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“In vivo anti-tumor efficacy of melanoma antigen-specific cytotoxic T lymphocytes generated using artificial antigen presenting cells (aAPC)”

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Background: A major goal in the field of tumor immunotherapy is to generate an effective cell-mediated anti-tumor immune response. While adoptive immunotherapy holds promise as a treatment for a variety of cancers, development of adoptive immunotherapy has been impeded by the lack of a reproducible and economical method for generating therapeutic numbers of antigen-specific cytotoxic T lymphocytes (CTL). We have reported that an artificial Antigen-Presenting Cell (aAPC), made by coupling HLA-Ig and anti-CD28 to beads, can reliably induce and expand antigen-specific CTL. These aAPC were better than dendritic cell mediated expansion of antigen specific CTL.

Design: The goals of this study were to test the in vivo anti-tumor effects of aAPC expanded melanoma antigen (MART-1; melanoma associated T cell reactive antigen-1)-specific CTL using SCID mouse model of human melanoma.

Results: We observed that adoptive transfer of MART-1 specific CTL could lead to reduction of tumor growth both in prevention and treatment experiments that was associated with decrease in tumor weight and increase in survival, respectively. In vivo imaging of mice using luciferase reporter assay revealed that these CTL could target the tumor in antigen-dependent manner. Interestingly, V β repertoire analysis using TCR spectratyping showed that only a subset of these CTL trafficked to the tumor site. The mechanism of selective trafficking of these cells is under investigation.

Conclusion: This is the first report to show that tumor antigen specific CTL expanded using aAPC are able to home to the tumor site and efficient in controlling the tumor growth in vivo. Our study would further define the potential clinical uses of HLA-based aAPC to enhance approaches for adoptive immunotherapy to treat cancer patients, specifically melanoma.