

Components from spider venom activate macrophages against glioblastoma cells: new potential adjuvants for anticancer immunotherapy

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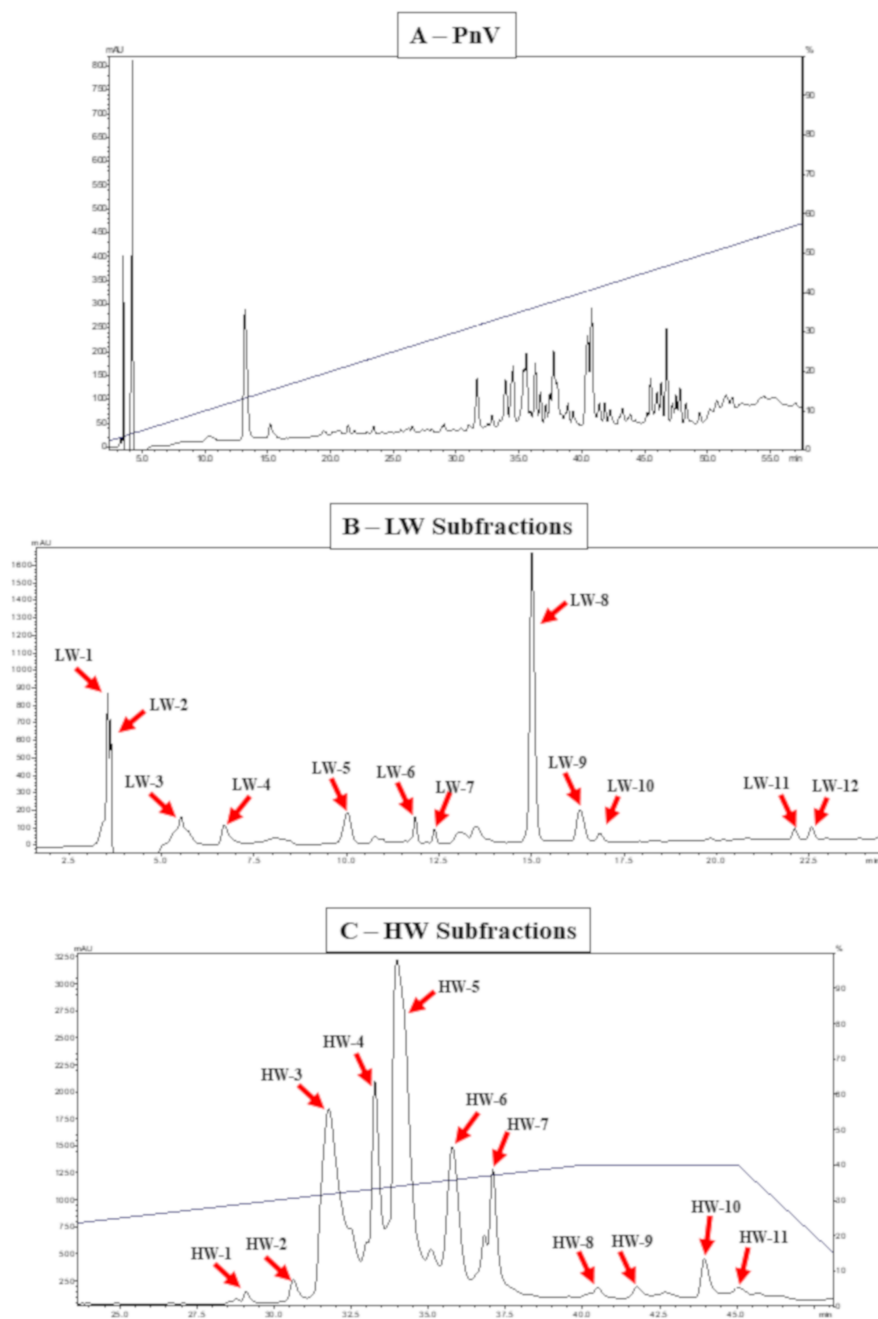
August 13, 2020

Abstract

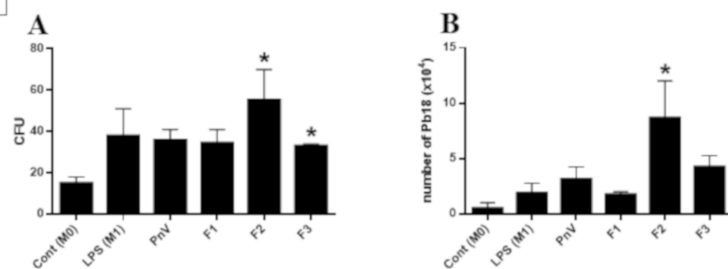
Immunomodulation has been considered an important approach in the treatment of various types of malignant tumors. However, adaptive immune cells have received more attention, while the modulation of innate immune cells is still an underexplored tool. A recent study by our group demonstrated that the Phoneutria nigriventer spider venom (PnV) administration increased the circulating NK cells and monocytes and the infiltration of macrophage in glioblastoma, in addition to decreasing the tumor size in a preclinical model. The hypothesis that PnV would be modulating the innate immune system led us to the main objective of the present study: to elucidate the effects of PnV and its purified fractions on cultured macrophages. After differentiation from bone marrow precursors, cells were pre-activated with IFN- γ and treated as follow: Control (untreated); LPS (1 $\mu\text{g/mL}$); PnV (14 $\mu\text{g/mL}$); PnV-fractions F1, F2 and F3 (1 $\mu\text{g/mL}$) or PnV-subfractions (1 $\mu\text{g/mL}$). Results showed that PnV and the three fractions activated macrophages. Further purification generated twenty-three subfractions named Low Weight (LW-1 to LW-12) and High Weight (HW-1 to HW-11). LW-9 presented the best immunomodulatory effect. Treated cells were more phagocytic, migrated more, showed an activated morphological profile and induced an increased cytotoxic effect of macrophages on tumor cells. However, while M1-controls (LPS) increased IL-10, TNF-alpha and IL-6 release, PnV, fractions and subfractions did not alter any cytokine, with the exception of LW-9 that stimulated IL-10 production. These findings suggest that molecules present in LW-9 have potential to be used as immunoadjuvants in the treatment of cancer.

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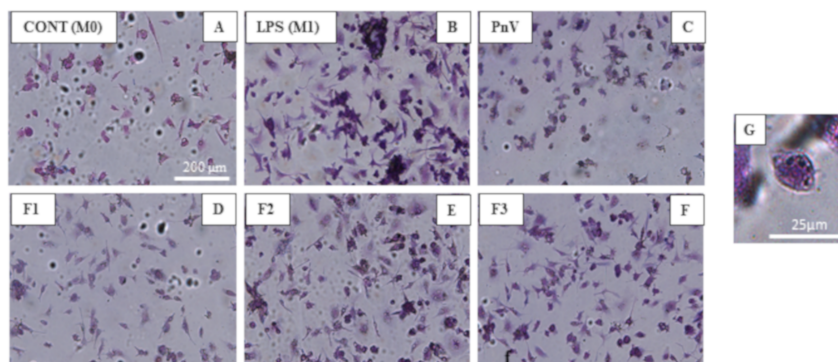
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2.1



2.2



2.3

