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Combined killing of cancer cells and cross presentation of tumor antigen by Vγ9Vδ2 T cells

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The human Vγ9Vδ2 T cells are a unique T cell type, and recent studies of the biology of Vγ9Vδ2 T cells emphasize the potential exploitation of these cells in immunotherapy of cancer. Vγ9Vδ2 T cells exhibit dual functionality in that they are both antigen presenting cells (APC) and cytotoxic towards cancer cells. We show that Vγ9Vδ2 T cells can kill cancer cell lines from various cancer types such as leukemia, melanoma, prostate-, and breast cancer, with a significantly increased killing upon treatment of the cancer cells with Zoledronic acid. In addition, we show that Vγ9Vδ2 T cells take up tumor antigens gp100 and MART-1 (long peptide and recombinant protein, respectively), and process these antigens for presentation of class I restricted peptides in the context of the HLA-A02.01 molecule, to be recognized by peptide specific cytotoxic CD8 T cells. Moreover, we show that specific inhibition of the proteasome by lactacystin impair recognition by peptide specific CD8 T cells, strongly suggesting proteasome involvement in presentation of the relevant class I restricted peptides. The dual functions; killing and antigen presentation combined with the ease of expanding Vγ9Vδ2 T cells in vitro from peripheral blood lymphocytes to billions of cells, makes Vγ9Vδ2 T cells attractive vehicles for adoptive cell therapy (ACT) in cancer therapy. Thus, Vγ9Vδ2 T cells are broadly tumor specific killers, that concurrently could induce or support tumor specific αβ-T cell responses.

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