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HLA type-independent generation of antigen-specific T cells for adoptive immunotherapy

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Adoptive immunotherapy with antigen-specific T cells has been successfully used to treat certain infectious diseases and cancers. Although more patients may profit from T cell therapy, its more frequent use is restricted by limitations in current T cell generation strategies. The most commonly applied peptide-based approaches rely on the knowledge of relevant epitopes. Therefore, T cells cannot be generated for diseases with unknown epitopes or for patients with unfavorable HLA types. We developed a peptide-based approach for HLA type-independent generation of specific T cells against various proteins. It is based on short-time stimulation with peptide libraries that cover most CD4+ and CD8+ T cell epitopes of given proteins. The procedure requires no prior knowledge of epitopes because libraries are synthesized solely on the basis of the protein's amino acid sequence. Stimulation is followed by immunomagnetic selection of activated IFN-c-secreting cells and nonspecific expansion. To evaluate the protocol, we generated autologous T cells specific for a well-characterized antigen, the human cytomegalovirus phosphoprotein 65 (pp65). Generated T cell lines consisted of pp65-specific CD4+ and CD8+ lymphocytes that displayed antigen-specific killing and proliferation. The protocol combines the biosafety of peptide-based approaches with HLA type independence and may help to advance adoptive immunotherapy in the future. (Eur. J. Immunol. 2005. 35)