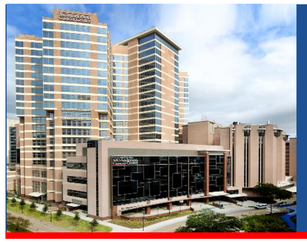

Analyzing CFT Images to Determine Optimum Time for F-19 MRI Acquisition in NK-cell Immunotherapy of Osteosarcoma

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Background

- As a part of innate immune system, NK-cells are first-line responders and they do not require antigen, making them promising candidates for immunotherapy.
- Cancer cells downregulate MHC-I to evade T-cells, which NK-cells can detect and destroy such cancer cells by direct cytotoxicity.
- Detecting whether the NK-cells have been delivered to specific tumor sites is challenging. F-19 MRI can be potentially used to detect the localization of NK-cells in the targeted tumor.
- Similarly, hyperpolarized C-13 MRI may be able to detect metabolic response to immunotherapy in a localized manner.
- In this study, we aimed to detect the localization of NK-cells in osteosarcoma which localized in lung of mice and use CFT imaging to inform on the optimum time to perform 19-F MRI after NK-cell immunotherapy.

Hypothesis

We expect NK-cells to localize in lung tumor after immunotherapy and we anticipate this will be visible by CFT at multiple time-points.

Methods

NK cells were labelled with DIR, a membrane label, that has an excitation spectrum of 750 nm and an emission spectrum of 782 nm. These NK cells were Injected collaterally.

↓

Sacrificed mice using standard protocol

↓

CFT was done using Xerra to generate high-resolution images

↓

Methods (continued)

3D image generated using vivo-quant by combining all image slices from Xerra

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Figure 1. ROI in lung tumor and liver indicated by orange region and blue region respectively

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Intensity of NK-cells was displayed using vivo-quant software, and the resulting intensities were quantified for longitudinal comparison

Results

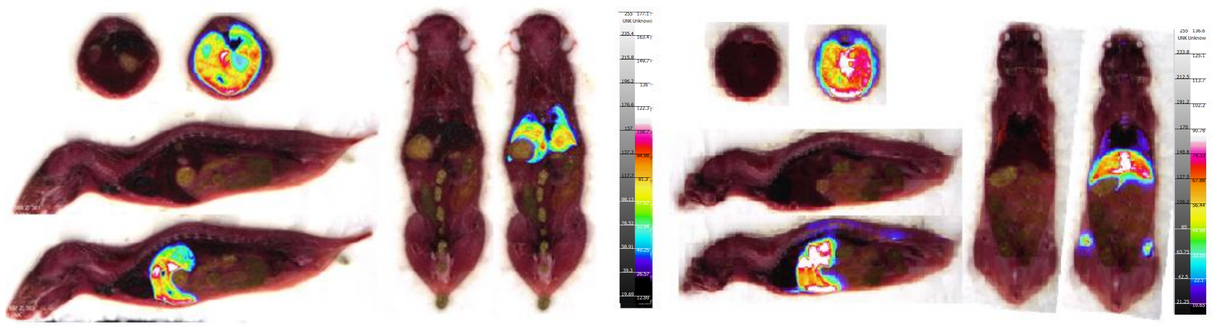

Figure 2. Axial(top-left), sagittal (bottom-left), and coronal (right) CFT images adjacent to white light images of mouse 4 hours (left) and 24 hours (right) after NK-cells administration. NK-cells are indicated by DiR.

Results (continued)

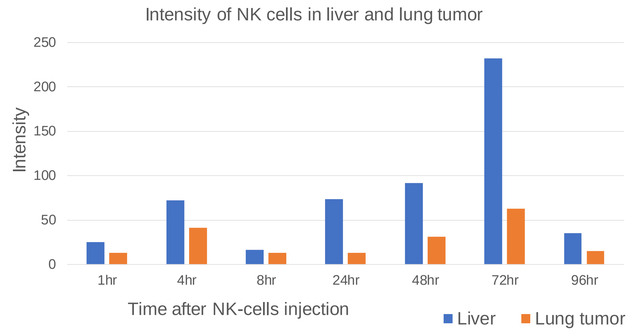

Figure 3. The intensity of NK-cells in liver and lung tumor at 730 nm.

- Localization of F-19 NK cell was indicated by DiR in the liver and lung tumor of all mice.
- Besides liver and lungs, localization of some NK-cells was observed in spinal cord and tail region in some mice.
- The ratio of the intensity of NK-cells in lung tumor vs liver was high for 4 hours and 8 hours after NK-cell immunotherapy.

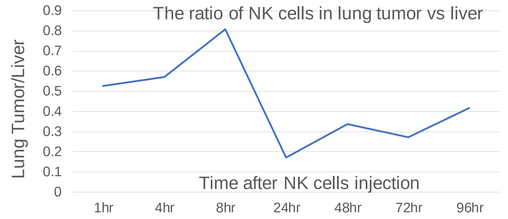

Figure 4. The ration of intensity of lung tumor vs. liver at different time-points after NK-cells administration

Discussion and Conclusions

- The significant number of NK-cells found in the lung osteosarcoma tumor suggests that NK-cell immunotherapy maybe observed using this novel theranostic imaging.
- The ratio of NK-cells in lung tumor/liver was higher during initial 8 hours, so 4-hour can be a good timing for doing 19-F MRI.
- The high intensity of fluorescence, further, suggests that 19-F MRI can be used to detect the localization of NK-cells in targeted organ(s) if 19-F imaging is sensitive enough.
- In order to verify the localization of NK-cells in-vivo, more data are needed because tumor burden and pathogenesis usually varies among different mice and the sensitivity of the 19-F MRI experiment needs to be optimized through hardware and better 19-F tags.
- Given this data, we form a new hypothesis for our next set of measurements that NK-cells will be visible with 19-F MRI at 4-8 hours after immunotherapy.

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