ILRI Tick Unit: Local research with global impact

Naftaly Githaka, Stephen Mwaura and Vish Nene

Why tick research at ILRI?

- Global economic losses due to ticks is ~\$17-19 billion.
- Vectors of many emerging of human and animal diseases.
- Acaricide resistance: a major obstacle to livestock production globally
- Direct impact of ticks
- Disease transmission
- Tick worry
- Anaemia
- Reduced productivity/low weights
- Ulceration of skin and teats
- Systematic immunosuppression
- Secondary infections Dermatophilosis

Irritation/restlessness

- Tick paralysis
- Tick facts
- They are not insects!
- ~900 species of hard and soft ticks worldwide.
- One tick lays ~500-20000 eggs!
- They feed for upto 14 days continuously.
- Tick genomes are very huge~10 GB (x3 human genome!).









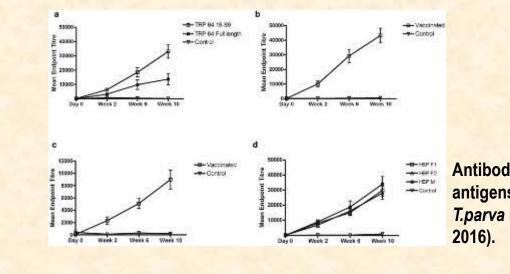
Basic research at ILRI tick Unit

Vaccines

•ECF recombinant vaccine support. Tick Unit provides parasite

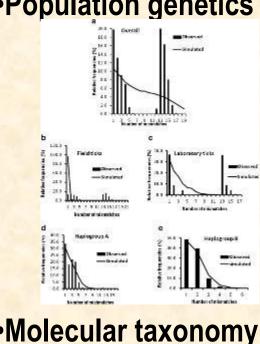
reagents.

Anti-tick vaccines



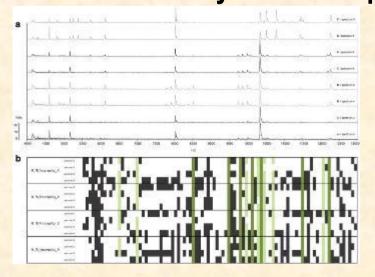
Vector Biology

•Population genetics of Rhipicephalus spp in eastern Africa.



Molelcular typing with COI and 12S genes revealed two distinct and welldifferentiated haplogroups among R. appendiculatus populations in Kenya. hese two haplogroups have no phylogeographic structure or correlation with their mammalian host species or the evolutionary and breeding history of the species. These findings suggest an ongoing speciation of R. appendiculatus in sub-Saharan Africa. It would be important to establish if the two haplogroups have any associated phenotypic differences which might influence parameters such as T. parva acquisition and transmission dynamics. In addition, identifying evolutionary forces driving the observed genetic differentiation may help explain the apparent population expansion of the two haplogroups within the sub-Saharan region (Kanduma et al., 2016).

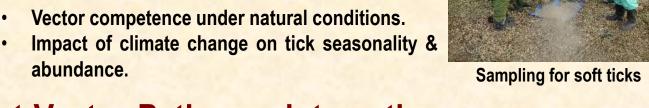
Molecular taxonomy of Afro-tropical ticks



Application of Matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) to identify field-collected ticks from East Africa (Rothen & Githaka et al., 2016).

•Tick ecology and disease dynamics at livestock-wildlife interfaces.

- · Link between vector resistance and anti
- microbial resistance in small-holding settings Role of wildlife as reservoir of tick vectors.
- Vector competence under natural conditions.



Host-Vector-Pathogen interactions

In vitro and in vivo laboratory models for highly pathogenic tick-

borne micro-organisms of livestock and humans.

ILRI Tick Unit

Background

·A rare and unique biological resource not only in Africa but also globally. •Built in 1979 to support research on East Cost fever (ECF) and other Tick Borne Diseases (TBDs).

Infrastructure

•Fly/tick proof cattle isolation pens (16 cattle). Rabbit rooms (48 rabbits). •Tick incubation rooms (8 incubators). Entomology Laboratory (14 microscopes).

Student data room (5). Tick colonies maintained

Rhipicephalus appendiculatus (7 different stocks and lines from Eastern and Southern Africa). Low (refractory) and High (susceptible) genetic lines of R. appendiculatus to T. parva infection. ·R.Zambeziensis

·Amblyomma variegatum Boophilus decoloratus, Boophilus microplus

Comparative advantages

biology, taxonomy, capacity building) Basic research & product delivery (10 peer-reviewed







Tick unit Building

Development/applied research at ILRI tick Unit

vaccine production for research purpose and backstopping of field deployment of past vaccine stocks. 2016 ITM vaccine production

The tick unit has recently produced 640,000 doses of Muguga Cocktail live vaccine against ECF commonly referred to as ITM (Infection & Treatment Method). 492 000 ticks, 400 rabbits and 40 cattle were used in the current production.



This current production ensures ILRI retails the technology to produce this important vaccine and provide materials for research purposes.

Acaricide resistance diagnostics

The tick unit is currently adapting protocols for detecting and quantifying chemical resistance in ticks (Larval packet test (LPT) and Adult Immersion Test (AIT) assays) to backstop similar efforts by regional veterinary services. We aim to classify by tick species, acaricide compound and by geographical locations in eastern Africa.

Pen and field trials of new acaricide formulations and other compounds with acaricidal properties.

This project aims to evaluate alternatives to existing compounds to mitigate acaricide resistance in tick vectors of veterinary importance.



Tick Unit projects (2014~)

- **Current or concluded grants**
- ILRI: Vish Nene (PI) & Stephen Mwaura (Co-PI)-Production of a new stock of ITM Muguga Cocktail vaccine against East Coast fever, \$407,370, May 2015-Sept 2016.
- Wellcome Trust: Naftaly Githaka (PI), Eshter Kanduma, Lucy Kamau & Patrick Kirera-International Public Engagement Award-Catalyzing the uptake and application of research output by small-scale rural farmers in Kenya, £17500, (April 2015-Sept November).
- ILRI-DAAD: Irene Kioo-Evaluation of anti-vector vaccine antigens targeting iron homostasis in ticks (graduate fellowship) (2015-2018).
- BBSRC: Lesley Bell-Sakyi (PI), Richard Bishop, Naftaly Githaka (Co-PI) & Vish Nene- Kenya-UK partnership to develop in vitro and in vivo laboratory models for highly pathogenic tick-borne microorganisms of livestock and humans, £30 000, (April 2014-March 2017.
- Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES)-Itabajara da Silva Vaz Junior (PI) & Naftaly Githaka (Co-PI)-Coperative agreement for development of vaccines against ticks, \$113,400 (2014-
- Genesis labs Inc: Vish Nene (PI) & Naftaly Githaka (Co-PI)- Development of a new host target vector control strategy using fipronil or another endectocidal agent to reduce the abundance of ticks and mosquitoes in western Kenya, **\$198.147**. (2014-2015).
- Proposals submitted (S) or under preparation (P)
- African Union Research Grant 2016: Christine Maritz-Olivier (University of Pretoria), Vish Nene (ILRI), Naftaly Githaka (ILRI), Christian Stutzer (University of Pretoria), Michael Crampton (CSIR BioSciences division, South Africa)-Integrated strategy for effective control of ticks and tick-borne diseases using acaricide resistance diagnostics, phylogeography and tick vaccines. \$1,049,012 (2017~) (S)
- EU H2020: Pirbright, ILRI et al., Understanding host-pathogen-environment interactions, € 6M (S)
- BBSRC: Lesley et al; The Tick Cell Biobank: outposts in Asia, Africa and South America, £120,000 (2017~ (S)
- BBSRC: University of Edinburgh, ILRI et al.; Networks in Vector Borne Disease Research: £2M (P).
- Wellcome Trust: Naftaly Githaka & Vish Nene: Intermediate Fellowship in Public Health and Tropical Medicine
- New partnerships on ticks and TBDs under discussion
- ILRI-University of Bern (Host-Vector-Pathogen interactions).
- ILRI-Directorate of Veterinary Services (DVS) (exchange of tick materials, joint proposals and sharing of facilities for

Public Engagement with Science at ILRI Tick Unit

Supported by Project: Catalyzing the uptake and application of research output by small-scale rural farmers in Kenya.







with ticks and tick-borne diseases.



Exploring tick biology with farmers-Mkulima mtafiti (the researching farmers)





A model farm integrating tick control, prevention of zoonoses and drought resilience.

A herd of Borans cattle under integrated tick management during science engagement.

Tick Unit peer-reviewed publications (2016)

- Costa, E.P., Façanha, A.R., Cruz, C.S., Silva, J.N., Machado, J.A., Carvalho, G.M., Fernandes, M.R., Martins, R., Campos, E., Romeiro, N.C., Githaka, N.W., Konnai, S., Ohashi, K., Vaz, I.S., Logullo, C., 2016. A novel mechanism of functional cooperativity regulation by thiol redox status in a dimeric inorganic pyrophosphatase. Biochim. Biophys. Acta-
- Gen. Subj. doi:10.1016/j.bbagen.2016.09.017 Olds, C.L., Mwaura, S., Odongo, D.O., Scoles, G.A., Bishop, R., Daubenberger, C., 2016. Induction of humoral immune response to multiple recombinant Rhipicephalus appendiculatus antigens and their effect on tick feeding success and
- pathogen transmission. Parasit. Vectors 9, 484. doi:10.1186/s13071-016-1774-0 †Rothen, J., †Githaka, N., Kanduma, E.G., Olds, C., Pflüger, V., Mwaura, S., Bishop, R.P., Daubenberger, C., 2016. Matrix-assisted laser desorption/ionization time of flight mass spectrometry for comprehensive indexing of East African ixodid tick species. Parasit. Vectors 9, 151. doi:10.1186/s13071-016-1424-6 †=Equal contribution
- 4. Lozano-Fuentes, S., Kading, R.C., Hartman, D.A., Okoth, E., Githaka, N., Nene, V., Poché, R.M., 2016. Evaluation of a topical formulation of eprinomectin against Anopheles arabiensis when administered to Zebu cattle (Bos indicus) under field conditions. Malar. J. 15, 324. doi:10.1186/s12936-016-1361-z
- Kanduma, E.G., Mwacharo, J.M., Githaka, N.W., Kinyanjui, P.W., Njuguna, J.N., Kamau, L.M., Kariuki, E., Mwaura, S., Skilton, R.A., Bishop, R.P., 2016. Analyses of mitochondrial genes reveal two sympatric but genetically divergent lineages of Rhipicephalus appendiculatus in Kenya. Parasit. Vectors 9, 353. doi:10.1186/s13071-016-1631-1
- Kamau, L.M., Skilton, R.A., Githaka, N., Kiara, H., Kabiru, E., Shah, T., Musoke, A., Bishop, R.P., 2016. Extensive polymorphism of Ra86 genes in field populations of *Rhipicephalus appendiculatus* from Kenya. Ticks Tick. Borne. Dis.
- doi:10.1016/j.ttbdis.2016.03.011 Toyomane, K., Konnai, S., Niwa, A., Githaka, N., Isezaki, M., Yamada, S., Ito, T., Takano, A., Ando, S., Kawabata, H.
- glands of Ixodes persulcatus Schulze. Ticks Tick. Borne. Dis. 7, 119–25. doi:10.1016/j.ttbdis.2015.09.006 Kanduma, E.G., Mwacharo, J.M., Mwaura, S., Njuguna, J.N., Nzuki, I., Kinyanjui, P.W., Githaka, N., Heyne, H., Hanotte, O., Skilton, R.A., Bishop, R.P., 2016. Multi-locus genotyping reveals absence of genetic structure in field populations of the brown ear tick (Rhipicephalus appendiculatus) in Kenya. Ticks Tick. Borne. Dis. 7, 26–35.
- Patel, E., Mwaura, S., Kiara, H., Morzaria, S., Peters, A., Toye, P., 2016. Production and dose determination of the Infection and Treatment Method (ITM) Muguga cocktail vaccine used to control East Coast fever in cattle. Ticks Tick. Borne. Dis. 7, 306-14. doi:10.1016/j.ttbdis.2015.11.006
- 10. Gomes, H., Moraes, J., Githaka, N., Martins, R., Isezaki, M., Vaz, I. da S., Logullo, C., Konnai, S., Ohashi, K., 2015. Vaccination with cyclin-dependent kinase tick antigen confers protection against *Ixodes* infestation. Vet. Parasitol. 211,
- 266-73. doi:10.1016/j.vetpar.2015.05.022 11. Norling, M., Bishop, R.P., Pelle, R., Qi, W., Henson, S., Drábek, E.F., Tretina, K., Odongo, D., Mwaura, S., Njoroge, T. Bongcam-Rudloff, E., Daubenberger, C.A., Silva, J.C., 2015. The genomes of three stocks comprising the most widely utilized live sporozoite Theileria parva vaccine exhibit very different degrees and patterns of sequence divergence. BMC
- Genomics 16, 729, doi:10.1186/s12864-015-1910-9 2. Murase, Y., Konnai, S., Yamada, S., Githaka, N., Isezaki, M., Ito, T., Takano, A., Ando, S., Kawabata, H., Murata, S., Ohashi, K., 2015. An investigation of binding ability of *Ixodes persulcatus* Schulze Salp15 with Lyme disease spirochetes. Insect Biochem, Mol. Biol. 60, 59–67, doi:10.1016/j.jbmb.2015.01.010
- 13. da Silva, R.M., Noce, B. Della, Waltero, C.F., Costa, E.P., de Abreu, L.A., Githaka, N.W., Moraes, J., Gomes, H.F., Konnai, S., Vaz, I. da S., Ohashi, K., Logullo, C., 2015. Non-classical gluconeogenesis-dependent glucose metabolism in Rhipicephalus microplus embryonic cell line BME26. Int. J. Mol. Sci. 16, 1821–39. doi:10.3390/ijms16011821

Our Vision & Mission

- A centre of excellence in tick research in Africa.
- To conduct cutting-edge scientific research on ticks and tick-borne diseases for better lives through livestock.
- To provide our clients with quality biological reagents and services on a timely manner.

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