

Report from an ILRI strategy workshop on tick research, Cape Town, 24 August 2014

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Introduction

A team of staff from the International Livestock Research Institute ([ILRI](#)) participated in the 12th Biennial Conference of the Society for Tropical Veterinary Medicine (STVM) and the VIII International Conference on Ticks and Tick-borne Pathogens ([TTP8](#)), held in South Africa in August 2014.

ILRI held a side event on 24 August to sensitize conference participants on ILRI's work on tick and tick-pathogen combination vaccines, vector-pathogen interactions, the molecular basis of vector competence, the influence of climate on the prevalence of tick-transmitted diseases and screening African ticks for the presence of human pathogens.

Background

The International Livestock Research Institute (ILRI) has previously had active programs on tick-related research including anti-tick vaccine evaluation and antigen identification, vector genomics and vector-pathogen interactions. These were designed to complement the long term activities on recombinant vaccine development for control of East Coast fever. ILRI still maintains a unique tick unit facility with tick colonies from four genera, *Rhipicephalus*, *Rhipicephalus (Boophilus)*, *Amblyomma*, and *Hyalomma*. The tick unit maintains selected lines of *Rhipicephalus appendiculatus* that have differential susceptibility to infection with *Theileria parva*. The cattle pens in the Tick Unit can hold up to 16 animals at BSL2 containment level, for use in specific experiments, including vaccine and acaricide trials or aspects of tick biology

Given the increasing burden of ticks and tick-borne diseases in many regions of the world, ILRI seeks to reenter the tick research arena, targeting areas where it has comparative/competitive advantage and the greatest potential for impact. A key driver in this decision is the spread of the invasive species *Rhipicephalus microplus* within eastern, western and southern Africa. As an institute with a global mandate, ILRI envisages a tick program that extends beyond Africa, particularly to South Asia.

As a first step in re-entering the tick research field ILRI invited distinguished scientists in the field of tick biology and control to attend a special session at TTP8 to discuss how the institute can best reintegrate into the global tick research arena, in synergy with the ongoing research activities of other groups.

Meeting objective

To identify current research gaps and opportunities for ILRI participation in tick and tick-borne disease control and tick biology research

Presentations

- Richard Bishop: How does ILRI reintegrate into the global tick research arena?
- Vish Nene: Current and future livestock vaccine research activities at ILRI.
- Jose De La Fuente: Tick Vaccinomics.
- Ala Lew-Tabor: Tick Reverse Vaccinomics

Discussions

Following the presentations the workshop participants split into three groups to discuss specific research areas. The discussions were led by an external expert, with ILRI staff acting as rapporteurs

The specific topics were

- Improved Tick control: Discussion Leader - Ala Lew Tabor (Group 1)
- Tick pathogen interaction: Discussion Leader - Jose De la Fuente (Group 2)
- Monitoring of livestock Tick Distribution in Africa: Discussion Leader - Maxine Madder (Group 3)

Group 1: Improved tick control: (Anti-tick vaccines, novel acaricide and acaricide resistance).

Professor Christine Maritz-Olivier
Dr Ard Nijhof
Professor Ben Mans
Professor Isabelle de Miranda Santos
Dr Michael Crampton
Professor Ala Lew-Tabor
Professor Ivan Morrison
Dr Lucilla Steinaa

Knowledge Gaps Identified

- The presence of co-infections in animals in the field and the lack of knowledge regarding how this may influence the outcome of vaccination.
- The need to test individual antigens rather than cocktails. The results from approaches using artificial salivary component cocktails are likely to be dependent on specific composition of particular cocktails
- Is there a possibility the ticks can evolve escape variants ('vaccine resistance') which will ultimately make a vaccine less effective?
- Are tick resistant animals changing tick populations through selection for more tolerant ticks?
- Will the use of 'rotational vaccination' delay the evolution of resistant ticks ?
- Vaccine trial standardization to allow comparisons between different laboratories is an important requirement. Presently, different breeds and animals of different ages are used in vaccine trials. There is a need for standardized protocols.
- Threshold levels of vaccine efficacy for effectiveness in the field need to be determined. This will likely require application of modeling

Potential ILRI role

- Analyze African tick populations through genetic analyses
- Isolation of homologues of known vaccine candidates from African tick species.
- Perform heterologous tick challenges-to antigens identified by other groups
- Evaluate the p67 sporozoite antigen with tick molecules and evaluate whether protection against tick challenge in the field is enhanced.
- Acaricide resistance to *Boophilus (Rhipicephalus)* is widespread in South America and particularly well studied in Brazil. However this has been little researched in East Africa.
- ILRI could lead the establishment of integrated tick management programs involving sustained anti-tick vaccination (based on BM86) combined with decreased acaricide usage following the examples of Cuba and Mexico

Group 2: Tick-pathogen interaction

Professor Jose de la Fuente
Dr. Anna Lacasta
Dr. Petr Kopacek
Professor Tim Kuurti
Dr. Manuel Rodriguez Valle
Dr. Lesley Bell Sakyi
Professor Libor Grubhoffer
Dr. Nicholas Svitek

Knowledge Gaps Identified

- Knowledge of tick-pathogen interactions remains relatively limited. There could be opportunities for ILRI collaboration with groups working in this field.
- There is requirement for a network exchanging well defined tick populations from different sources
- Tick cell lines represent an underutilized tool for research on basic aspects of vector-pathogen interaction. More could be done using *in vitro* systems. Look for endogenous viruses in tick cells that may have effects on transmission. The potential for culture of *Theileria* in tick cells is little studied.
- Factors determining susceptibility to infection and hence vector competence are little known. One example is the role of the microbiome, which is a researchable area. The role of symbiotic bacteria and their manipulation lags behind research in mosquitoes.
- There is no systematic understanding of how tick salivary gland proteins and other biomolecules modulate pathogen infection. This would benefit from a coordinated approach.
- Transgenic ticks would be very useful tools. While many transgenic mosquitoes exist, this approach has not yet been pursued for ticks.
- Mutagenesis of tick-borne pathogens, which has already been pioneered for *Anaplasma* could help identify some of the key loci and molecules involved in vector pathogen interaction, for example receptor-mediated interactions.
- Induction of sporogony in vitro using cell lines is possible but only as a research tool; it is not possible to generate sufficient amounts for vaccine development.

- ILRI Currently concentrates on research on ECF, but not other TBDs. However, Ticks and TBDs are a major problem in the field in Africa. A recent SADEC livestock disease index places TBDs well above FMD in importance.
- A more detailed understanding of the biology of pathogen survival and multiplication inside the tick. This includes tissue specific responses at different stages of the infection cycle.

Potential ILRI Role

- ILRI could play a role in projects relating to many of these research gaps, but this would be on a strategic basis and in collaboration with external research groups.

Group 3: Monitoring of livestock tick distribution In Africa

- Maxime Madder
- Saskia Hendrickx
- Etsuya Tanaka
- Abdalla Latif
- David Odongo
- Richard Bishop
- Naftaly Githaka

Knowledge Gaps Identified

- Current initiatives to map tick distribution are small scale and isolated. To date, there has been research performed in Benin, Ivory Coast, Burkina Faso, Togo, Zimbabwe, and Tanzania. There are no similar studies for Kenya, Uganda, Sudan, and central Africa. A continent-wide project is required to generate a comprehensive map of tick distribution and density on the African continent.
- There is an urgent requirement for improved tick identification protocols. Western Africa is one key area where *Rhipicephalus* spp ticks are present but often misidentified. It is also possible that hitherto unknown taxa are present.
- Molecular analysis has revealed the presence of hybrid ticks: unanswered questions related to this discovery include:
 - Are the hybrid genotypes/phenotypes assisting the ticks to adapt to new habitats?
 - Are the hybrids viable? These seem to be found only in areas with *Rhipicephalus microplus*
 - What is the potential impact of *hybrids* on deployment of tick vaccines?
 - Is there selective pressure that favours the hybrids?
- In western Africa, tick spread is linked to movement of humans and livestock; are there other factors that may be involved in catalyzing the spread in other regions? Are the factors driving the spread similar in southern and eastern Africa?
- The origins of newly introduced ticks need to be traced since different geographic strains of *R. microplus*, exhibit important phenotypic differences, including different levels of acaricide resistance and different responses to anti-tick vaccination. Is *R. microplus* adapting to host species in Africa other than cattle as it has in other parts of the world, particularly Latin America

Potential ILRI Role

- Establish a reference centre for ticks: to test levels of acaricide resistance in East African in collaboration with veterinary authorities. Initially in Kenya in collaboration with DVS.
- Play a lead role in identifying cryptic tick species in East and West Africa using novel technologies including molecular taxonomy and mass spectrometry to supplement morphological analysis
- In collaboration with partners, such as ASARECA, AU-IBAR and CRP 3.7 (Specifically in Tanzania and Southern Kenya) determine the impact of recent tick incursions (particularly *B. microplus*) on livestock production and pathogen spread.
- Map distribution of tick susceptible and resistant breeds to inform livestock breeding programs? This could extend beyond Africa to Latin America, particularly Nicaragua.
- Lead field surveillance and modeling of potential losses from introduction of *R. microplus* in East Africa.
- Investigate the impact of other tick species, particularly *Amblyomma*

Key issues arising from plenary discussion

- Currently Bm86 is the only antigen to be deployed against ticks creating opportunities for deployment of additional antigens in anti-tick vaccination. An improved version of Bm86 is under development by a group led by Professor Christine Maritz-Olivier
- Reverse vaccinology approaches have made significant progress towards identification of vaccine candidates for *B. microplus*, although more testing is still required
- A tick-challenge model for *T. parva* infection has never been developed and the mechanism of immunity in cattle that are infected by ticks is unknown
- Mapping of tick distribution, particularly that of *B. microplus* in East Africa provides a research niche for ILRI that is potentially attractive to both donors and of interest to the tick scientific community