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Vg9Vd2 T cells in neoplastic and infectious diseases: From bench to bedside

Miroslav Malkovsky
University of Wisconsin Medical School, USA

Most vaccine strategies are designed to elicit adaptive immune responses to a variety of microbial or tumor-associated antigens and target predominantly αβ T cells and B cells. In contrast to these cells, Vγ9Vδ2 T lymphocytes typically recognize nonpeptidic antigens generated by the DOXP (many eubacteria, algae, plants, apicomplexa) and mevalonate (eukaryotes, archaebacteria and certain eubacteria) pathways of isoprenoid synthesis. Vγ9Vδ2 T cells can be also activated by certain nitrogen-containing bisphosphonates (N-BPs). These activated Vg9Vd2 T cells can kill very effectively various tumor and virus-infected cells. We have shown that intravenous administration of N-BPs combined with low doses of IL-2 induces a large pool of CD27+ and CD27-effector/memory Vγ9Vδ2 T cells in the peripheral blood. In AIDS patients, these events are associated with decreases of the peripheral blood virus load. However, Vg9Vd2 T lymphocytes exposed to IL-2, IL-15 and TGF-b display regulatory functions in vitro typically associated with ab CD4+CD25+ Tregs. Vg9Vd2 Tregs derived by this method express the transcription factor FOXP3 and, similar to ab Tregs, suppress the proliferation of anti-CD3 and anti-CD28 stimulated-PBMCs in the presence of IL-2. The presence of high numbers of these cells may interfere with anti-cancer or anti-infectious immune responses. Several clinical trials focused on γδ T-cell activation in vivo in patients with various cancers are currently in progress. The findings from these trials could guide novel combinations of suitable Vg9Vd2 T-cell activations with conventional therapies that may further improve the armament of clinical oncologists as well as specialists in infectious diseases.

Biography

Miroslav Malkovsky received his Ph.D in 1979 from Charles University, Prague. At present he is Professor for Department of Medical Microbiology and Immunology, University of Wisconsin Medical School; University of Wisconsin Comprehensive Cancer Center; and Wisconsin Regional Primate Research Center (WRPRC), Madison, Wisconsin.

guittarr@hotmail.com