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Anti-tick vaccines: homology modeling of a tick antigen Bm91 from Boophilus microplus

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Short Abstract: An alternative method of tick control involves the artificial induction of immunologically-based resistance to infestation. The 3D-structure of Bm91, a tick-antigen from B. microplus, was predicted by means of homology modeling using HACE as template. This work has contributed towards future drug design and development of ectoparasite specific anitigens.

Long Abstract:

Ticks are blood-sucking ectoparasites of enormous economical and medical importance. In the past years chemicals have been used to control ticks. An alternative involves the artificial induction of immunologically-based resistance to infestation.

In this study Bm91, which is an effective antigen against the cattle tick B. microplus, was investigated. Bm 91 is a carboxy-dipeptidase with biochemical specificity very similar to mammalian agiotensin-converting enzymes (ACE; Peptidyl-dipeptidase A. EC 3.4.15.1). The 3D-structure of Bm91 was predicted by means of homology modeling using human ACE as template. To obtain related sequences, the sequence of Bm91 was submitted to BLAST (Basic local alignment search tool) and FUGUE2. A multiple alignment of the relevant ACE was done using T-COFFEE. MODELLER 8 was used to obtain the 3D-model of the target protein. The sequence of Bm91 was analyzed for antigenic properties using ANTIGENIC followed by a hydrophilic analysis using PEPWINDOWALL. Normal mode analysis was done by ElNémo.

Analysis of alignment shows that Bm91 has many conserved regions within the family of ACE. This ranges from single conserved amino acids as well as structural- and functional-motifs. Although the sequence identity is relatively low (35%), significantly low RMS values (range 0.51-0.61Å) and high quality Ramachandran plots where obtained. Normal mode analysis of Bm91 reveals a “closing up” of the substrate binding site. It is postulated that the “closing up” of the substrate binding site is responsible for holding the substrate in place and forcing the substrate closer to the active site.

This work has contributed towards future drug design studies and development of ectoparasite specific anitigens.