Evaluating immune checkpoint blockade treatment efficacy via $^{89}$Zr-CD4 and $^{89}$Zr-CD8 PET imaging in breast cancer mouse models

Yun Lu, B.S.1,2, Hailey Houson, Ph.D.1,2, Alessandro Mascioni, Ph.D.1,2, Fang Jia, Ph.D.1,5, Patrick Song1,2, Tiara Napier, M.S.1,2, Amer Mansur1,3, Carlos A. Gallegos1,3, Benjamin M. Larimer, Ph.D.1,2, Suzanne Lapi, Ph.D.1,2,4, Anna Sorace, Ph.D.1,3

1Radiology, 2O’Neal Comprehensive Cancer Center, 3Biomedical Engineering, 4Chemistry, University of Alabama at Birmingham; 5ImaginAb, Inc.

Introduction

- Immune checkpoint blockades have shown a great promise in cancer therapy.
- However, as the overall response rate varies, there is a profound unmet need to monitor the treatment efficacy and predict therapeutic responders.
- This study evaluates whether CD4 and CD8 immuno-PET can predict and evaluate immunotherapy treatment efficacy in controlled pre-clinical mouse models.

Methods

- In vivo blocking and biodistribution studies were performed to validate the specificity of $[^{89}Zr]$-mouse-CD4 and $[^{89}Zr]$-mouse-CD8. 10 times of non radio labeled minibody was served as blocking agent.
- 4T1 and MMTV-HER2 mouse models of breast cancer (N=80 per model) were imaged on Days 0, 2, and 6 during treatment (saline, anti-PD1, anti-CTLA4, or combinational therapies) and evaluated for long-term changes in tumor response.
- Therapeutic responders were determined through the thresholding of tumor mass at the end of study.
- Intra tumoral and splenic CD4+ and CD8+ cells were characterized in vivo via $[^{89}Zr]$-mouse-CD4 and $[^{89}Zr]$-mouse-CD8 position emission tomography (PET) imaging during immunotherapy treatment.
- An additional of mice (N=16) were euthanized on day 7 post treatment for biological validation studies.
- Autoradiography and immunofluorescence staining (CD8 and CD4) were performed to validate the biological accuracy of $[^{89}Zr]$-mouse-CD4 and $[^{89}Zr]$-mouse-CD8 PET imaging.

Results

Figure 2: $[^{89}Zr]$-CD4 PET imaging indicates immunotherapy treatment efficacy. (A) Day 0 SUV$_{\text{mean}}$ of MMTV-HER2 tumors. (B) Day 0 SUV$_{\text{mean}}$ of 4T1 tumors. (C) SUV$_{\text{mean}}$ changes from day 0 to day 6 in MMTV-HER2 tumor model. (D) SUV$_{\text{mean}}$ changes from day 0 to day 6 in 4T1 tumor model.

Figure 3: $[^{89}Zr]$-CD8 PET imaging indicates immunotherapy treatment efficacy. (A) Day 0 SUV$_{\text{mean}}$ of MMTV-HER2 tumors. (B) Day 0 SUV$_{\text{mean}}$ of 4T1 tumors. (C) SUV$_{\text{mean}}$ changes from day 0 to day 6 in MMTV-HER2 tumor model. (D) SUV$_{\text{mean}}$ changes from day 0 to day 6 in 4T1 tumor model.

Conclusions

1. $[^{89}Zr]$-CD4 and $[^{89}Zr]$-CD8 PET imaging can accurately evaluate CD4+ and CD8+ cell populations in vivo.
2. Biomarkers for predicting immunotherapy response varies with different targeted drugs and tumor models.