

Peter A. Savage

savagep@mskcc.org

Spontaneous T lymphocyte responses to a widespread endogenous antigen in a transgenic mouse prostate cancer model

Peter A. Savage and James P. Allison
Memorial Sloan-Kettering Cancer Center and the Howard Hughes Medical Institute
New York, NY 10021

Male transgenic adenocarcinoma of mouse prostate (TRAMP) mice express SV40 T antigen under the control of a prostate-specific promoter, resulting in the development of spontaneous adenocarcinoma by 14-20 weeks of age. In a screen for endogenous tumor-reactive T cell responses in the TRAMP model, we identified a novel infiltrating CD8 $\alpha\beta$ ⁺ T cell population that is consistently overrepresented in TRAMP prostate tumors. To facilitate the study of this T cell population and to define its contribution to tumor immunity or tolerance, we generated clonotypic TCR β and TCR $\alpha\beta$ transgenic mice, and are currently characterizing the phenotype and function (effector or suppressor) of clonotypic T cells in the prostate tumors of TRAMP, TRAMP x TCR β , and TRAMP x TCR $\alpha\beta$ transgenic mice. In efforts to characterize the antigen driving this response, we found that clonotypic T cells could be stimulated *in vitro* using HPLC-purified peptide extracts from primary TRAMP prostate tumors. Surprisingly, the stimulatory activity was also found in the spleen and liver of wild-type male and female B6 mice, as well as male TRAMP mice, indicating that the peptide antigen is widespread. Currently, 2-D HPLC purification and tandem mass spectrometry are being employed to isolate and identify the antigenic peptide. In sum, here we outline the discovery of a spontaneous CD8 $\alpha\beta$ ⁺ T cell response directed at a natural self antigen in a transgenic mouse prostate cancer model. Characterization of this model will provide insight into the role of T lymphocytes in tumor immunity, and will facilitate the design of new and improved immunomodulatory therapies for the treatment of human cancer.

