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

Negar Omidvari, 2Terry Jones, 3Pat M Price, 2Fatma Sen, 4Barbara Shacklett, 5Stuart Cohen, 1,2Ramsey D Badawi, 6Ian Wilson, 1,2Simon R. Cherry

1Department of Biomedical Engineering, UC Davis, 2Department of Radiology, UC Davis, 3Department of Surgery and Cancer, Imperial College, London, United Kingdom, 4Department of Medical Microbiology and Immunology, School of Medicine, UC Davis, 5Department of Internal Medicine, UC Davis, 6ImaginAb, Inc., Inglewood, CA

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 89Zr-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 \( K_i = \frac{K_1 k_2}{k_2 + k_3} \) 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), \( K_i \), 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 89Zr-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.