Santos L C P, J Cancer Sci Ther, 3:7
doi: http://dx.doi.org/10.4172/1948-5956.S1.18

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference & Exhibition on
Cancer Science & Therapy
15-17 August 2011 Las Vegas, USA

Antitumor activity of the vh complementarity-determining region 3 (cdr3) synthetic peptide derived from monoclonal antibody a4 in melanoma cells

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Malignant melanoma is a skin cancer with increased worldwide incidence. Tumor-specific monoclonal antibodies (mAb) have been used as an alternative to conventional chemotherapy for treatment of metastases. Recently, we showed that a murine melanoma B16F10-directed mAb, named A4, recognizes the cell adhesion molecule protocadherin β13 and is cytotoxic in vitro and in vivo against melanoma cells. MAb A4 is internalized, induces activation of caspase-9, 3 and 6, degradation of total- and phospho-β-catenin, TCF-4 down-regulation and apoptosis in melanoma B16F10-Nex2.1 cells. Similarly, the antibody V_H CDR3 (A4 H3) is cytotoxic in vitro against B16F10-Nex2 cells and have the properties of a microantibody. Presently, we aimed at determining the cytotoxic mechanism triggered by A4 H3 in melanoma cells. A4 H3 competes with mAb A4, suggesting that it also recognizes protocadherin β13. As with mAb A4, peptide A4 H3 induced tumor cell apoptosis, as shown by induction of superoxide anion production, chromatin condensation and DNA degradation. MAb A4 and peptide A4 H3 were also cytotoxic in vitro to several human tumor cells, and A4 H3 showed a significant antimetastatic effect in the syngeneic murine melanoma model. We conclude that peptide A4 H3 is functionally similar to mAb A4 in vitro and in vivo, and both are promising new therapeutic agents against melanoma.

Biography

Luana Cheven Perbore dos Santos graduated in Biological Sciences at the Campinas State University, completed her M.Sc. in Microbiology and Immunology and is engaged in the PhD program at the Experimental Oncology Unit, Federal University of São Paulo, Brazil. She presented oral communication at the International Congress of Immunology, and was awarded in poster sections in two other meetings (Biochemistry and Cell Biology) both held in Brazil.