**IMMUNOMODULATORY AND ANTITUMOR PROPERTIES OF THE BACTERIAL METALLOPROTEASE OLIGOPEPTIDASE A IN THE MURINE MELANOMA B16F10 MODEL**

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**Introduction:** Proteolytic enzymes from different sources have been evaluated for the treatment of several diseases. When administered as an exogenous drug, proteases may display a number of pharmacological properties, including antitumor effects. **Objective:** To verify the antitumor activity of recombinant oligopeptidase A (OpdA), a M3A oligopeptidase from *Escherichia coli*, with hydrolytic properties similar to Zn-dependent mammalian thimet oligopeptidase (EP 24.15) and neurolysin (EP 24.16). **Methodology and Results:** Intraperitoneal treatment of C57Bl/6 mice, endovenously challenged with syngeneic B16F10-Nex2 melanoma cells, with inactive but not with active OpdA induced a significant reduction in the number of pulmonary metastatic nodules. A major immunomodulatory effect was suggested to explain the anti-melanoma activity of the inactive protease. To evaluate the possible immunomodulatory properties of the inactivated metalloprotease, bone marrow derived dendritic cells (BM-DCs) from wild-type (WT), TLR-4, TLR-2, MyD88 and TRIF knockout (KO) mice were stimulated with OpdA. BM-DCs from WT animals were activated by inactivated OpdA, as demonstrated by the increased expression of CD80, CD86, CD40, MHC-II molecules, and the secretion of IL-12, TNF-α, IL-10 and NO. The TLR-4/MyD88 and TRIF signaling pathways are involved in this activation, since BM-DCs from KO animals were not activated. **Conclusions:** Our results suggest that the antimelanoma effect of inactivated OpdA due to a potent immunomodulatory effect of the metalloprotease activating antigen presenting cells to induce a protective immune response, and that this effect is dependent on the TLR4/MyD88/TRIF signaling pathway. **Acknowledgements:** CNPq, CAPES and FAPESP. **Key words:** OpdA, Immunomodulation, B16F10