

“Molecular Imaging to Assess Tumor-associated Macrophages with Targeted Nanoparticles”

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Abstract: The tumor microenvironment has recently become the focus of much attention, as it appears to play an important role in tumorigenesis and tumor maintenance. Recent data indicate that the amount of tumor-associated macrophages (TAM) correlates with a poor prognosis. Indeed, TAM have been found to promote neovascularization, invasiveness and tumorigenesis rather than inhibiting tumor growth as initially suspected. However, in spite of their importance, there is currently no clinically applicable methodology to quantify TAM in patients; such a methodology would aid considerably in prognosis stratification. To address this need, we aim to develop a method to noninvasively measure TAM presence and activity *in vivo* using quantitative PET imaging utilizing nanoparticles that specifically target TAM. Importantly, this work brings together three major novel research directions: i) nanotechnology comprising of nanocarriers modified with small molecules; ii) the newly discovered biology of TAM and iii) the PET nuclide Zirconium-89 (^{89}Zr), which makes this approach, for the first time, feasible due to its extended half life compared to conventional PET tracers like ^{18}F . Through utilization of PET, combined with biodegradable nanoparticles, the translation of this approach into the clinic is readily possible. The approach also defines a new paradigm for cancer diagnosis - the assessment of TAM for improved individual prognosis stratification. This project is a collaborative alliance and builds on the combined knowledge of three investigators, two from MSKCC (Drs. Jan Grimm and Jason Lewis) and one from MGH & Harvard/The Broad Institute (Dr. Ralph Weissleder).