Cancer Immunotherapy with Human Vγ2Vδ2 T Cells

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PhD Candidate

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Human γδ T cells expressing Vy2Vδ2 TCRs monitor foreign- and self-prenyl pyrophosphate metabolites in isoprenoid biosynthesis to mediate immunity to microbes and tumors. Vy2Vδ2 cells have been used for adoptive cancer immunotherapy with some partial and complete remissions. Most trials have used continuous zoledronate exposure to expand Vy2Vδ2 cells. Zoledronate inhibits farnesyl pyrophosphate synthase causing isopentenyl pyrophosphate to accumulate that then stimulates Vy2Vδ2 cells. Because zoledronate exposure is toxic, we hypothesized that a short period of exposure would reduce T cell toxicity but still be sufficient for monocytes uptake.

Supporting this hypothesis, pulse zoledronate exposure with IL-2 resulted in more uniform expansion of Vy2Vδ2 cells with higher purity and cell numbers as compared with continuous exposure. These Vy2Vδ2 cells also had higher levels of CD107a and perforin and slightly increased tumor cytotoxicity. Importantly, adoptive immunotherapy with Vy2Vδ2 cells derived by pulse stimulation controlled human PC-3 prostate cancer cells in immunodeficient NSG mice significantly better than those derived by continuous stimulation.

Pulse zoledronate stimulation of Vy2Vδ2 cells with IL-15 also resulted in higher purity and cell numbers. Like with CD8 αβ T cells, IL-15 preserved early memory Vy2Vδ2 T cell subsets better than IL-2. However, despite this fact, adoptive immunotherapy with Vy2Vδ2 cells derived with IL-15 showed similar inhibition of PC-3 tumor growth as those derived with IL-2. Thus, pulse zoledronate stimulation maximizes the purity, quantity, and quality of expanded Vy2Vδ2 cells. This simple modification to existing protocols would likely enhance the effectiveness of adoptively transferred Vy2Vδ2 T cells.

Mohanad Nada
Biographical Sketch

Mohanad was born and raised in a small town in Tikrit, Iraq. He is the oldest son of ten children for Mr. Hameed Nada and Mrs. Lamya Bunyan. During his studies in Tikrit medical school, Mohanad developed a special interest in tumor immunology and cancer immunotherapy. He investigated the role of T lymphocytes in breast cancer patients in Iraq during his Master study. Due to his outstanding performance in his master studies, Mohanad was awarded a scholarship from the Iraqi government (HCED) to pursue his doctoral studies in tumor immunology at the University of Iowa. Mohanad joined the immunology graduate program in Fall, 2011, and he worked with Dr. Craig Morita since then to develop cancer immunotherapy using γδ T cells.

Mohanad met his wife, Auster, during their studies in Tikrit medical school in Iraq. They have been happily married since 2008. Mohanad and Auster were blessed with three wonderful boys, Ayham, Anas, and Kinan. When he is not working, Mohanad enjoys spending family time with his wife and kids. Mohanad also likes to play tennis regularly.

After finishing his PhD, Mohanad plans to stay for one more year as a postdoctoral fellow working with Dr. Morita. Then, we will finish his medical education. Mohanad plans for a future career in Medicine as a scientist physician where he can combine clinical work and his research interest.