse model of TEM1. Our findings suggest that our TEM1-targeted ¹²⁴I-PET antibody probe can specifically and sensitively detect TEM1 expression *in vivo*, thus demonstrating the potential of using PET technology to image the TEM1 tumor status of patients and monitor the effectiveness of TEM1-targeted therapeutic interventions.

Biography

Ann-Marie Chacko completed her Ph.D. at the University of Pennsylvania in Pharmacology with a focus in Radiopharmaceutical Chemistry. She continued her postdoctoral training at Penn and is currently a Research Associate in Penn Radiology, leading translational efforts in bringing macromolecular radiopharmaceuticals (i.e., proteins and nanoparticles) as diagnostics and therapeutics to the clinic. She is a recipient of a KL2 Career Development Award from the Penn Clinical and Translational Research Award (CTSA), and is currently pursuing her master's in Translational Research (MTR).

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