ALTERNAGIN-C, AN ECD-DISINTEGRIN FROM *Bothrops alternatus* SNAKE VENOM, MODULATES GENE EXPRESSION OF VEGF RECEPTORS IN HUMAN ENDOTELIAL CELLS

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Angiogenesis is an essential process in both physiological and certain pathological conditions. The interactions between vascular endothelial growth factor (VEGF) and its receptors VEGFR-1 and -2 are critical in these processes. VEGFR-2 mediates the VEGF-dependent mitogenic effect, while VEGFR-1 is a decoy receptor. Alternagin-C (ALT-C), an ECD-disintegrin, induces human umbilical vascular endothelial cell (HUVEC) proliferation by up-regulating vascular endothelial growth factor (VEGF) expression in fibroblasts. This work shows that ALT-C modulates the gene expression of VEGFR-1 and -2 in HUVEC using real-time PCR. Cells were treated with soluble ALT-C (1, 10, 100nM) for 4, 24, and 48h. Amplification detection was based on the SYBR® Green fluorescence. The comparative expression was normalized to β-actin expression and calculated by $\Delta\Delta$Ct method. Results were obtained from independent experiments in duplicate. At 1nM ALT-C, mRNA levels of both receptors decreased between 4h and 48h. VEGFR-1 expression was not different of control at 10nM, but VEGFR-2 expression was up-regulated after 48h. At 100nM ALT-C the effects are opposite to those observed for 1nM ALT-C regarding to VEGFR-1. However, VEGFR-2 expression at 100nM was lower than or equal to controls. Since VEGFR-2 is involved in the HUVEC proliferative response, these results contribute to the understanding of the ALT-C dose-dependent mechanism of action.

Keywords: disintegrin, endothelial cell, cell proliferation, VEGFR expression.
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