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*Serine Proteinases in Venom of the Yucatan Rattlesnake *Crotalus simus tzabcan**

Biological Sciences

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Faculty Sponsor(s): Mackessy, Stephen

Snake venoms comprise a complex mixture of macromolecules, primarily proteins, that can cause cataclysmic destructive changes to living tissues when injected by a snake. Somewhat enigmatically, these same molecules have high potential for medicinal purposes, because most venom components are mimics of natural regulators of body functions. Previous studies have revealed that serine proteases in venoms interact with the blood coagulation cascade, a complex series of protease-mediated reactions in the body which regulate and the thrombin-like serine proteases (TLSP) act preferentially on fibrinogen. The isolation and manipulation of these proteins could directly contribute to the treatment of clotting disorders, acute hypertension, and even some cancers. New drug candidates are necessary because current drugs have undesired side effects and several newer candidates have recently failed in clinical trials. To address this need, I am examining TLSPs from the venom of the Yucatan Rattlesnake (*Crotalus simus tzabcan*), a species whose venom has not been investigated but which contains abundant serine proteases. Isolation of a TLSP has just been completed using a three step chromatographic purification protocol (low pressure size exclusion, ion exchange and reversed phase). Initial characterization of this purified protein include determination of its mass, specific activity and possible inhibitors. In addition, I will evaluate other physical characteristics of the protein such as extent of glycosylation, which can influence physiological stability and resistance to endogenous proteases, and specific activity toward fibrinogen and other natural substrates. Identification of these properties are the first steps toward a future therapeutic, and if these are positive, biological testing in a rodent model will be undertaken. This research further demonstrates the potential for new and more specific-acting drugs from natural sources, and animal venoms contain a wealth of candidate molecules potentially useful for treating human diseases.