Flexibility Controls Specificity of Snake Venom Metalloproteases

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Protein-Protein interfaces have crucial functions in many biological processes[1]. The large interaction areas of such interfaces show complex interaction motifs. Even more challenging is the understanding of (multi-)specificity in protein-protein binding. Many proteins can bind several partners to mediate their function[2].

A perfect paradigm to study such multi-specific protein-protein interfaces are snake venom metalloproteases (SVMPs)[3]. Inherently, they bind to a variety of basement membrane proteins of capillaries, hydrolyze them, and induce profuse bleeding. However, despite having a high sequence homology, some SVMPs show a strong hemorrhagic activity, while others are (almost) inactive[4].

Our results indicate that the activity to induce hemorrhage, and thus the capability to bind the potential reaction partners, is related to the backbone flexibility in a certain surface region[4]. A subtle interplay between flexibility and rigidity of two loops seems to be the prerequisite for the proteins to carry out their damaging function. Presumably, a significant alteration in the backbone dynamics makes the difference between SVMPs that induce hemorrhage and the inactive ones.

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