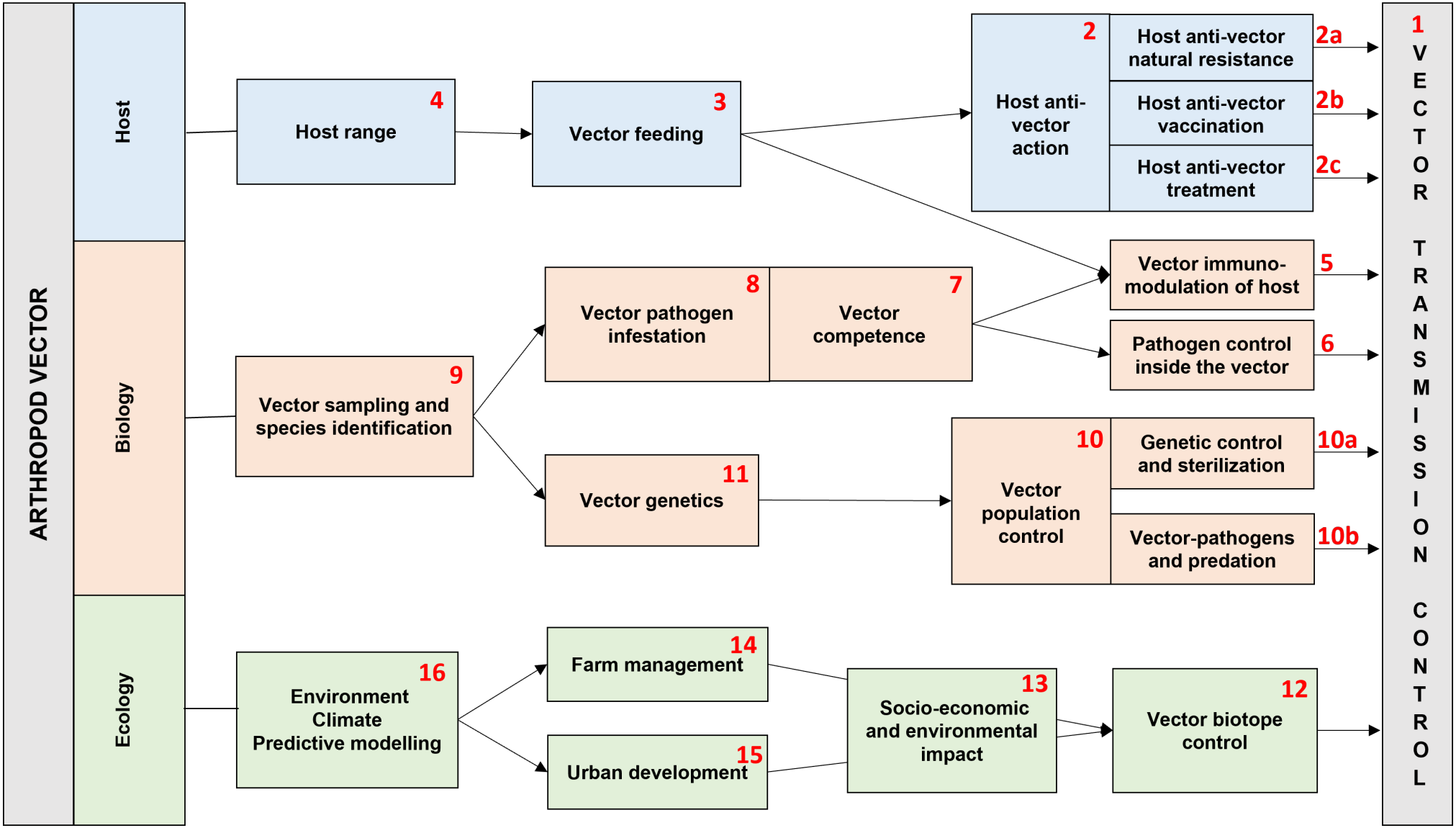
STAR-IDAZ
International Research
Consortium on Animal Health

Roadmap Lead Summaries

Disease/pathogen				
Roadmap type	**Vector Transmission and Control**			
Version: Date	V10	15/06/2023		
	V11	16/08/2023		
	V12	03/12/2023		
	V13	05/04/2024		
	V14	20/08/2024		

The generic roadmap for Vector Transmission Control considers the control of transmission through three routes; 1. Control of the host (blue), 2. Control through the vector (orange), and 3. Looking at the vector ecology or biotope (green). The generic roadmap can be used in conjunction with STAR-IDAZ roadmaps for specific vector-transmitted diseases.

Roadmap for Vector Transmission Control (VTC)



Lead Summary 2: Host-vector action

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Identify how hematophagous vectors find their hosts and how they feed on them and use the knowledge to disrupt their infestations as well as pathogen transmission:

- What are the various naturally occurring behavioural or physiological mechanisms that regulate host preferences of parasitic, hematophagous arthropods,
- What are the hosts' innate and acquired immune responses,
- What drugs or other chemicals target the vector, or
- What other biological interventions are effective, such as microbes that disrupt the vector's habitat or its host preference and thus their ability to find and infest the host and/or transmit pathogens
- Can animal nutrition affect immunity to vectors and VBDs?

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identifying naturally occurring physiological or anatomical vector resistance mechanisms among hosts, i.e., differences between host species and breeds regarding levels of vector infestation and pathogen transmission and whether it is possible to select for animals with the protective traits or otherwise co-opt these differences in other technological solutions (e.g., repellents).

Determining how different target livestock and poultry species or breeds respond to vector bites by inflammation and innate and adaptive immune responses to limit infestation or infection so that this can be genetically selected for or induced by prophylactics such as vaccines or other technologies. (E.g., while much of the research on mosquito feeding has been conducted in mice, there is a need for more studies on how other host species respond.)

Furthering understanding of vector pathways that can be targeted by chemical intervention to control infestation or identifying biologics that limit vectors on the host or in the environment.

Solution Routes

What approaches could/should be taken to address the research question?

These are outlined individually below in 2a, 2b and 2c.

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of host-vector interaction, especially vector attraction to specific hosts and subsequent feeding

Identification of naturally more resistant and susceptible animals within livestock and poultry breeds to be used to study the mechanisms of resistance

Understanding vector biology and physiology to develop new chemical targets

State of the Art

Existing knowledge including successes and failures

Several publications examine individual hosts and host breeds that present contrasting phenotypes of vector infestations and vector-transmitted pathogen infections (e.g., ticks, mosquitos or biting flies and greater vs lesser attraction to particular individual hosts; *Trypanosoma brucei*,; greater or lesser parasitemia and pathology in different breeds of cattle).

No genetic improvement through breeding or gene-editing or transgenesis are available yet because neither SNPs or specific genes that correlate with resistance have been identified.

A commercial vaccine is available for only one tick species despite decades of research. Vaccines for other vectors such as tsetse flies or mosquitos are not available.

Different ways to administer chemical controls are known but are dependent upon the type of host and are particularly concerning for food animals.

Resistance to chemical acaricides for vector control, particularly ticks, is of enormous concern worldwide thus having animals that are naturally resistant or vaccines to protect against vectors is of substantial importance.

Projects

What activities are planned or underway?

See below in 2a, 2b and 2c

Lead Summary 2a: Host anti-vector natural resistance

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Define mechanisms of vector control mediated by the host's innate and acquired resistance mechanisms (host anatomical characteristics such as skin thickness, host skin microbiome, inflammatory responses, innate immune responses, MHC variability and acquired immunity) using animals that present with different levels of previous exposure to the vector, or histories of vaccination, or acaracide or other chemical or drug treatments. Certain drugs used to treat VBDs potentially have a negative impact upon generation of host immunity to the very VBDs that are being treated. (Sourcing such animals and defining mechanisms is needed in order to be able to select and breed vector-resistant animals or to genetically edit animals to enhance resistance.)

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Developing phenotypic and genetic resistance assessment protocols.

Identifying populations of naïve animals showing differences in degrees of susceptibility vs resistant to vectors. For example, determine why certain breeds of cattle have lower tick loads than others (e.g., Bovidae in Indian subcontinent are more resistant, as are *Bos indicus* relative *Bos taurus*.) Does it represent co-evolution of cattle living in tick-infested areas?)

Determining whether livestock can be bred to increase their natural resistance to vectors.

Determining if host natural resistance is vector-species specific.

Determining whether expression of innate resistance differs with environmental factors such as heat, humidity, nutrition, etc.

Cataloguing the host's behavioural factors (e.g., tail swishing; licking) that contribute to animal resistance to or repelling of ticks or other pathogen vectors.

Determining the role of skin thickness and morphological structure (skin anatomy and physiology) in natural resistance.

Determining the relationship between skin reactions and resistance to vectors.

Determining which innate immune cells and other inflammatory components (neutrophils, macrophages, complement, acute phase reactants, etc.) are involved in natural resistance mechanisms.

Studying genetic variation in both the host and parasite populations to identify genetic factors that influence susceptibility to infection, e.g., the pathogen's resistance to complement-mediated killing or the host's ability to mount complement-mediated protective responses.

Identifying genetic polymorphisms including SNPs involved in conveying natural resistance that can be exploited to develop genetically edited hosts that can resist vector infestations without loss of productivity.

Identifying biomarkers of resistance in hosts.

Understanding the mechanisms behind histamine resistance. While it is known that ticks and mosquitoes are susceptible to histamine early in the feeding cycle but become resistant to histamine after some days. Others have suggested that repetitive feeding on rich blood makes them histamine resistant. The mechanisms behind this resistance are not well understood.

Solution Routes

What approaches could/should be taken to address the research question?

Assuming populations of naturally resistant and susceptible animals can be identified and that these are stable phenotypes, naïve animals representing these two groups need to be bred to create herds of naïve animals.

Using these animals, it may be possible to identify genetic markers including SNPs or other genetic polymorphisms that may be used as templates for gene editing studies.

These herds of animals can also be used to evaluate behavioural, inherent physiological, and innate immune responses that differ between the two groups.

Collectively, this knowledge will serve as criteria for selecting more resistant individuals from different breeds that are resilient to their environments for additional reasons (e.g., resistance to particular pathogens, heat-resistance, greater productivity with local grazing or feeding systems, etc.)

Dependencies

What else needs to be done before we can solve this need?

Establish herds of hosts with different levels of natural resistance for comparative studies.

State of the Art

Existing knowledge including successes and failures

Babesia is a protozoan parasite that is transmitted by ticks and causes babesiosis in humans and animals. The host complement system plays an important role in controlling babesia infections by killing the parasites directly or marking them for destruction by other immune cells. Some strains of babesia have evolved mechanisms to evade the host complement system, allowing them to survive and replicate within the host. Understanding these mechanisms could provide new insights into how babesia and other TBD cause disease and lead to new approaches of control.

Some breeds of cattle such as Nelore cattle in Brazil have a level of natural resistance to ticks. The crosses of Gir and Holstein to yield Girolandos and also crosses of Hereford and Gir to yield Braford were evaluated. The various breeds were evaluated by transcriptomics to see association with resistance using GWAS and found 4 pathways associated: MAPK, ROS, complement and wound repair.

Latif AA, Punyua DK, Capstick PB, Newson RM. Tick infestations on Zebu cattle in western Kenya: host resistance to Rhipicephalus appendiculatus (Acari: Ixodidae). J Med Entomol. 1991 Jan;28(1):127-32.

Projects

What activities are planned or underway?

Lead Summary 2b: Host anti-vector acquired resistance (vaccines)

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To increase host resistance to vectors by elucidating protective adaptive immune responses and determining the vector antigens that provoke such responses.

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identifying antigens (components) of vectors that induce protective adaptive immune response.

For ticks, why is the homologue of BM86 (an antigen used as a protective vaccine) not transcribed in some individual ticks of the same species, and how does this impact vaccine efficacy?

There is currently no standardized method for testing the efficacy of some anti-vector vaccines, which makes it difficult to compare results across studies. This lack of standardization also makes it difficult to determine which vaccines are most effective and thus a protocol needs to be established.

Determining whether there is an efficient way to test whether a protective vector antigen is effective across a range of vector species. For example, could in vitro feeding of ticks with antibodies be used to demonstrate this?

Determining whether vaccines are working better in 1-host ticks than 3-host ticks because of differences in feeding lengths. Again, could this be addressed by in vitro feeding systems?

Evaluating which isotype (class) of antibody is needed to be induced in order for anti vector vaccines to be effective; that is, what effect does IgM, IgG, and IgE isotypes have?

Developing anti-vector vaccines to affect all life stages of vector.

Determining if an ongoing tick infestation at the time of vaccination affect vaccine efficacy.

How effective are antibodies elicited by natural exposure to vector saliva in neutralizing functions of salivary proteins?

What are the profiles of antibody responses of hosts elicited by exposure to vector salivary proteins during natural exposure and how do they interfere with vaccines against vectors based on these proteins (through antigen masking, antigen imprinting, inhibitory FcR signalling)?

Determining which compounds ticks produce in their guts to protect themselves from vaccines, and how to overcome these protective mechanisms.

Developing and testing vaccines for ticks can be challenging due to regulatory requirements and safety concerns. It can be difficult to obtain regulatory approval for new vaccines, which can slow down the development process. How can this be improved?

Determining whether vaccinated animals rechallenged by natural exposure to the vector results in boosting the immune response. It seems immune animals don't develop a memory response against the BM86 hidden antigens – is that true for all tick antigens? It has been proposed that T cells maintain memory a long time while B cells are more short-lived and thus does the BM86 vaccine only induce a T-independent B cell response?

Why do *Bos indicus* (Zebu cattle) make more Abs to tick saliva proteins than taurine cattle?

Can haemolymph antigens of the vector be used as vaccine candidates which would require transcytosis of antibodies through the gut?

Solution Routes

What approaches could/should be taken to address the research question?

Tick genomes could provide valuable insights into potential vaccine targets and thus it is necessary to continue to collect these.

Determine which gut antigens are transcribed in various tick species through transcriptomic studies.

Identify and target salivary antigens and other potential "cryptic antigens" beside gut antigens.

Conduct long term trials to assess vaccine efficacy and duration of immunity.

Use artificial feeding to determine the role of various Abs to kill the tick as well as to see which tick antigens are secreted.

Dependencies

What else needs to be done before we can solve this need?

Vector saliva biochemistry: define the actual functions of molecules in saliva in a more systematic way using high throughput evaluation/screening of their functions particularly those affecting the host immune responses. Such knowledge also can feed into anti-vector drug discovery projects.

Determining in general how the vector modulates the host immune system potentially preventing the host from developing a protective immune response.

Need to know how many ticks an individual host can tolerate and still give a economically viable level of productivity and for the host to be considered to be in a state of well-being; that is, what level of reduction in infestation must a vaccine achieve for both of these aspects to be considered worthwhile.

State of the Art

Existing knowledge including successes and failures

There is a current commercial vaccine for *Rhicephalus (boophilus) microplus* using the BM86 antigen. Studies are underway to evaluate its ability to induce cross-protection to other tick species.

Vaccine trials that addressed the role of complement in immunity to tick-borne pathogens have shown contradictory results. One study published in the *Journal of Immunology* found that complement activation enhanced the immune response to tick-borne encephalitis virus, while another study in the *Journal of Virology* suggests that complement inhibition may be a useful strategy for improving vaccine efficacy against tick-borne diseases. These are apparently contradictory results that need to be clarified to determine their whether both are reproducible observations and if so, what is pathogen-specific reason for such differing outcomes.

It is known that if the vector targets are so-called "hidden antigens" then there is a need for frequent boosters.

RNA vaccination has been shown to induce tick resistance and pathogen transmission. (Sajid A, Matias J, Arora G, Kurokawa C, DePonte K, Tang X, Lynn G, Wu MJ, Pal U, Strank NO, Pardi N, Narasimhan S, Weissman D, Fikrig E. mRNA vaccination induces tick resistance and prevents transmission of the Lyme disease agent. Sci Transl Med. 2021 Nov 17;13(620) Epub 2021 Nov 17. PMID: 34788080.)

Ixodes scapularis saliva components that elicit responses associated with acquired tick-resistance (2020)

A Vaccinomics Approach for the Identification of Tick Protective Antigens for the control of Ixodes ricinus and Dermacentor reticulatus infestations in companion animals (2019)

New approaches and omics tools for mining of vaccine candidates against vector-borne diseases (2016)

Transcription factors as a target for Vaccination against ticks and mites (2017)

Phlebotomus papatasi exposure cross-protects mice against Leishmania major co-inoculated with Phlebotomus duboscqi salivary gland homogenate (2015)

DNA plasmid coding for Phlebotomus sergenti salivary protein PsSP9, a member of the SP15 family of proteins, protects against Leishmania tropica (2019)

Manning JE, Oliveira F, Coutinho-Abreu IV, Herbert S, Meneses C, Kamhawi S, Baus HA, Han A, Czajkowski L, Rosas LA, Cervantes-Medina A, Athota R, Reed S, Mateja A, Hunsberger S, James E, Pleguezuelos O, Stoloff G, Valenzuela JG, Memoli MJ. Safety and immunogenicity of a mosquito saliva peptide-based vaccine: a randomized, placebo-controlled, double-blind, phase 1 trial. Lancet. 2020 Jun 27;395(10242):1998-2007.

Maruyama SR, Garcia GR, Teixeira FR, Brandão LG, Anderson JM, Ribeiro JMC, Valenzuela JG, Horackova J, Veríssimo CJ, Katiki LM, Banin TM, Zangirolamo AF, Gardinassi LG, Ferreira BR, de Miranda-Santos IKF. Mining a differential sialotranscriptome of *Rhipicephalus microplus* guides antigen discovery to formulate a vaccine that reduces tick infestations. Parasite Vectors. 2017 Apr 26;10(1):206. Doi: 10.1186/s13071-017-2136-2

David Odongo: used infected blood as a vaccine – no heterologous strain protection to Heartwater.

Projects

What activities are planned or underway?

Lead Summary 2c: Host anti-vector treatment (excluding vaccines)

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To decrease vector challenge by treating the host with chemicals or biological agents (e.g., chemical poisons, chemical repellents, fungi).

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Anti-vector treatments need to be developed that are non-toxic to the animal host, the environment and to humans.

Acaracide resistance in vectors is a huge problem worldwide and the acaracides also are an environmental contaminant. There are a number of challenges in this arena:

1. Determine how can the residual effect be increased to minimise treatment frequency and thus development of resistance?
2. Determine whether it is possible to delay acaracide resistance by proper use.
3. Develop diagnostic tests to inform farmers regarding which acaracides that ticks in their area are susceptible to in order to prevent misuse and overuse of acaracides
4. Determine how frequency of use and dose of acaracides impact selection of acaracide resistant ticks
5. Understand the variety of modes of actions that acaracides could be developed to disrupt, thus having a greater variety to employ

Finding for alternatives to acaracides is a top priority – fungi could be a strong option for this

There are restrictions on use of insecticides for mosquito control – in urban areas in particular – determine how this affect vector challenge to livestock and poultry

Formulation is another important consideration when developing new tick control products since it can affect the efficacy, safety, and ease of use of the product. For example, topical formulations may be more effective at controlling ticks than oral formulations but may be more difficult to apply and the farmer has to weigh the cattle with pour-on. New pour-on acaricides have very long half-life in the blood; cattle lick themselves so intake that way. Oxazoline is a synthetic made in last 5 years that is given as a tablet to dogs or cats but resistance is developing. In dairy cattle it is secreted in milk so have a 42-day withdrawal time. In beef cattle it is used differently (greater quantity) because don't have milk. Registered in Brazil. Target Product Profile (TPP) important, e.g., pour on/spray preferred by farmers to injections.

Determining if systemic application (oral) is better than dipping/spraying and could this be employed without affecting the ability to market or consume food animal products? Advantage is that if use systematic treatment can eradicate ticks from pasture.

Laboratory conditions may not always reflect real-world conditions when it comes to acaricide resistance. It is important to conduct field studies to determine how well different products and strategies work in actual tick-infested environments but this is expensive.

Solution Routes

What approaches could/should be taken to address the research question?

Delivery methods to ease application and contribute to proper use of acaricides:

- For application of anti-vector drugs use of boluses for long treatment (like anthelmintic application is done) may be an option.
- Consider delivery methods for delayed release for anti-vector antibodies or for drugs such as by microneedle patches.
- The use of oral acaricides, similar to anthelminthics, has been proposed as a way to reduce the risk of resistance developing. This approach could be particularly useful for controlling ticks in wildlife populations where topical treatments may be difficult to apply.

Delaying acaricide resistance:

- One approach suggested is the use of combination therapies, which involve using multiple acaricides with different modes of action at once
- Another approach is to rotate the use of different acaricides to prevent ticks from developing resistance to any one product
- Anecdotally, resistance is thought to occur in about 10 years but controlled studies need to be done to evaluate effectiveness of the proposed alternative strategies

Still need to continue to identify unique vector biochemical pathways to target

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of insect physiology.
Mapping of where the various vector species are found.
Mapping of drug resistance in vectors.
Mapping of pathogens being carried by the vectors.

State of the Art

Existing knowledge including successes and failures

Oxazoline is a synthetic product that has shown promise in controlling ticks on livestock. It can be applied topically as a pour-on insecticide and has been shown to be effective against several species of ticks. However, further research is needed to determine long-term effectiveness of oxazoline and potential environmental impacts. Has a super long half-life.

University of Florida looking at potassium ion channels for novel drug target focusing on the AB422 protein for rapid engorgement.

Anthelminthic treatment knowledge: slow release

Preference for non-histamine blood so can attach to host

Cattle tick *R. (boophilus) microplus* in Brazil are resistant to 6 of the acaricides that includes all classes of acaricides. 75% of ticks in Brazil are resistant to 3 to 5 compounds. Doing sequencing to find SNPs associated with resistance.

The “larval packet test” is the gold standard for testing for acaricide resistance.

Projects

What activities are planned or underway?

University of Florida taking a chemical approach rather than a vaccinology approach and are focusing on the potassium ion channel AB422 protein for rapid engorgement as a drug target.

Lead Summary 3: Vector Feeding

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Gain a fuller understanding of vector feeding

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Determining possible changes in components of vector saliva during feeding on the host

Determining if there are differences in the saliva of male and female ticks

Determining whether artificially collected saliva fully reflects what is secreted during vector feeding

Determining whether infected vectors feed more than uninfected vectors

Determining if pathogens acquired with blood meals kill vector if the vector immune system such as the TLRs are inactivated?

Solution Routes

What approaches could/should be taken to address the research question?

Establish the constituents of vector saliva and how they aid feeding and influence pathogen uptake or survival in the vector

Improve understanding of the inflammatory response at vector feeding sites and how this affects uptake of blood meal

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of vector physiology

State of the Art

Existing knowledge including successes and failures

At Washington State University they have established a very effective artificial feeding system for colony-maintained vectors and experimentation of drugs, chemicals and antibody effects on ticks

Projects

What activities are planned or underway?

Lead Summary 4: Host Range

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Define the hosts of the various vector species that transmit livestock and poultry pathogens.

Establish the host ranges of particular vectors including when and where the vectors are opportunistically feeding in order to survive in the absence of livestock or poultry hosts

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Field sampling in areas where the pathogens are known to be present is required to find opportunistic hosts and to then accurately identify the range of vector species

Determining whether host range varies with life-cycle stage of vectors

Modelling how climate change will influence the vector range since the hosts are expected to have larger and/or different ranges in response to climate change (rain, heat, humidity)

Determining which chemical molecules emitted by hosts are responsible for vector attractivity and how we can use this knowledge to reduce vector populations by the push-pull strategy of control

Determining the molecular basis for host preferences

Determining whether the emission of attractants differs by breeds of livestock

Solution Routes

What approaches could/should be taken to address the research question?

Field collection to determine range and analysis of gut contents to determine host species (both preferred and opportunistic)

Development of more effective traps for mosquitoes and tsetse flies, taking into account their chemical ecology and host preferences both to control the vectors and for sampling them

Dependencies

What else needs to be done before we can solve this need?

Determine their chemical ecology

State of the Art

Existing knowledge including successes and failures

Some work on tsetse fly attractants and repellents is being done to implement a push-pull strategy of control (i.e., repel from the hosts and attract to the traps)

Projects

What activities are planned or underway?

Yale University and KALRO in Kenya have a large program for this with regard to tsetse flies.

Lead Summary 5: Vector Immunomodulation of the Host

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To decrease pathogen transmission by reducing the vector's down or up-modulation of the host immune reaction

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Elucidate mechanisms of host immunomodulation by vectors to determine how the vector is reducing protective host immune responses

Identify immunosuppressive components in vector saliva and thus their role in transmission of pathogens

Further research is needed to develop new vaccines or treatments that target the specific mechanisms by which mosquito saliva enhances disease transmission. (Is this by immunosuppressants in the saliva or is it other factors such as anti-coagulants?)

Identify the specific components in mosquito saliva that attract dendritic cells and how this attraction contributes to immune responses

Determine what are the interactions between host compounds and vector saliva and how this affects immunosuppression

Determine the difference in feeding regularity and other behaviours of infected vs. noninfected vectors. E.g., infected sandflies regurgitate gut contents and spread infection

Determine which vector factors are facilitating pathogen transmission and how they relate to those causing immunosuppression

Increase our understanding of the effects of mosquito feeding on immune responses in flavivirus-resistant mice: while mosquito feeding has been shown to modulate cytokines in flavivirus-susceptible mice, it is not clear whether this effect is also present in flavivirus-resistant mice. Further research is needed to determine how mosquito feeding impacts immune responses in different mouse strains and how this may relate to disease susceptibility in humans and livestock and poultry

Solution Routes

What approaches could/should be taken to address the research question?

Collection of saliva by artificial membrane feeding of vectors

Biochemical analysis, identification and isolation of components (proteins, fatty acids and others) in vector saliva

In vitro studies with leukocytes to determine the immunomodulatory effects of total saliva or isolated compounds from the saliva

Study of innate and acquired immune responses of the host with or without vector infestation to understand whether or what kind of immunomodulation is induced by the vector

Comparative studies of histology of skin biopsies of vector and non-vector infested host

Vaccination of the host against vector factors aiding pathogen transmission or reducing host immune responses

Dependencies

What else needs to be done before we can solve this need?

Knowledge of the role of vector salivary factors in pathogen transmission is needed.

The inoculation volume required for transmission of vector-borne disease or immunomodulation of the host is not well understood. Further research is needed to determine the minimum volume

required for transmission or immunomodulation as well as the factors that influence inoculation volume.

State of the Art

Existing knowledge including successes and failures

It is known that *Aedes aegypti* saliva alters leukocyte recruitment and cytokine signalling during West Nile virus infection, but our understanding of the specific mechanisms behind this effect is still limited. Further research is needed to identify the specific components in mosquito saliva that contribute to these changes and how they impact disease outcomes.

Immunosuppressive effects of sialostatin L1 and L2 isolated from the taiga tick Ixodes persulcatus are known (Schulze (2020))

So, we know quite a lot about mosquito saliva that has about 100 components - mainly proteins (compared with 300 in tick saliva). Of the 100 mosquito components, we know the roles of a few, including their immunomodulatory activity (e.g., Sialokinin). In simple terms the inoculation of very small volumes of mosquito saliva into the feeding site can have profound effects, some even lasting for days after feeding. Dendritic cells attracted to the feeding site, are often the initial target cell to establish viral infection. This means that virus delivered by a mosquito establishes an infection more efficiently than if delivered by needle. We have immunosuppressive effects of saliva, for example down regulation of Interferon. if delivered with saliva, the virus can establish more efficiently, spread more efficiently with elevated titers and potentially more severe disease symptoms (all compared with needle inoculation).

Edwards, J.F., Higgs, S. & Beaty, B.J. (1998). Mosquito feeding-induced potentiation of Cache Valley Virus (Bunyaviridae) in mice. J. Med. Entomol. 35: 261-265.

Zeidner, N.S., Higgs, S., Happ, C.M., Beaty, B.J. & Miller, B.R. (1999). Mosquito feeding modulates Th1 and Th2 cytokines in flavivirus susceptible mice: an effect mimicked by injection of sialokinins, but not demonstrated in flavivirus resistant mice. Parasite Immunol. 21: 35-44.

Limesand, K.H., Higgs, S., Pearson, L.D., & Beaty, B.J. (2000). Potentiation of vesicular stomatitis New Jersey virus infection in mice by mosquito saliva. Parasite Immunol. 22: 461-467.

Limesand, K.H., Higgs, S., Pearson, L.D. & Beaty, B.J. (2003). The effect of mosquito salivary gland treatment on vesicular stomatitis New Jersey virus replication and interferon α/β expression in vitro. J. Med. Entomol. 40: 199-205.

Wanasen, N., Nussenzveig, R.H., Champagne, D.E., Soong, L. & Higgs, S. (2004). Differential modulation of murine host immune response by salivary gland extracts from the mosquitoes Aedes aegypti and Culex quinquefasciatus Med. Vet. Entomol. 2004. 18: 191-199.

Schneider, BS., L Soong, NS Zeidner, & Higgs, S. (2004). Aedes aegypti Salivary gland extracts modulate anti-viral and TH1/TH2 cytokine responses to Sindbis virus infection. Vir. Immunol. 17: 565-573.

Schneider, B.S., Soong, L., Girard, Y.A., Campbell, G., Mason, P. & Higgs, S. (2006). Potentiation of West Nile Encephalitis by mosquito feeding. Viral Immunology. 19: 74-82.

Schneider, B.S., McGee, C.E., Jordan, J.M., Stevenson, H.L., Soong, L. & Higgs, S. (2007). Prior exposure to uninfected mosquitoes enhances mortality in naturally-transmitted West Nile virus infection. PLoS ONE 2(11): e1171

Schneider, B.S. & Higgs, S. (2008). The enhancement of arbovirus transmission and disease by mosquito saliva is associated with modulation of the host immune response. Trans. Roy. Soc. Trop. Med. Hyg. 102: 400-408.

Schneider, B.S., Soong, L., Coffey, L.A., Stevenson, H.L. & Higgs, S. (2010). Aedes aegypti saliva alters leukocyte recruitment and cytokine signaling by antigen-presenting cells during West Nile virus infection. PloSONE 5: e11704.

Thangamani, S., Higgs, S., Ziegler, S., Vanlandingham, D., Tesh, R. & Wikel, S. (2010). Host immune response to mosquito-transmitted chikungunya virus differs from that elicited by needle inoculated virus. PloSOne. 5:e12137.

Projects

What activities are planned or underway?

Lead Summary 6: Pathogen Control inside the vector

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To decrease pathogen load in vectors by increasing vector resistance to pathogen infestation

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Determine vector physiological and immunological pathways that decrease pathogen replication in the vector

Co-evolution/symbiotic evolution makes it difficult to disrupt and boost immune response of ticks to pathogens that parasitize the vector, it might be easier to control the vector than it is to control the pathogens within it

Investigating the symbiotic relationship between ticks and their hosts could provide insights into new strategies for tick control. For example, understanding how ticks acquire and transmit pathogens could lead to new approaches for interrupting the transmission cycle.

Need to consider cost-effectiveness and applicability in field by considering delivery and technologies (e.g., micro capsules)

Determine how to stimulate tick innate immunity: can RNAi be used for mosquito larvae, how can we deliver such a stimulus for ticks (spray and micro capsules) – pharmaceuticals

There is limited understanding of the feasibility of using RNA for tick control? How can it be delivered as a commercial product? Need for more effective methods for delivering RNA technology. While there have been studies on delivering RNA technology to cattle via microcapsules or pharmacological formulations, there is still a need for more effective methods. Further research is needed to identify new delivery methods that can be used commercially and improve treatment outcomes.

There is a need for more research on pathogen competence and symbiosis in insect vectors: While there have been studies on competition between bacteria in flies and symbiosis within tsetse flies, there is still a need for more research on these topics. Further research is needed to better understand how different pathogens interact with each other and with their insect hosts.

Transgenesis has been used to modify both mosquitoes and bacteria, however our understanding of the impact of these modifications on vector capacity is still limited. Further research is needed to determine how transgenesis can be used to reduce disease transmission by insect vectors.

Is it feasible to use application of plasmids for tick control in the field?

Bacterial and viral microbiota/infection can alter the pathogen transmission of the vector

Solution Routes

What approaches could/should be taken to address the research question?

Genetically modify vectors to prevent pathogen replication and/or transmission

Analyse natural differences in pathogen concentrations between vector populations (species): it might be that certain vector phenotypes or genotypes are more able to control the pathogen within them

Increase our understanding of innate and acquired resistance of insect vectors: e.g., while it is known that female tsetse flies can develop resistance to viruses and Spiroplasma, our understanding of the mechanisms behind this resistance is still limited. Further research is

needed to identify the factors that contribute to innate and acquired resistance in insect vectors and how this resistance may impact disease transmission.

Dependencies

What else needs to be done before we can solve this need?

Improved our understanding of the vector pathogen interaction including the pathogen cost to the vector

State of the Art

Existing knowledge including successes and failures

Induce systemic tick immunity through gene editing – not practical/feasible

Jasinskas A, Barbour AG (2005). The Fc Fragment Mediates the Uptake of Immunoglobulin G from the Midgut to Hemolymph in the Ixodid Tick Amblyomma americanum (Acari: Ixodidae). Journal of Medical Entomology, Volume 42, Issue 3, 1 May 2005, Pages 359–366,

Zhong J, Jasinskas A, Barbour AG (2007). Antibiotic treatment of the tick vector Amblyomma americanum reduced reproductive fitness. PLoS One 2: e405

Shi et al. 2022 Bidirectional interactions between Arbovirusses and the bacterial and viral microbiota in Aedes aegypti and Culex quinquefqsciatus. mBIO13, 5

Hobson-Peters et al. 2013 A new insect-specific flavivirus from northern Australia suppresses replication of West Nile Virus and Murray Valley Encephalitis Virus in Co-infectde mosquito cells. PLOSone 2013, 8,2 e56534

Hall-Mendelin et al. 2016 The insect-specific Palm Creek virus modulates West Nile virus infection in and transmission by Australian mosquitoes. Parasites and Vectors 9, 414.

Schutz et al 2018 Dual insect specific virus infection limits Arbovirus replication in Aedes mosquito cells. Virology 518, 406-413.

Projects

What activities are planned or underway?

Lead Summary 7: Vector Competence

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To establish which vector species are capable of transmitting any particular pathogen and the necessary conditions for cyclical transmission

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Determine if there are variations in time and temperature requirements where cyclical transmission occurs

Need to identify differences in competence between vector species/strains, recognising there are wider variation between both different species and different populations of the same species with respect to susceptibility to infection and transmission.

Need to identify vector factors that define pathogen acceptance and proliferation. E.g., determine why some species of mosquito are susceptible to a particular virus and others are not. That is, define the molecular determinants of vector infection. Need a system biology approach (understanding the molecular, cellular and physiological interactions between vector and pathogen)

Increase our knowledge about host co-infections and their impact on tick-borne diseases. Ticks are known to transmit multiple pathogens, but our understanding of how co-infection impacts disease transmission and host immune responses is still limited. Further research is needed to identify the specific mechanisms behind co-infection and develop more effective treatments for these diseases.

Have knowledge gaps about the vector midgut microbiome: While it is known that the tick midgut is relatively empty compared to the ovaries in terms of microbiome composition, our understanding of the role of this microbiome in tick biology and disease transmission is still limited. Further research is needed to identify the specific functions of the tick midgut microbiome and how it interacts with host cells. Where is the microbiome present/identify real microbiota in ticks and mosquitos (ovaries) – could be strategy for poultry mites, vector control and transmission control in general

Determine why infected ticks live for shorter periods than non-infected ticks but still feed normally, including considering immune upregulation and energy expenditure

Bacterial and viral microbiota/infection can alter the pathogen transmission of the vector

Solution Routes

What approaches could/should be taken to address the research question?

Has feeding on uninfected blood an influence on infected ticks? Feeding on infected animals followed by “clean” animals. Artificial feeding on “spiked” blood followed by feeding on clean animals.

Identification of receptors for pathogen entry into vector cells or body compartments

The Ig binding protein in ticks is another area of research that could provide new insights into tick biology and control. This protein is involved in the tick's immune response and could be a potential target for vaccines or other control measures.

Dependencies

What else needs to be done before we can solve this need?

Determine how the host-vector interaction affects transmission so that this effect can be negated when trying to elucidate the vector-

pathogen interaction including pathogen survival in the vector and successful transmission to the host

State of the Art

Existing knowledge including successes and failures

This includes discussion of Wolbachia and transgenic approaches.

Higgs, S. (2013). Alternative approaches to control dengue and chikungunya: transgenic mosquitoes. Public Health. 24: 35-42.

Shi et al. 2022 Bidirectional interactions between Arbovirusses and the bacterial and viral microbiota in Aedes aegypti and Culex quinquefqsciatus. mBIO13, 5.

Hobson-Peters et al. 2013 A new insect-specific flavivirus from northern Australia suppresses replication of West Nile Virus and Murray Valley Encephalitis Virus in Co-infected mosquito cells. PLOSone 2013, 8,2 e56534

Hall-Mendelin et al. 2016 The insect-specific Palm Creek virus modulates West Nile virus infection in and transmission by Australian mosquitoes. Parasites and Vectors 9, 414.

Schutz et al 2018 Dual insect specific virus infection limits Arbovirus replication in Aedes mosquito cells. Virology 518, 406-413.

Projects

What activities are planned or underway?

Lead Summary 8: Vector-pathogen infestation

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To identify which arthropods are the vectors and which samples are optimal for confirming infection in an arthropod vector

To identify animal pathogens in carrier vector

To control pathogen replication and/or transmission through elucidation and understanding vector physiology/immunology

To define vector species and establish the feeding and environmental conditions necessary for survival and long-term maintenance of particular vectors

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Molecular based diagnostics for tick resistance to pathogens – test needs to be rapid, field appropriate – lots of associated challenges; molecular understanding of tick resistance to pathogen

Determine whether and which bacteria trigger the immune system of vector

Gain understanding of vector innate and acquired immune responses.

Determine which physiological and immunological processes can influence the presence/replication of the pathogen, microbiome, etc.

Population genomics: resistance, vector competence, infested/infected

Mosquitos have an ability to encapsulate parasites. They have components of an immune system that experimentally can influence virus infection

Collection of pathogen-infested vectors and their breeding

Solution Routes

What approaches could/should be taken to address the research question?

NGS on various vector samples to determine the pathogens they carry

The microbiota of ticks is another area of research that could provide new insights into tick biology and control. Understanding how the microbiota interacts with the tick's immune system and affects its ability to transmit pathogens could lead to new approaches for controlling tick-borne diseases.

What are the mechanism of losing the immunity after acquiring it from infection with babesia or malaria?

Sterile male technique (Lead 4a)

Female uninfected can only mate with uninfected males (Tsetse) (Lead 4a)

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of pathogen replication and transfer between compartments in the vector.

Techniques to study physiology and immunology of vectors

State of the Art

Existing knowledge including successes and failures

Molecular detection of tick-borne pathogens in bovine blood and ticks from Khentii, Mongolia (2019)

Microbial control of arthropod-borne disease (2017)

Engineered symbionts activate honeybee immunity and limit pathogens (2020)

Mosquito transgenics – Denge virus when infected chain response to kill mosquito – Uni Sao Paulo

Van den Hurk, A.F., Hall-Mendelin, S., Pyke, A.T., Frentiu, F.D., McElroy, K., Day, A., Higgs, S. & O'Neill, S.L. (2012). Impact of Wolbachia on infection with chikungunya and yellow fever viruses in the mosquito vector Aedes aegypti. PloS Neglected Tropical Diseases 6(11): e1892.

Vector potential and population dynamics for *Ambylomma inornatum* (2015)

Liu WL, Hsu CW, Chan SP, Yen PS, Su MP, Li JC, Li HH, Cheng L, Tang CK, Ko SH, Tsai HK, Tsai ZT, Akbari OS, Failloux AB, Chen CH. Transgenic refractory Aedes aegypti lines are resistant to multiple serotypes of dengue virus. Sci Rep. 2021 Dec 13;11(1):23865.

Yen PS, James A, Li JC, Chen CH, Failloux AB. Synthetic miRNAs induce dual arboviral-resistance phenotypes in the vector mosquito Aedes aegypti. Commun Biol. 2018 Feb 8;1:11.

Projects

What activities are planned or underway?

Lead Summary 9: Vector sampling and species identification

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Determine the best methods to sample the vectors of concern

Develop methods for rapid and accurate identification of vector species

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Develop new ways for data mining population size and density (population genomics could include resistance, competence, presence of pathogens). There is a need for measuring effective population size and genetic diversity.

Mosquito attractiveness to the host; to develop more attractive traps, light traps…

Evaluate vector load on vertebrate host via host blood analysis for anti-vector antibodies

Vector migration/invasion: how do certain vectors displace other vectors from a area/region

What is best method to sample? Enormous variation within seasons and localities.

Solution Routes

What approaches could/should be taken to address the research question?

Variation in seasons – cyclical

Population genetic tools need to be developed so that we have a more stable measure for determining the size of the population and to monitor it– looking at genetic diversity for high level cycles in population

Dragging is a commonly used method for sampling ticks, but it can be time-consuming and may not capture all stages of the tick life and there is a need to exploring alternative methods such as bait boxes and host-seeking traps that can be more effective in capturing ticks at different stages of their life cycle.

Identification of molecular markers (i.e., SNPS) for resistance to acaricides, etc.

Dependencies

What else needs to be done before we can solve this need?

Vector whole genome sequences

Environmental DNA sampling

State of the Art

Existing knowledge including successes and failures

Field sampling methods for mosquitoes, sandflies, biting midges and ticks

VectorNet project 2014-2018 (2018)

There has been studies in Kenya that looked at attractants for mosquitos – it is know that they like to bite faces and feet. Chemicals have been characterized and synthesized and added to cloth traps and it gave a reduction in vector density

Projects

What activities are planned or underway?

Lead Summary 10: Vector population control

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Decrease vector prevalence and consequently vector challenge of the host

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Targeting the specific vector without environmental impact on other arthropod populations

Sterilization, predation, and reduction through vector pathogens

Development of treatment regimens to decrease development of resistance to chemical controls

Developing cost-effective products or methods to reduce vector challenge. Cost effectiveness is an important consideration when developing new tick control measures. Products that are too expensive or difficult to apply may not be practical for use in the field, particularly in developing countries where tick-borne diseases are a major public health concern.

Effective tick control requires a long-term approach that takes into account changes in tick populations over time. Policy strategies should be developed that are sustainable and adaptable to changing conditions. For example, promote the use of integrated pest management strategies and encourage the development of new tick control technologies.

Determine if species displacement is because they are more aggressive species and how does that change disease transmission.

Maintenance of vector colonies for basic and applied research including supplying materials for genetic control and sterilization studies, and to study their competence for pathogen transmission.

Artificial feeding systems are needed for the studies described here although transcriptomics between artificial and natural-fed vectors needs to be done also to validate the use of such a system.

Solution Routes

What approaches could/should be taken to address the research question?

In vivo trials involving:

a) Chemical controls;
b) Vector predation as a method of control;
c) Vector pathogens including viruses, bacteria and fungi as control methods

Maintenance of colonies of vector species and artificial feeding systems

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of vector physiology

Validation of artificial feeding systems

State of the Art

Existing knowledge including successes and failures

Washington State University has a program of artificial feeding of ticks

Projects

What activities are planned or underway?

Lead Summary 10a: Genetic control and sterilization

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To decrease vector populations through genetic modification and/or by disrupting breeding

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Determine fitness of sterilized arthropods

Determine fitness of genetically modified vectors

While gene drive systems have been used to spread genes through mosquito populations, there is still a need for more effective systems. Further research is needed to identify new gene drive systems that can be used safely and effectively in mosquito populations.

Upregulate the mosquito anti-viral responses (i.e., genetically engineered mosquitoes) to prevent virus infestation because upregulating these genes may influence other genes and physiological process that makes the mosquito less fit.

At the stage of releasing engineered mosquitoes in the hope of reducing malaria. Success will depend on many things but compared with ticks, mosquitoes, although short-lived, have a high reproductive rate and disperse widely. Can a similar approach be taken for other vector species? Gene editing to create sterile male ticks could help reduce tick populations, could large scale rearing be achieved. This involves using CRISPR/Cas9 or other gene editing technologies to modify the genes responsible for tick reproduction, making it more difficult for them to reproduce.

There is a need for more effective strategies for monitoring and evaluating genetically engineered mosquito releases

There is a need for more research on public attitudes towards genetically engineered mosquitoes

Solution Routes

What approaches could/should be taken to address the research question?

Male sterilization through genetic modification

Radiation

Chemical treatments

Sterile male competitive technique – sterile male mates slower?

Female reproduction reduction (using RNAi)

Wolbachia control approaches.

Insect specific viruses

Dependencies

What else needs to be done before we can solve this need?

Vector genome sequences need to be available

State of the Art

Existing knowledge including successes and failures

Molecular and functional characterization of Bm05br antigen from *Rhipicephalus microplus* (2015)

Radiation of vectors (*Glossina*) for sterilization and release into the wild

Projects

What activities are planned or underway?

Lead Summary 10b: Vector pathogens and predation

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Control of vectors through their natural pathogens

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Identification of vector viruses, bacteria, fungi, protozoa, helminths that reduce viability of survival of the vector (E.g., test how agriculture fungi could be used in ticks/other vectors) but don't also target useful species

Determine the natural variation from ticks in response to entomopathogenic exposure

Regulatory issues (legislation and regulation) for delivering entomopathogens for cattle need to be considered

Research into human inhalation of fungus when using enviro-spray

Determine whether there could be variation in effect of entomopathogenic fungi on tick colonies (lab bred) compared to wild tick populations – thicker exoskeleton

Formulation needed to maintain the shelf life to keep entomopathogenic spores viable for travel and to be UV tolerant and thermostable.

Gain an understanding of the impact of these control methods on different lifecycle stages of the vectors

Determine how to mass rear parasitoids of ticks

Solution Routes

What approaches could/should be taken to address the research question?

Release entomopathogenic fungi including field trials to spray on cattle in farm and/or environmentally sprayed as well. Strains of fungi more selective to target ticks than other arthropods could reduce unplanned impact.

Test vector specific viruses

Bacterial – immerse ticks (Lora Mendez, Manuel Fernandez 2010)

After establishing the natural predators of the vector need predator production and release of the predators of the vector. For example, parasitoids of ticks can be very specific and eat tick larvae

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of vector ecology

State of the Art

Existing knowledge including successes and failures

Paul Allen School at Washington State University has a great program on artificial feeding of ticks

Fiorotti J. and Isabelle Santos (Sao Paulo):

- Used fungi to control ticks but problem is host (I.e., tick) immunity to them is generated.
- Are making fungi that are ROS resistant. Showed had more catalase and SOD and PR1 (enter cuticle of tick) activity.
- Vaccinated animals with 13 antigens and integrated these fungi with vaccinated animals and found it reduced tick infestation.
- Some Ags are part of the tick immune system

Projects *What activities are planned or underway?*

Lead Summary 11: Vector genetics

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Increase knowledge of vector genetics for:

- species identification of vectors
- designing genetic control methods of vectors
- identify vaccine targets
- to control pathogen replication in and/or transmission from the vector

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Sequence, assemble and annotate vector genomes

Edit genes to reverse resistance to chemical controls and make the vector susceptible again

Find mutations inducing resistance in ticks for host pathogens.

Compare gene homologues and expression levels among species of ticks for those gene products that could serve as vaccine antigens

Lack of knowledge about the impact of environmental factors on gene spread: While gene drive systems have been used successfully in laboratory settings, it is not clear how they will behave in natural environments. Further research is needed to determine how environmental factors like temperature, humidity, and host behaviour may impact gene spread in mosquito populations.

Solution Routes

What approaches could/should be taken to address the research question?

Generate enough genomes of vectors that carry pathogens of concern that they can be compared.

Identification of SNPs or other polymorphisms that convey resistance to chemical controls

Dependencies

What else needs to be done before we can solve this need?

Our understanding of tick biology is still limited, which makes it difficult to identify suitable vaccine targets. There is a need for more research on tick physiology, genetics, and immunology to identify potential vaccine targets.

State of the Art

Existing knowledge including successes and failures

Look at already elucidated genomes of other arthropods

Genetically modified tick (CRISPR-CAS) gene that affects length of hypostome – allowing monitoring

Complete tick genomes for several species that are well annotated

Projects

What activities are planned or underway?

Lead Summary 12: Vector biotope control

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

To decrease vector challenge through control in the environment

To evaluate the impact of climate change on the tick-host-biotope interface and possible interventions to mitigate eventual new problems brought about by climate change

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Need to establish vector niches to target Environmental toxicity

Define the different vector host: competition who are the vectors feeding on outside the domestic animals; wild versus domestic (buffalo-cattle; bats-cattle)

Need to understand competition – could influence spread of different species – leading to displacement, outcompeting, faster breeding (important in relation to climate change).

Need to understand hybridisation – could be difference in level of transmission/specificity to pathogen

Socio-economic studies to understand farmers perceptions of vector-borne diseases and preference of control methods – link to acaricide choices, farm management strategies

Hybridization between different species of ticks can lead to the emergence of new tick-borne diseases or the spread of existing diseases to new areas. It is important to monitor for hybridization events and to study the genetic makeup of tick populations in order to better understand their potential for disease transmission. Researchers are currently using molecular techniques such as DNA sequencing to identify hybridization events and track the spread of tick-borne diseases.

Changing husbandry systems could also be a way to reduce the risk of tick infestations in livestock. For example, keeping cattle indoors or using local breeds that are better adapted to the local environment could help reduce exposure to ticks. Harvesting grass by machine could also help reduce the risk of ticks by reducing the amount of vegetation available for ticks to live on; rotational grass management/rotational grazing

Need to understand the role of climate change on ectotherm ticks and their biology (number of generations/year, host preferences, etc.)

Need to understand the role of pastures, agrosilvopastoral systems (that produce the shade that vectors prefer, as do their entomopathogens, but reduce host heat stress), fires and flooding on persistence of vectors in biotope

Need to understand the role of vector-borne pathogens on resistance of ticks to desiccation and the role of climate on the vectorial capacity of vectors

Need to understand the role of species of pasture on persistence of ticks in environment and if species that have a negative impact on tick biology (e.g., molasses grass, *Melinis minutiflora*) can be bred for desirable agronomical traits without losing their negative impact on tick biology

Need to understand the role of heat stress on the host's immunity and on its responses to vectors and what are the interventions to mitigate negative impacts.

Animal movement big factor of tick resistance spreading.

While mosquito feeding is known to play a role in disease transmission, our understanding of the impact of environmental factors like temperature, humidity, and host behaviour on this process is still

limited. Further research is needed to identify the environmental factors that contribute to disease transmission and how they may be mitigated.

How environmental factors may impact microbiome composition. Research is needed to determine how environmental factors like temperature, humidity, and host behaviour may impact tick microbiomes.

There is a need for a dedicated Vector Control Agency that focuses on developing and implementing strategies for controlling ticks and other disease-carrying vectors. This agency could work with local communities, government agencies, and other stakeholders to develop integrated pest management strategies that incorporate both chemical and non-chemical control methods. The agency could also conduct research on new control methods and technologies.

Solution Routes

What approaches could/should be taken to address the research question?

Use of vector attractants and anti-vector chemicals

Pasture management and/or agro-silvo-pastoral systems

Push-pull mechanism (into traps) – doesn't address repopulation, long term control

Brugger K, Rubel F. Tick maps on the virtual globe: First results using the example of Dermacentor reticulatus. Ticks Tick Borne Dis. 2023 Mar;14(2):102102.

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of environmental needs of the vector and the impact of climate changes in host physiology and how changes in host physiology will relate to vector biology

Renew atlas of vector subspecies – project on this for Tsetse -could participatory science be used to help understand spread of different species

Environmental control needs to be coordinated otherwise new population will fill gap

VectorNet mapping for vector diseases (ticks, mosquitoes), in Europe and neighbouring countries (when funding available from EFSA) – maps available on website - also support capacity building in blank spots to collect samples (e.g. Syria, Iceland)

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

FAPESP (São Paulo, Brazil) has been addressing the impact of pastures on climate change and biodiversity

Lead Summary 13: Socio-economic & environmental aspects of vector control

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Can biotope control of the vector have environmental and socio-economic impact

What are the side effects of biotope control on the environment and human society

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Solution Routes

What approaches could/should be taken to address the research question?

Consultations could be carried out with public health socio-economists regarding vectors of great impact on animal and human health to understand the social economic impact and side effects of biotope or vector control.

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Projects

What activities are planned or underway?

Lead Summary 14: Farm management

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

Control of vector population through hygiene measures

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Environmental cost and benefits of this approach
Influence of grassland management (species, rotation) on transmission
Develop grass that resist ticks in Brazil
Rotation of fields, change grass species, cut the grass, zero-grazing. Rotation impact on tick population – reduce height of grass, can expose larva to UV sunlight and reduce tick population that way (depending on life cycle of tick and grazing intervals – calculations)
Production systems could be preferred by certain vector species
Husbandry approach changes risk of exposure, zero grazing vs open field grazing
Sustainable integrated management approach to controlling vectors that recognises production system used in that area/region
Understanding what kind of solutions can be applied to the different production systems -need socio-economic approach
Understand economic loss in productivity – to encourage uptake of control strategies/vaccines (WOAH looking at economic impact of various diseases) – consider if cheap for farmer but environmental loss for community – local/regional information
Selective breeding for grasses that are good for tick controls (molasses grass – good for tick control but farmers don't like to burn) – need to consider impact on natural grasslands farmers do not like it because it does not resist fire and tramping by cattle; it is invasive in South America.
To reduce contact between livestock and tick populations there is a need to develop husbandry models that promote practices such as indoor housing, zero grazing, and pasture rotation to reduce tick exposure. These models should be tailored to the specific needs of different animal species and environments.

Solution Routes

What approaches could/should be taken to address the research question?

Control of vector breeding sites – control of stagnant water (insects), dry vegetation (ticks)
Control of hibernation sites
Control/timing of grass cutting/habitat changes
Rotational use of grazing land/fields - habitat grazing

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of vector ecology

State of the Art

Existing knowledge including successes and failures

Making vector-borne disease surveillance work: new opportunities from the SDG perspectives (2019)

Projects

What activities are planned or underway?

Lead Summary 15 Urban development

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

How can urban development interfere with the vector population and pathogen transmission

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Analysis of socio-economical preparedness: farmer versus community

Solution Routes

What approaches could/should be taken to address the research question?

Dependencies

What else needs to be done before we can solve this need?

State of the Art

Existing knowledge including successes and failures

Labruna MB: human-modified landscapes

changes in behaviour of capybaras: in the night foraging in urban paddocks, during the day in the forest where there are no predators anymore but a lot of ticks. In the their natural environment not in the forest and thus less ticks on capybaras: rhus in human modified landscape more infested ticks in human area.

Projects

What activities are planned or underway?

Lead Summary 16: Environment, climate and predictive modelling

Research Question

What are we trying to achieve and why? What is the problem we are trying to solve?

How can we interact with the biotope to reduce vector population or disease transmission

Define the natural vector biotope or eco-environment

Do climate-changes alter the distribution of the vector population

To identify the potential range of particular vectors and their associated pathogen based on environmental parameters.

To predict possible spread of particular vectors and their associated pathogen based on climatic conditions

Impact of climate change on permissiveness of vectors, for example culicoides gut leakiness associated with higher temperatures leading to BTV transmission in 'non-permissive' species

Challenge(s)

What are the scientific and technological challenges (knowledge gaps needing to be addressed)?

Understanding the vector biotope to help in predictive modelling for determining parameters to control vector populations on the farm or environment

Changes to vector biotope through habitat/environmental changes (due to climate change, land development) predictive modelling

Economic impact of vectors

Socio economics - understanding which production systems will work: animal husbandry – zero grazing; rotational land use – used in Africa – farmers don't like it in Brazil; rice field then cattle grazing. Integrated management.

Develop new ways of data mining to describe populations genetics and distributions.

Mapping of climate change and change in land use (habitat).

Field sampling of vector in different geographical locations under influence of climate change

Field sampling at different seasonal periods for cyclical

Modelling of climate change and associated environmental/habitat/land-use changes and impact on host/vector changes – destroy habitat/preserve habitat

Also link to preserving/protecting landscape for conservation or changes in land use

Modelling based on level of antigens/antibodies in milk (when is the largest infestation of cattle with ticks) – help overcoming only identifying ticks when engorged, proxy for tick numbers

Understanding the ecological drivers of tick populations in different environments can help researchers predict how they may respond to climate change.

Algorithms that can predict based on temperature, time of year etc, when tick population rise (peak tick season) to id better time interventions – could also include any resistance

Accurate data on the environmental conditions needed for the survival and maintenance of a particular vector

When tick/vector season going to occur, could predict when most effective to begin control methods (i.e. more effective during low density than when high density, allow small exposure for natural immunity before control methods)

Ecological analysis and predictive modelling can be used to better understand the distribution and abundance of tick populations. This information can be used to predict when the tick season will start and to develop more effective tick treatment strategies. By analyzing environmental factors such as temperature, humidity, and

vegetation, researchers can gain insights into the ecological drivers of tick populations. Predictive models can then be developed to forecast tick abundance and distribution based on these environmental factors.

Tick mapping is an important tool for understanding the distribution and abundance of ticks in different regions. In Africa, there is a need for more comprehensive tick mapping efforts in order to better understand the risk of tick-borne diseases in different areas. These efforts could involve field surveys, remote sensing techniques, and citizen science initiatives. By mapping tick populations, researchers can identify areas where disease risk is highest and develop targeted interventions to reduce this risk.

Solution Routes

What approaches could/should be taken to address the research question?

Review of literature on changes in the distribution of the vector

Satellite imagery supported by field studies

Dependencies

What else needs to be done before we can solve this need?

Improved understanding of vector ecology

State of the Art

Existing knowledge including successes and failures

Clinglobal Mapping Project (BMGF funded)

- Ecto- and endoparasite frequency and economic impact
- Sampled 7000 cattle from 7 countries in Central and East Africa
- Has 2 publications on ticks and pathogen infections and follow on work around cattle genetics for susceptibility

KENTTEC is a model of control but needs lots of labour. If do long-term may be able to need fewer people as go along. Not research money – more government decision to support. In Europe have 6 people/vector and take literature data and put in a database and map all the vectors. Do capacity building.

GIS modelling – Robert Miller, USDA project using location tracking to trigger surveillance systems and cascade of actions (including lab to carry out testing) and map resistant populations

Probst J, Springer A, Topp AK, Bröker M, Williams H, Dautel H, Kahl O, Strube C. Winter activity of questing ticks (Ixodes ricinus and Dermacentor reticulatus) in Germany - Evidence from quasi-natural tick plots, field studies and a tick submission study. Ticks Tick Borne Dis. 2023 Nov;14(6):102225.

*Baylis, M. Potential impact of climate change on emerging vector-borne and other infections in the UK. Environ Health **16** (Suppl 1), 112 (2017).*

Sanders CJ, Shortall CR, England M, Harrington R, Purse B, Burgin L, Carpenter S, Gubbins S. Long-term shifts in the seasonal abundance of adult Culicoides biting midges and their impact on potential arbovirus outbreaks. J Appl Ecol. 2019 Jul;56(7):1649-1660.

Climate and emergence of rift valley fever: Anyamba A, Chretien JP, Small J, Tucker CJ, Formenty PB, Richardson JH, Britch SC, Schnabel DC, Erickson RL, Linthicum KJ. Prediction of a Rift Valley fever outbreak. Proc Natl Acad Sci U S A. 2009 Jan 20;106(3):955-9.

Projects

What activities are planned or underway?