CD8-Targeted Total-Body PET Imaging of T Cells in Patients Recovering from COVID-19

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Background: CD8+ T cells are key players in immune response. Following viral infection or vaccination, a small portion of antigen-specific T cells differentiate into memory cells, forming a long-term protective memory against reinfection. However, in vivo information about COVID-19-specific T cell immunity is limited, since 95% of T cells are not in the circulation and tissue sampling has been minimal. This pilot study aims to provide an *in vivo* measure of tissue distribution of CD8+ T cells after COVID-19 infection, using total-body imaging of a labeled minibody with high affinity to human CD8.

Materials and methods; 5 COVID-19-recovered patients and 3 healthy controls were studied. Subjects received ~0.5 mCi of ^{89}Zr-Df-Crefmirlimab-Berdoxam and had 60-min total-body PET/CT scans at 6-h and 48-h post-injection. Control subjects and 3 COVID-19 patients had an additional 90-min dynamic scan. Scans of 3 COVID-19 patients were repeated after 4 months. Volume-of-interest were drawn on spleen, liver, lungs, bone marrow, lymph nodes, tonsils, and blood-pool. Two-tissue compartmental modelling was performed on the dynamic data to derive $K_i = \frac{K_1 k_3}{k_2+k_3}$ and $V_T = \frac{K_1}{k_2}\left(1+\frac{k_3}{k_4}\right)$.

Results: In all subjects, activity decrease in bone marrow and spleen between 6–48 h was observed with parallel activity increase in lymph nodes and tonsils, suggesting cell-trafficking (Figure 1). Tissue-to-plasma ratio (0–7 h), Ki, and V_T were higher in bone marrow of the COVID-19 patients than controls and were the highest in one COVID-19 patient, infected twice with the virus.

Conclusions: Total-body imaging of CD8+ T cells with sub-millicurie levels of ^{89}Zr-labeled tracer resulted in the ability to quantify rates of uptake and concentrations of the tracer in lymphoid tissues throughout the body, along with T cell migration over a 48-h period. Current data suggest that the bone marrow T-cell pool in COVID-19-recovered patients is larger or has increased CD8 expression compared to controls.

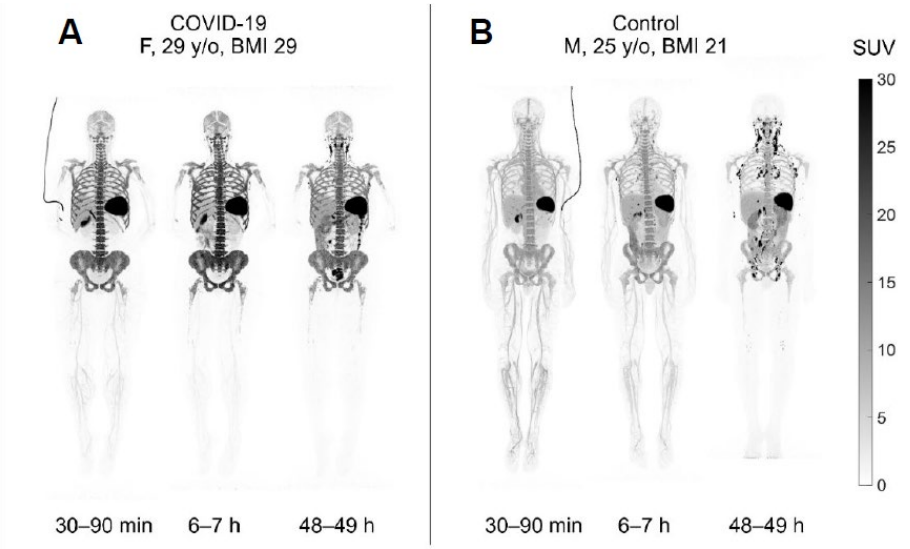

Figure 1. Example SUV maximum intensity projections of (A) a recovered COVID-19 patient, compared to (B) a healthy subject scanned on the uEXPLORER at three timepoints. Increase in lymph node uptake and decrease in bone marrow and spleen uptake is observed between 6 h and 48 h imaging time points.