Nonclinical safety evaluation of T-cell based immunotherapies

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Evasion of immune surveillance represents a major mechanism limiting the effectiveness of traditional therapies against tumor cells. However, an increasing number of approaches designed to stimulate or directly utilize the immune system in overcoming this limitation are currently undergoing preclinical and clinical testing, including immunotherapies utilizing autoreactive effector cells. The relatively recent expansion in the understanding of basic mechanisms in T cell biology, combined with continuously improving molecular biology techniques, have made possible an explosion of clinical trials involving the adoptive transfer of genetically engineered T cells for the treatment of both hematological and solid malignancies. However, one significant factor potentially limiting the widespread use of T cell therapies for a variety of cancer types includes the expression of target antigens on cancer cells as well as on other normal, and essential, tissues. This presentation will review the field of adoptive T cell therapies, with a particular focus on chimeric antigen receptor T cells, highlight experimentally-verified and theoretical safety concerns for such therapies, and review current thinking concerning non-clinical safety assessment approaches for such therapies.