Manipulation of effector and memory CD8 T cells via IL-2-antibody complexes

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The development and implementation of vaccines has arguably been the most successful public health intervention to date. The World Health Organization estimates that 1-2 million lives are saved by vaccines each year, with many more spared the burden of combatting debilitating diseases. Thus far, all prophylactic vaccines elicit high antibody titers to confer protection; however, certain chronic pathogens and tumors cannot be controlled by humoral immune responses. Thus, much effort has been devoted to manipulating both the quantity and quality of T cells, particularly CD8+ T cells, for therapy. CD8+ T cells, also referred to as cytotoxic T cells, have the capacity to specifically identify and kill infected or malignant cells through the production of lytic enzymes and effector cytokines. Additionally, these CD8+ T cells can respond more efficiently to subsequent exposures of the same pathogen or tumors, a characteristic of adaptive immunity, termed memory. Such features make them an attractive target for clinical use; however, our incomplete understanding of all the factors that control CD8+ T cell responses has led to failed, or only minimally effective, T cell-mediated therapies. Clearly, more research into potential immunization strategies and immunological mechanisms that regulate CD8+ T cell responses is necessary.

My dissertation focuses on manipulating various stages of the CD8+ T cell response through DC immunization and IL-2/mAb complexes, along with its therapeutic implications. This approach is investigated as both a potential cancer immunotherapy, as well as research tool for elucidating mechanisms controlling memory CD8+ T cell formation. The thesis work presented here seeks to contribute to the advancement of cellular vaccines and immunotherapies for the treatment of human disease.