

INVITED LECTURE H11

Variegin, a novel thrombin inhibitor from tropical bont tick and its interaction with thrombin

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Hematophagous insects depend on potent anticoagulant and antiplatelet agents for securing sumptuous blood meals. We recently isolated and characterized a novel thrombin inhibitor from the salivary gland extracts of tropical bont tick (*Amblyomma variegatum*). It is one of the smallest thrombin inhibitor found in nature. We examined the structure-function relationships of variegin using a number of deletion mutants. Recently, we have determined the X-ray crystal structure of thrombin-variegin complex at 2.5 Å resolutions. Based on the structure as well as the prior knowledge on thrombin inhibitors, we designed several peptides to understand the interaction between thrombin and variegin. These peptides cover a diverse spectrum of potency, kinetics and mechanism of inhibition, including peptides with affinities ranging from sub-picomolar to nanomolar values, with fast and slow tight binding, displaying competitive and non-competitive inhibition.