Reversing Tumor-Induced T Cell Suppression through Activation of TLR8 Pathway

Wang, Cindy (School: Ladue Horton Watkins High School)

The purpose of this project is to study how the Toll-like receptor 8 (TLR8) pathway prevents tumor-induced T cell suppression. Tumor-induced immunosuppression is important to study because it is a critical barrier blocking immunotherapy from achieving its full potential. One form of immunosuppression is tumor-induced T cell senescence, which can be reversed by poly-G3 (poly-G), an activating ligand of the TLR8 pathway. However, the underlying mechanism of poly-G is not known. We hypothesize that poly-G prevents tumor-induced T cell senescence by downregulating tumor glucose metabolism. We tested this hypothesis by culturing cancer cells with or without the treatment of poly-G and measuring the levels of key metabolites from glucose metabolism. We found that poly-G treatment decreases the levels of key metabolites, especially those from glycolysis. Through quantitative RT-PCR, we found that the expression levels of various glycolytic proteins, including glucose transporters, glycolytic enzymes, and transcription factors in cancer cells are also reduced by poly-G treatment. Taken together, our results indicate that poly-G treatment prevents T cell senescence by downregulating tumor glucose metabolism, thus increasing glucose availability to T cells and alleviating T cell senescence. Our findings suggest that targeting tumor glucose metabolism may represent a novel approach to prevent tumor-induced immunosuppression and subsequently boost the efficacy of cancer immunotherapy.

Awards Won: