EVENT ABSTRACT

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Analysis of the global CD8 T cells during Mycobacterium tuberculosis infection.

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Tuberculosis is a world-wide re-emerging infectious disease caused by Mycobacterium tuberculosis (Mtb) and both BCG vaccine and therapy are not fully effective in containing its spreading.
We investigated the frequency of Mtb epitope-specific HLA-E-restricted CD8 T cells in adult patients affected by tuberculosis (TB) before and after 6 months of anti-mycobacterial therapy and in healthy subjects. Using peptides/HLA-E tetramers, we found a high frequency of peptide-specific CD8 T cells in peripheral blood of patients with active TB, which consistently decrease after therapy. HLA-E-specific T cells produced in vitro high levels TNF, but very poor IFN-gamma and/or IL-2 and exerted cytotoxic activities toward peptide-pulsed HLA-E transfected target cells. Monitoring of epitope-specific HLA-E-restricted CD8 T cells by the use of tetramers in PBMC of Mtb patients during chemotherapeutic treatment, showed their frequency decreased, a pattern opposite to HLA-A*0201-restricted CD8 T cells, whose frequency instead increased after therapy. Our results indicate that HLA-E-restricted CD8 T cells behave and function differently than HLA-A-restricted CD8 T cells and could be an useful parameter to check the efficacy of therapy.
Moreover, since HLA-E is an highly conserved molecule with a very limited polymorphism and it's not down-regulated by HIV infection, often associated to TB reactivation, the evaluation of ex-vivo frequencies of peptides-specific HLA-E CD8 T cells could be useful to predict subjects that are at high risk to develop the disease and these peptides could be suitable candidates for a more effective vaccine against Mtb in HIV subjects.

Keywords: Mycobacterium tuberculosis, HLA-E tetramers, Cytokines, TB patients, CD8 T cells

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