ANTITUMOR EFFECT OF IXOLARIS, A FVIIa/TISSUE FACTOR COMPLEX INHIBITOR, IN B16F10 MELANOMA

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Melanoma is a highly metastatic cancer and there is strong evidence that its procoagulant behavior contributes to this aggressive pattern. In this context, it has been hypothesized that anticoagulants might attenuate the disease progression. The aim of this study was to evaluate the effect of Ixolaris, a FVIIa/TF complex inhibitor, on the procoagulant properties of the metastatic murine melanoma cell line B16F10 as well as in the *in vivo* tumor growth. Flow-cytometric analyses showed that B16F10 cells constitutively express the clotting initiator Tissue Factor. In addition, flow cytometry also demonstrates the exposure of the procoagulant lipid phosphatidylserine on cell surface. As a result, B16F10 significantly shortened the coagulation time of murine plasma. This effect was progressively reverted by increasing concentrations of Ixolaris. *In vivo* assays were further performed upon subcutaneous inoculation of cells in C57BL/6 mice. Animals were treated daily with Ixolaris (50 or 250 μg/kg, i.p.) and tumor growth was measured after 15 days. A significant decrease in the tumor size was observed for both Ixolaris doses (74% and 67%, respectively) as compared to control animals. Remarkably, Ixolaris showed no effect on cell viability after *in vitro* treatment with 1 μg/ml for 24, 48 or 72 h. Taken together, our data indicate that Ixolaris targets the procoagulant properties of B16F10 resulting in reduced tumor growth.