STRUCTURAL AND FUNCTIONAL INSIGHTS OF INFESTINS 1 AND 4 IN THE BLOOD FEEDING OF *TRIATOMA INFESTANS*.

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Blood feeding insects have to find a way to avoid coagulation. *Triatoma infestans*, a Chagas' disease vector, has a protein called infestin that participates in this vital function. Infestin is composed of seven Kazal domains with different protease inhibition specificities. Infestin's domain 1 bound to trypsin and domain 4 were crystallized and had their structures solved by X-ray diffraction. Although both domains share the Kazal structure, they differ in that while infestin 1 inhibits thrombin, infestin 4 inhibits factor XIIa from the coagulation cascade. This differentiation is clearly related to the interface of the proteins buried during interaction. We have mapped the amino acid residues involved in these interactions in the structures and suggest how inhibition occurs. Furthermore, we were able to select mutants of infestin 4 using a phage-display system that have a more selective and powerful inhibition against factor XIIa. Comparisons with the mutants and other inhibitors are made to understand the high affinities displayed by infestins.

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