

Relationship Between CD8 Dependent Antigen Recognition and Tumor Cell Recognition.

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Most of the human tumor antigens identified to date are nonmutated self proteins. Therefore, an efficient immune response which targets self antigens expressed by tumor cells could lead to autoimmune destruction of normal tissues as well as the tumor. Immunologic tolerance generally precludes T cells expressing high affinity TCRs reactive with self antigens from being part of the normal T cell repertoire. Therefore, it is predicted that most tumor reactive T cells would express relatively low affinity TCRs which may account for their inability to control the growth and metastases of tumors. In order to understand how TCR affinity impacts on tumor cell recognition, we have cloned and expressed the TCR genes from several HLA-A2 restricted, melanoma reactive, human T cell clones. We have used CD8 dependence as a means of determining if a TCR has sufficient affinity to mediate recognition of physiologic levels of antigen presented on tumor cells. In general, we found that CD8 dependence is a property of the TCR and is an indicator of a TCR's capacity to recognize tumor cells. However, the TCR expressed by a CD8⁻ T cell clone (TIL 1383I) transfers tumor cell recognition to Jurkat cells despite their low relative avidity as measured in peptide titration assays. In contrast, the TCR expressed by another CD8⁻ T cell clone (T4H2) failed to transfer tumor cell recognition to Jurkat cells despite their high relative avidity. These results suggest that T cells can modulate their sensitivity to antigen and their capacity to recognize physiologic levels of antigen independent of the affinity of their TCR.