Single-cell sequencing to define the sequences, phenotypes and functionalities of tumor antigen-specific $CD8^+$ T cells from lymphoma patients

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With the support of this Young Investigator Award, we have established a flow cytometry sorting based single-cell sequencing technology in our laboratory, which can simultaneously determine the TCR sequence and functional phenotype of a single T cell. The establishment of this single-cell technology allows us to deeply decode single tumor antigen-specific T cells from mice and humans. Furthermore, we have recently started using an automatic 10x platform to perform high-throughput single-cell sequencing. The preliminary results are very promising and we are currently optimizing experimental conditions and refining the data analysis pipeline. Based on our previous peptide-major histocompatibility complex (pMHC) dodecamer technology (Huang et al, PNAS, 2016), we have simultaneously developed an antibody dodecamer to isolate antigen-specific T cells for mass cytometry and sequencing analyses. We will apply this technology to study tumor-specific T cells from different cancers.

I have presented our research results domestically and internationally. I was invited by the President of Nanjing Medical University as the keynote speaker in the 2016 symposium, “Jinling Medical Symposium of Nanjing Medical University” at the International Conference on Biomedical Engineering and Clinical Medicine. I also presented our dodecamer work at the American Association of Immunologists (AAI) annual meeting. In addition, I was invited to speak at the 2016 UChicago Biophysics Program, 2017 University of Minnesota-University of Chicago Joint Immunology Retreat, and 2017 UChicago Biomedical Science Cluster Retreat.

Using the preliminary data generated from this supported project, we have written and submitted an NIH R21 grant to the National Cancer Institute. Although we were not funded in the first round, the score—20^{th} percentile--was good and the review was generally positive. We are currently revising the proposal for a second submission.

Finally, with the support of this award, we have published the following two papers:

1. Rosenberg J and Huang J. $CD8^+$ T cells and NK cells: parallel and complementary soldiers of immunotherapy. ***Current Opinion in Chemical Engineering***, 2018; 19: 9-20.
2. Wendel et al. Reduced clonal and functional diversity of follicular helper T cells in human lymph nodes during chronic HIV infection. ***Science Immunology***. (in press).