From vector spit to spitomes and beyond: How much work is there to do?

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The habit of blood sucking evolved independently in several arthropod orders or families. In their adaptation to blood feeding, these arthropods evolved a sophisticated salivary cocktail that disarms their hosts hemostasis and inflammation, thus allowing more blood to be removed while preventing host behavioral defenses from killing the robber. Accordingly, anti-clotting, anti-platelet and vasodilatory substances have been found in the saliva or salivary gland homogenates of blood sucking arthropods (BFA). Immunomodullators are also found, mainly in ticks that feed for several days on their hosts. In the last 8 years, several salivary gland transcriptomes from BFA have been analyzed, uncovering over 70 different salivary proteins in fast feeders, such as mosquitoes and sand flies, and several hundreds in hard ticks. Many of these proteins comprise novel families, a small number of which have now been functionally characterized. Interestingly, many of these proteins act on neutrophil products, reaffirming the role of these leukocytes in hemostasis. It is also becoming apparent a convergent mechanism of pharmacological antagonism, which we name kratagonism, that relies on the sequestration of host agonists by different protein families, including members of the lipocalin and odorant binding superfamily. We also find that every genus of a blood sucker so far studied contains at least 2-3 novel protein families that await functional studies. Accordingly, the combined BFA spitomes or BFA sialoverse constitute a large mining ground for novel pharmacological reagents. Considering that each single novel protein requires a minimum of 1 year of work for the discovery of its function, and that there are over 500 different genera of blood sucking arthropods, a minimum of 1,000 scientist working years will be required to map this mining ground.

Protease Inhibitors - aspects and applications of low molecular weight and proteic inhibitors.