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Abstract LB-188: Sensitivity of ^{89}Zr-labeled anti-CD8 minibody for PET imaging of infiltrating CD8+ T cells FREE

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Abstract

Background- The ability to monitor CD8 positive tumor infiltrating lymphocytes (TILs) *in vivo* is important for evaluating response to immunotherapies and assisting in the development of more effective immune cell targeted single and combination therapies. “ImmunoPET” imaging of tumor infiltrating T cells can provide a specific and sensitive modality to aid selection of patients for specific immunotherapy regimens and determine whether the therapy is working. Here, we report initial results to define the number of CD8+ T cells that can be detected with ^{89}Zr-Df-IAB22M2C, an anti-CD8 immunoPET probe, using different animal models

Methods- IAB22M2C, a humanized anti-CD8 minibody, was conjugated with desferrioxamine (Df) and radiolabeled with ^{89}Zr. NOD scid mice were implanted with varying ratios of CD8+ T and tumor cell admixtures either intramuscularly (IM) without Matrigel or subcutaneously (SC) with Matrigel. One or six days later, CD8+ T-cells were visualized with ^{89}Zr-Df-IAB22M2C. The same probe was used to detect CD8+ T cells in NSG™ mice engrafted with human PBMCs for 1 and 4 weeks to monitor the temporal progression of Graft versus Host Disease (GvHD).

Results- CD8+ T cells implanted in the muscles of mice were imaged one day later and SC implanted Matrigel plugs imaged 6 days later. Both approaches yielded similar results and indicated that the lower limit of detection was between 1.6 and 4 million CD8+ T cells in a volume of ~480 mm^3 in the presence of normal tissue background activity. The sensitivity of detection increased 10-fold when *ex vivo* radiolabeled CD8+ T cells were implanted SC with Matrigel. NSG ™ mice engrafted with human PBMCs provide a reliable model for xenogeneic T cell driven Graft versus Host Disease (GvHD). Human CD8$^+$ T cells were readily detectable in the spleens of mice 1 week post PBMC engraftment using ^{89}Zr-Df-IAB22M2C. As GvHD progressed 4 weeks later, expansion

and trafficking of the engrafted T cells to extra-lymphoid tissues including lungs could be followed. Terminal biodistribution showed a 2-3 fold increase in radioactivity uptake in lungs by week 4 post-engraftment; a result that was confirmed by IHC analysis. T cell enumeration and IHC analyses are in progress to further define the sensitivity range using an optimal dose and specific activity of ^{89}Zr-Df-IAB22M2C.

Conclusion- These studies show that the lower limit of CD8+ T cell detection by ^{89}Zr-Df-IAB22M2C is between 1.6-4.0 million cells in the presence of normal tissue background activity and that the probe can be used to monitor CD8+ T cell trafficking in a GvHD model *in vivo.* ^{89}Zr-Df-IAB22M2C has sensitivity properties that may enable the detection of CD8+ T cells in human tumors. Clinical trials with ^{89}Zr-Df-IAB22M2C in melanoma patients will commence later this year.

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