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Peptide vaccination induces specific effector and memory T cells but fails to enhance preexisting T cell immunity

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Peptide vaccines were shown to induce specific T cell reponses in the majority of patients with resected primary melanoma. We evaluated the immunogenicity of tyrosinase peptides in the combination with the adjuvants GM-CSF and KLH in patients with relapsed resected stage III/IV melanoma (median 4.5 (± 4.2) previous relapses, range 1–20 relapses). Twentythree patients received tyrosinase peptides mixed with KLH administered 4 times 2 weekly and then 2 times 4 weekly with GM-CSF daily for 4 days. Using intracellular cytokine and tetramer staining Tyrosinase specific IFNγ-producing T cells ranging from 0.05 to 1.4% of CD3+CD8+ T cells were already detected in 13 of the 23 patients before vaccination was initiated. In 12 of these patients we were unable to boost the frequency of tyrosinase-specific T cells by 6 vaccinations. In contrast, induction of tyrosinase-specific T cells was achieved in 7 out of 10 patients without preexisting immunity with 0.08–0.3% specific T cells of CD3+CD8+ T cells after 6 vaccinations. Prolonged immunization for a total of 12 cycles resulted in induction of further increase of the frequency of peptide-specific T cells up to 1.9% in 5 of 6 patients. The phenotypic characterization of preexisting as well as of vaccine-induced T cells showed the presence of both tyrosinase-specific memory and effector T cells and vaccination did not result in a major phenotypic shift in the prevaccination T cells. There were also no major differences in the proliferation capacity of Tyrosinase specific T after short-term in-vitro stimulation with IL-2 between the group with inducible T cell responses and patients with a preexisting T cell response. In summary our results indicate that a preexisting T cell response to a peptide significantly impairs the ability of the vaccine to expand specific T cells.