Efficient induction of tumoricidal cytotoxic T lymphocytes by HLA-A0201 restricted, melanoma associated, L(27)Melan-A/MART-1(26-35) peptide encapsulated into virosomes in vitro

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Cancer immunotherapy requires the induction of HLA class I restricted cytotoxic T lymphocytes (CTL) specific for tumor associated antigens (TAA). While a number of TAA have been identified, there is an urgent need for the development of adjuvants capable of stimulating CTL responsiveness. Previously, we reported the capacity of immunopotentiating reconstituted influenza virosomes (IRIV) to enhance CTL responses specific for synthetic peptides simultaneously added to cultures in soluble form. This effect was based on IRIV mediated activation of CD4(+) T cells. Here we investigated the "in vitro" immunogenicity of a novel virosome formulation coupling in a single reagent the adjuvant power of IRIV to the capacity of liposomes to efficiently encapsulate synthetic peptides. As a model epitope we chose L(27)Melan-A/Mart-1(26-35) HLA-A0201 restricted peptide from a melanoma-associated antigen widely used in tumor immunotherapy. The reagent thus developed induced the proliferation of CD4(+) T cells characterized by a T helper 1 cytokine profile and CXCR3 expression. Most importantly, it significantly enhanced the generation of L(27)Melan-A/Mart-1(26-35) specific CTL, as compared to soluble peptides, in particular at low nominal epitope concentrations (<1 microg/ml). These effector cells were able to efficiently kill HBL melanoma cells expressing Melan-A/MART-1 and HLA-A0201. The adjuvant effects observed were also detectable in the absence of CD4(+) T cells. Taken together our results suggest that this highly immunogenic antigenic formulation might qualify for clinical use in active, antigen-specific, melanoma immunotherapy.

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