Spontaneous and Therapy-induced T Cell Responses to Cancer

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It has rarely been questioned that spontaneously occurring cancer cells have to escape T cell attack, even though this has not been directly demonstrated. Recently, it was shown that sporadic immunogenic cancer at the time of initial recognition induces an aberrant rather than a protective T cell response, resulting in tolerance at the premalignant stage. Tumors which grew in the primary host despite initially functional tumor-reactive CTLs had a regressor phenotype upon transplantation. Thus, in a clinically relevant model, cancer cells do not need to escape. General CTL hyporesponsiveness is a late event, probably involves immature myeloid cells, requires immunogenic tumors, and appears to be a symptom, not the cause of tumor growth. Tumor-infiltrating lymphocytes reflect cancer-induced inflammation, rather than immunosurveillance. In contrast, tumors induced by virus infection induce an effective T cell response and need to escape immunosurveillance by local tolerance. In contrast to endogenous T cells, adoptively transferred T cells have been shown to reject large established tumors. In such models, T cells recognize the tumor antigen as foreign. The task is to generate human T cell receptors (TCR) that recognize human tumor-associated (self) antigens as foreign and use these TCRs for gene therapy, which will facilitate clinical application.

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Bibliography

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