Glycosaminoglycans Modulate Elastase Amidolytic Activity and *Anoïkis*

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Neutrophil elastase (NE), one of the most destructive enzymes, can degrade extracellular matrix components and activate several proteases, when not controlled by endogenous inhibitors, giving rise to irreversible damages. Several compounds, as glycosaminoglycans (GAGs), may influence the action of NE. Therefore, the aims of the present study were to verify the action of GAGs on the activity and structure of NE, and their effects on fibroblast death, induced by this enzyme. The catalytic efficiency of NE on the MeO-Suc-Ala-Ala-Pro-Val-pNan hydrolysis was reduced by heparan (HS), dermatan and chondroitin 6-sulfate (C6S). In addition, the secondary structure of NE, determined by circular dichroism, was also modified by the same GAGs. Cellular viability and DNA fragmentation, determined by flow cytometry, were used as parameters to analyze the events involved in the possible elastase-induced cell death and the influence of GAGs in this process. NE, in the presence of HS and C6S, reduced the cell viability. Also, the occurrence of anoïkis, a programmed cell death induced by the loss of cell/matrix interactions, caused by proteases, is possible considering NE increased the DNA fragmentation. Besides, CeEI, an elastase inhibitor from *Caesalpinia echinata* seeds, increased the cell viability and reduced DNA fragmentation, confirming the NE involvement in this process. It is possible that GAGs, that have no effect in the DNA fragmentation, can modulate the NE activity in this cell death model. These results are particularly important for the understanding of several processes where NE is involved, such as disruption of extracellular matrix components and cell migration (FAPESP, CNPq, CAPES).