

Novel Vaccinology Approaches against Ticks

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Over the past few years, the science of developing vaccines have had, and continue to prevent diseases. Veterinary vaccines have a major role in reducing animal suffering, protection of animal health and enhance efficient animal productivity. Ticks are considered among the most important disease transmitting vectors second to mosquitoes. Tick borne diseases affect both human and livestock animals in many tropical and subtropical areas [1,2]. Ticks transmit several viral infections, bacterial and protozoan diseases causing Encephalitis, Crimean-Congo Hemorrhagic fever, Kyasanur forest disease, Lyme disease, Rocky Mountain spotted fever, monocytic and granulocytic ehrlichiosis, and babesiosis.

Control of ticks and tick borne diseases has passed several steps started by using the biological control and the use of acaricides which showed partial success and many drawbacks on the environment and animal productivity. Other strategies had evolved using immunization protocols of native purified proteins followed by the cloning of the gut cell surface molecule BM86; the most successful vaccine against the cattle tick *Rhipicephalus microplus* with some limitations against non *Rhipicephalus* species.

Recently, other approaches have been developed based on the genomics of the tick species. The genome sequence of the target tick species will explore potential protein coding sequences that can be used as candidate vaccines [3]. Vaccinology in the genome era is considered to be the second revolution in the 20th century [4]. This approach is known as the reverse vaccinology which utilizes the information of the entire genome of the parasite to predict and localize potential functional proteins through the open reading frames in the genome. These potential candidates are then cloned and expressed and finally their immunogenicity is validated in animal models.

In ticks, the genome size varies between ~10⁹ bp (*Amblyomma americanum*) and ~7×10⁹ bp (*Rhipicephalus microplus*). The efforts to characterize the genomes of other ticks like *Ixodes scapularis* and the current studies implying the use of cDNA libraries of *R. annulatus* [5,6], *R. microplus* [7], *A. variegatum* [8], *I. scapularis* [9] in the identification of novel molecules, will impact on the discovery of new tick-protective antigens. The use of the information deduced from the open reading frames in conjugation with functional analysis using technologies such as RNAi, bioinformatics, mutagenesis, transcriptomics, proteomics will allow for rapid discovery of novel tick vaccines.

High-throughput studies for some tick species have been accomplished such as the deer tick; *I. scapularis*, blacklegged tick; *Ixodes pacificus*, the Rocky mountain wood tick; *Dermacentor andersoni*, the tropical bont tick; *Amblyomma variegatum*, the castor bean tick; *Ixodes ricinus* [10], *Rhipicephalus haemaphysaloides* [11], the Gulf coast tick; *Amblyomma maculatum* [12] and the coarse bontlegged tick; *Hyalomma marginatum rufipes* [13]. The authors have investigated the sialotranscriptome and proteome in tick salivary glands of previously mentioned tick species. Several protein families have been identified as shown in table 1. These annotated databases can be used in the development of new strategies to control tick infestations and the discovery of new candidates for animal vaccination.

Two projects studying the sialotranscriptome of the cattle and camel ticks; *Rhipicephalus annulatus* and *Hyalomma dromedarii*, respectively, are currently in progress.

Tick species	Proteins/Genes
<i>Hyalomma marginatum</i> (Salivary glands cDNA library from adult fed females)	Secreted genes Housekeeping genes Unknown group of genes Transposable elements Metalloproteases Proteins with antimicrobial functions Basic tail proteins Madanin thrombin inhibitor proteins Lipocalin proteins Glycin rich proteins Mucins proteins Immunity related proteins
<i>Ixodes ricinus</i> (Salivary glands cDNA libraries from: unfed, 24hours fed, partially 4 days fed, and fully engorged-7 days fed female ticks)	Housekeeping genes Reverse transcriptase-like proteins Collagen-like secreted proteins Basic tail secreted proteins Kunitz domain containing proteins 18.9 kDa group (related to feeding) RGD-domain containing proteins WC-containing proteins (unique proteins) Histamine-binding proteins Metalloproteases α-2 macroglobulin Calreticulin Defensins Neuropeptide-like proteins Carboxypeptidase inhibitors Ixoderin B Phospholipases
<i>Rhipicephalus haemaphysaloides</i> (Proteins extracted from salivary glands of fed and unfed adult females)	Signal transduction proteins Transcription factors Cell apoptosis factor Molecular chaperones Synthesizing immunosuppressant proteins

Table 1: Examples of annotated protein families or genes identified in some tick species.

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