

## CYTOTOXIC, THROMBOLYTIC AND EDEMATOGENIC ACTIVITIES OF THE SNAKE VENOM METALLOPROTEINASE LEUCUROLYSIN-A

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Leucurolysin-a (leuc-a), a 23 kDa non-hemorrhagic metalloproteinase is found in venom of the viper *Bothrops leucurus*. We examine the biological consequences of leuc-a, including thrombolytic activity, direct effects on endothelial cells in culture and edematogenic activity *in vivo*. We demonstrate fibrinolytic activities of leuc-a upon fibrin  $\alpha$ ,  $\beta$ , and  $\gamma$  chains. While not causing hemorrhaging, leuc-a has thrombolytic activity in whole blood clots. Endothelial cells are highly resistant to leuc-a in culture. Nevertheless, cell morphology changes (detachment) are induced by leuc-a and cell adhesion to fibronectin decreased due to leuc-a. This mild cellular impact is unlike that of crude venom, where lower concentrations triggered cell death and a more pronounced decrease in cell adhesion. Also, leuc-a increased microvessel permeability with marked edema in mice peritoneum and foot pads. These *in vivo* effects were weaker when crude venom was tested. In conclusion, albeit not hemorrhagic, leuc-a is fibrinolytic, thrombolytic and induces a prominent edema which appears to be significant in the local effects observed after *B. leucurus* venom accidents. Supported by CAPES, CNPq, Fundação Araucária-PR, FAPEMIG.