CD40L expression permits CD8+ T cells to execute immunologic helper functions.

Abstract:
CD8(+) T cells play an essential role in immunity against intracellular pathogens, with cytotoxicity being considered their major effector mechanism. However, we here demonstrate that a major part of central and effector memory CD8(+) T cells expresses CD40L, one key molecule for CD4(+) T-cell-mediated help. CD40L(+) CD8(+) T cells are detectable among human antigen-specific immune responses, including pathogens such as influenza and yellow fever virus. CD40L(+)
CD8(+) T cells display potent helper functions in vitro and in vivo, such as activation of antigen-presenting cells, and exhibit a cytokine expression signature similar to CD4(+) T cells and unrelated to cytotoxic CD8(+) T cells. The broad occurrence of CD40L(+) CD8(+) T cells in cellular immunity implicates that helper functions are not only executed by major histocompatibility complex (MHC) class II-restricted CD4(+) helper T cells but are also a common feature of MHC class I-restricted CD8(+) T cell responses. Due to their versatile functional capacities, human CD40L(+)
CD8(+) T cells are promising candidate cells for immune therapies, particularly when CD4(+) T-cell help or pathogen-associated molecular pattern signals are limited.