Memory Functions and Death Proneness in Three $CD4^+CD45RO^+$ Human T Cell Subsets[1]

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We propose a classification of human $CD4^+CD45RO^+$ memory T cells into three new subsets based on cell surface expression levels of CD43. The first subset consists of cells whose CD43 expression is relatively high; this subset also contains the highest proportion of recall Ag-reactive precursors, and its constituent cells respond far more strongly than cells in either of the other subsets to immobilized CD3 Ab in addition to secreting substantially more IFN-γ and IL-4. Cells of the second subset express similar levels of CD43 to naive cells, and they also respond weakly to TCR-mediated stimuli as judged by either their ability to proliferate or capacity for cytokine production. The third subsets consists of cells whose CD43 expression levels are clearly down-regulated; its cells appear to be anergic to TCR-mediated stimuli, and when examined ex vivo many of them appear to be undergoing either spontaneous apoptosis via a caspase-independent pathway or Fas-mediated apoptosis via a caspase-dependent pathway, even in the resting state. An analysis of telomere lengths revealed that the typical telomere of a cell in the second subset was significantly longer than the typical telomere in the first or third subset. Taken together, these results appear to indicate that $CD4^+CD45RO^+$ T cells fall into three functionally differing subsets, one being a subset of cells with fully matured memory phenotype, a second being a less mature subset of cells that retain longer telomeres and whose memory functionality is marginal, and a third consisting of anergic cells that give every appearance of being death-prone and/or in the process of dying. *The Journal of Immunology,* 2002, 169: 39–48.

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