THE ROLE OF CATHEPSINS B, L AND S IN B16F10-NEX2 MELANOMA ANGIOGENESIS

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In tumorigenesis process, angiogenesis is crucial for the tumor progression, being a prerequisite for the rapid clonal expansion and formation of macroscopic tumors. Tumors appear to activate the angiogenic switch by changing the balance of angiogenesis inducers and counteracting inhibitors. High expression and activity of cathepsins was found in many tumors which may participate in angiogenesis process. Our objectives were to verify the cathepsins B, S and L activity in B16F10-Nex2 melanoma and endothelial cells. The effect of those enzymes in angiogenesis process with an *in vitro* Matrigel assay was also investigated. Using fluorogenic substrates and specific inhibitors, we determined the cathepsins catalytic activities on cellular surface of melanoma and endothelial cells. We observed that the cysteine-protease inhibitor E-64 and an specific cathepsin L inhibitor (RF-14) promoted a reduction of angiogenesis, indicating the participation of cathepsins in the process. In contrast, the inhibition of cathepsin B by the specific inhibitor CA-074 promoted stimulation of angiogenesis. The effect of cathepsin S in angiogenesis will also be analyzed. Our results indicated that, in B16F10-Nex2 melanoma, cathepsins are capable to induce and inhibit angiogenesis, suggesting that antagonic factors may regulate or trigger the angiogenic switch. The data provided suggest that specific cathepsin inhibition can be a tool in therapeutic approaches. Supported by CNPq and FAPESP.