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Meeting Abstract

T-help, TRAIL, and CTL memory

Stephen P. Schoenberger[1*], Edith M. Janssen[1], Nathalie Droin[1], Edward Lemmens[1], Thomas Griffith[2] and Douglas Green[3]

[1]*La Jolla Institute for Allergy and Immunology, La Jolla, CA, USA*
[2]*University of Iowa, Iowa City, IA, USA*
[3]*St. Judes Childrens Hospital, Memphis, TN, USA*
[*]*Presenting author*

Abstract

Cytotoxic CD8+ T lymphocytes (CTLs) are especially suited to the detection and eradication of incipient tumors due to their capacity to recognize neoplastic cells based on the mutated, over-expressed or tissue-specific genes they express. The strategic use of CTLs as effectors in cancer immunotherapy must be predicated on a more detailed understanding of their immunobiology. Although numerous studies have demonstrated that CTLs are dependent on CD4+ "helper" T lymphocytes for various aspects of their function, a clear picture of the underlying mechanisms has only recently become apparent. My presentation will discuss the studies that our laboratory has performed on the mechanism through which T-help is provided, and on consequences for the function and fate of CTLs of its provision or absence. The emerging picture is that T-help is provided to CTLs early during their primary activation and serves to direct cells towards a specific program of development and differentiation. "Helped" CTLs are endowed with the capacity for secondary expansion upon re-exposure to antigen while "helpless" CTLs undergo activation-induced cell death (AICD) by a TRAIL-mediated mechanism when restimulated. This is not an unavoidable fate for the "helpless" CTLs, however, as various cytokines can prevent their death by TRAIL through distinct mechanisms. The relevance of these findings to cancer immunotherapy will be discussed.