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The V_H CDR2 peptide C7H2 interferes in actin dynamics, induces apoptosis in B16F10-Nex2 cells *in vitro* and activates dendritic cells to reduce metastasis in a melanoma syngeneic model

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Abstract

Malignant melanoma is the main cause of death in patients with skin cancer. Chemotherapy is not effective in the metastatic disease and immunotherapy is being encouraged, but still with few objective results.

Recently, we showed the *in vitro* and *in vivo* antitumor effects of peptide V_H CDR2 from monoclonal antibody C7 (C7H2) tested as synthetic peptide on B16F10-Nex2 cells (PLoS One 3, e2371, 2008). We have shown that the C7H2 induces beta-actin polymerization and inhibits depolymerization of F-actin. Such an effect on actin dynamics causes apoptosis in murine melanoma B16F10-Nex2 and several lines of human cancer cells. Chromatin condensation, DNA degradation, annexin-V binding, caspase 8 and caspase 3 activation, lamin disruption, degradation of organelles seen by electron microscopy and abundant production of superoxide anions, characterized tumor cell apoptosis. Since the *in vivo* protective effect of C7H2 was not observed in NOD/Scid-IL2rgamma^{null} mice, syngeneic dendritic cells (DCs) were tested in the metastatic melanoma model. DCs primed with melanoma antigens were poorly protective in animals challenged intravenously with B16F10-Nex2 cells. DCs primed with melanoma antigens and treated with C7H2 peptide were highly effective in reducing the number of lung metastatic nodules. Since peptide C7H2 seems to act directly on tumor cells, and also through the activation of DCs, which induce a protective anti-metastatic effect *in vivo*, it is a promising compound to be developed as an anticancer drug.

Biography

Denise Costa Arruda graduated in Pharmacy at Federal University of Santa Catarina, Brazil, completed her Ph.D at the University of São Paulo (USP), and postdoctoral studies at Federal University of São Paulo (UNIFESP), Brazil. At USP and at the Experimental Oncology Unit (UNIFESP) she has published 9 papers in reputed journals, in collaboration with international research groups, and got awards for poster presentation in two international meetings.