A NOVEL STRATEGY TO IMPROVE ANTIGEN PRESENTATION FOR ACTIVE IMMUNOTHERAPY IN CANCER. FUSION OF THE HUMAN PAPILLOMAVIRUS TYPE 16 E7 ANTIGEN TO A CELL PENETRATING PEPTIDE

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Aim: Fundamental for an effective therapeutic cancer vaccine is facilitating the delivery of exogenous antigens to antigen presenting cells, ensuing processing and presentation via the MHC-class I and induction of an effective immune response. In this regard, we propose the use of cell-penetrating peptides fused to a tumor antigen. To demonstrate this concept we designed a fusion protein comprising a novel our proprietary cell-penetrating and immunostimulatory peptide (CIGB 550) linked to the human papillomavirus 16 (HPV 16) -E7 antigen (CIGB550-E7). The E7 viral protein alone is often poorly recognized by the immune system. HPV 16 infection has been linked to the development of cervical, anal and head and neck cancers.

Methods: Mice: Female C57BL/6 mice, 6–8 weeks old. Immunizations: The immunizations with CIGB550-E7 were given subcutaneously in the flank, in a final volume of 0.2 mL/dose. Tumor cells: The TC-1 cells were injected subcutaneously in the leg of C57BL/6 mice at 5 × 10^4 or 2 × 10^5 doses. Starting 7–10 days later and every 3–4 days thereafter, the area was observed and palpated for the presence of a tumor nodule. Tumor diameters were measured.

Results: 1. Coupling E7 to CIGB550 takes advantage that allows it to enter to the cells and thereby significantly improves the presentation of E7-derived peptides to T-cells 2. Therapeutic immunization with CIGB550-E7 vaccine induces regression of palpable tumors and survival increase. 3. In vitro analyses indicated that immunizations with this vaccine leads to the induction of a Th1-like cell mediated immune response based IFN-gamma secretion T cells and significant IFN-gamma increase following antigenic recall, using the ELISPOT assay.

Conclusions: The relevance of this result is the design of an original vaccine with promissory perspectives to treat HPV16 related malignancies, based on the covalent linkage of CIGB550 and HPV16 E7 antigen. Our data underline the efficacy of this approach at inducing broad immune responses in vivo, and offer a new strategy that could improve subunit cancer vaccine in a clinical setting.

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