

# LOCALLY GENERATED ELASTIN PEPTIDES INCREASE INVASIVE POTENTIAL OF MELANOMA CELLS DOMINANTLY BY GALECTIN-3

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Melanoma is a highly malignant tumor type and elastin protein plays a key role in the progression of melanoma. The VGVAPG and VAPG peptide-sequences are repeating several times in the human elastin and they are most likely to be the breakdown products after the degradation of elastin.

We demonstrate the elastin protein and the VGVAPG sequence with histochemical and immunohistochemical methods. We present evidence that both VGVAPG and VAPG elastin peptides could bind to three identical receptors: galectin-3, integrin  $\alpha\beta 3$  and elastin-binding protein.

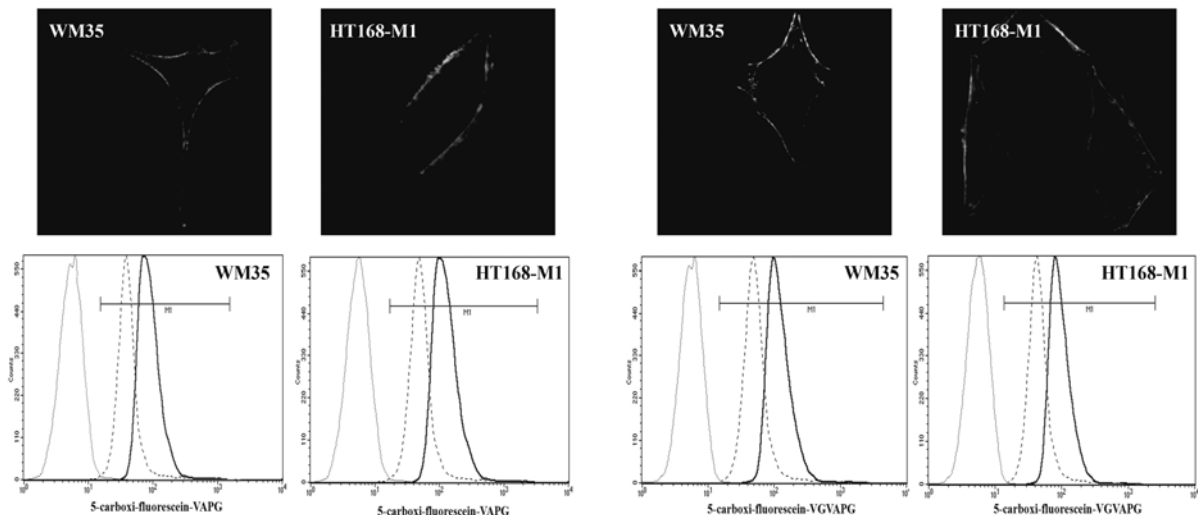


Figure 1: Expression of carboxy-fluorescein VGVAPG and VAPG on the cell surface of melanoma cells; and the binding of peptides to galectin-3, integrin  $\alpha\beta 3$  and elastin-binding protein receptors.

We investigated the effects of VGVAPG and VAPG elastin peptides on several metastatic markers of human melanoma cell lines with different invasive potential (WM35 and HT168-M1). Immunocytochemistry, flow cytometry and quantitative real-time PCR were applied to evaluate the changes of the expressions.

In conclusion: interaction between phylogenetically conserved elastin sequences (VGVAPG, VAPG) and melanoma cells appears to be a significant point of tumor progression: (i) elastin and its fragments are potential substrates of MMP-2 and MMP-3; (ii) they have chemotactic effect on the melanoma cells; (iii) elastin peptides increase the expression of CXCR-4 and CXCL-12 chemokines; (iv) the cleaved peptide fragments have the ability to increase the expression of the elastin-degrading MMP-2 and MMP-3 enzymes; (v) they could increase the expression of CD44, ICAM-1 and NCAM-1 major adhesion molecules and (vi) increase the expression of the angiogenic VEGF-C. All these effects are mediated dominantly by galectin-3 receptor.