STAR IDAZ International Research Consortium on Animal Health

World Organisation for Animal Health

JUNE 26TH, 2025

STAR IDAZ IRC Contribution to Vector-Borne Diseases:

The Vector Transmission Control Roadmap and the Report on Immunobiological Control of Cattle Ticks

WOAH Regional Seminar

Vector-Borne Diseases in the European Region

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University of Sao Paulo, Brazil
Scientific Committee – STAR IDAZ IRC

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Improving Global Research Coordination on Major Infectious Diseases of Animals and Zoonoses

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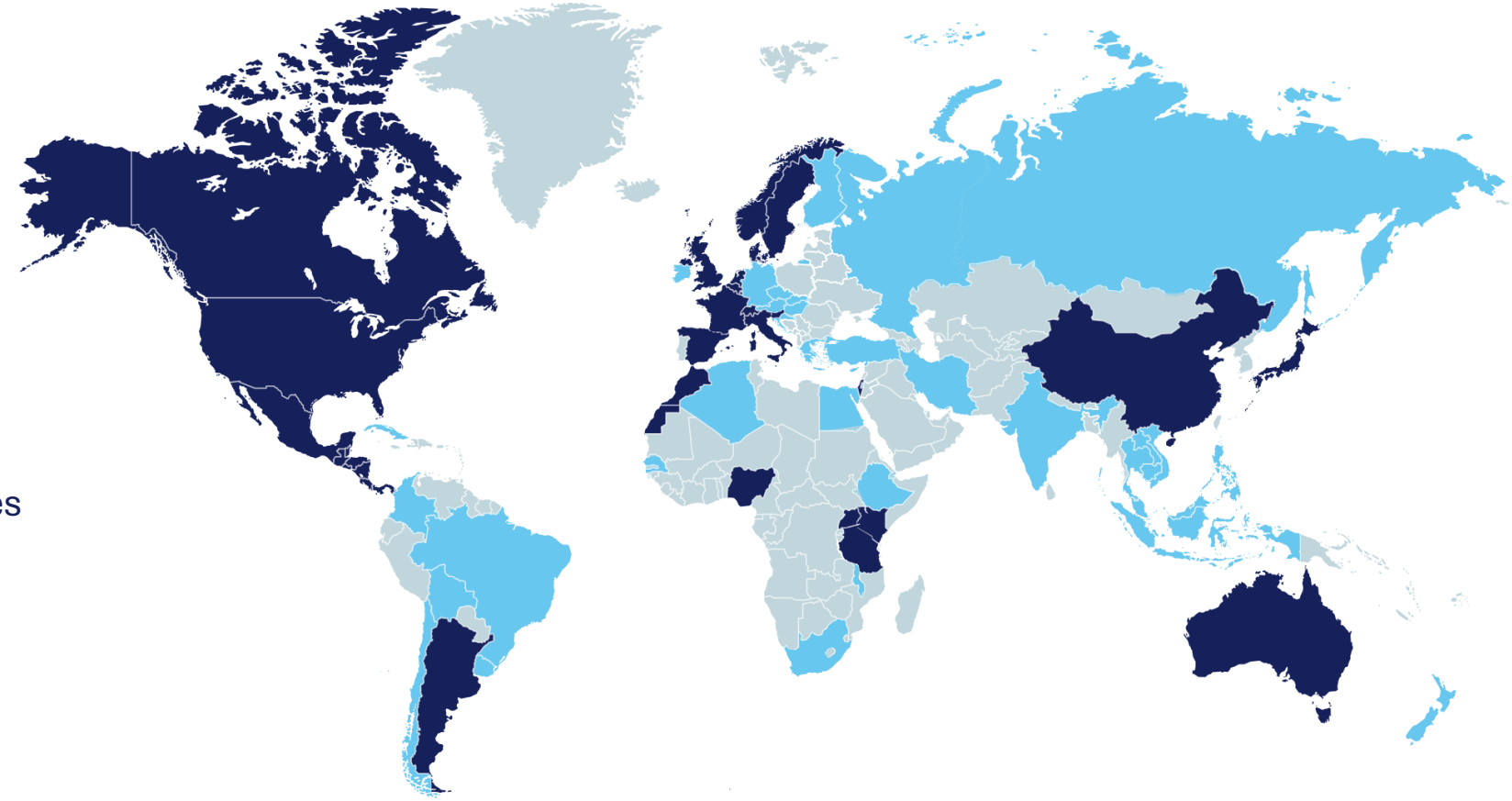
Global **St**rategic **A**lliances for the Coordination of **R**esearch on the Major **I**nfectious **D**iseases of **A**nimals and **Z**oonoses



SCAN ME

36 PARTNER ORGANISATIONS

23 COUNTRIES

+$2.5B RESEARCH INVESTMENT

4 REGIONAL NETWORKS

55+ ASSOCIATED COUNTRIES

Join Now

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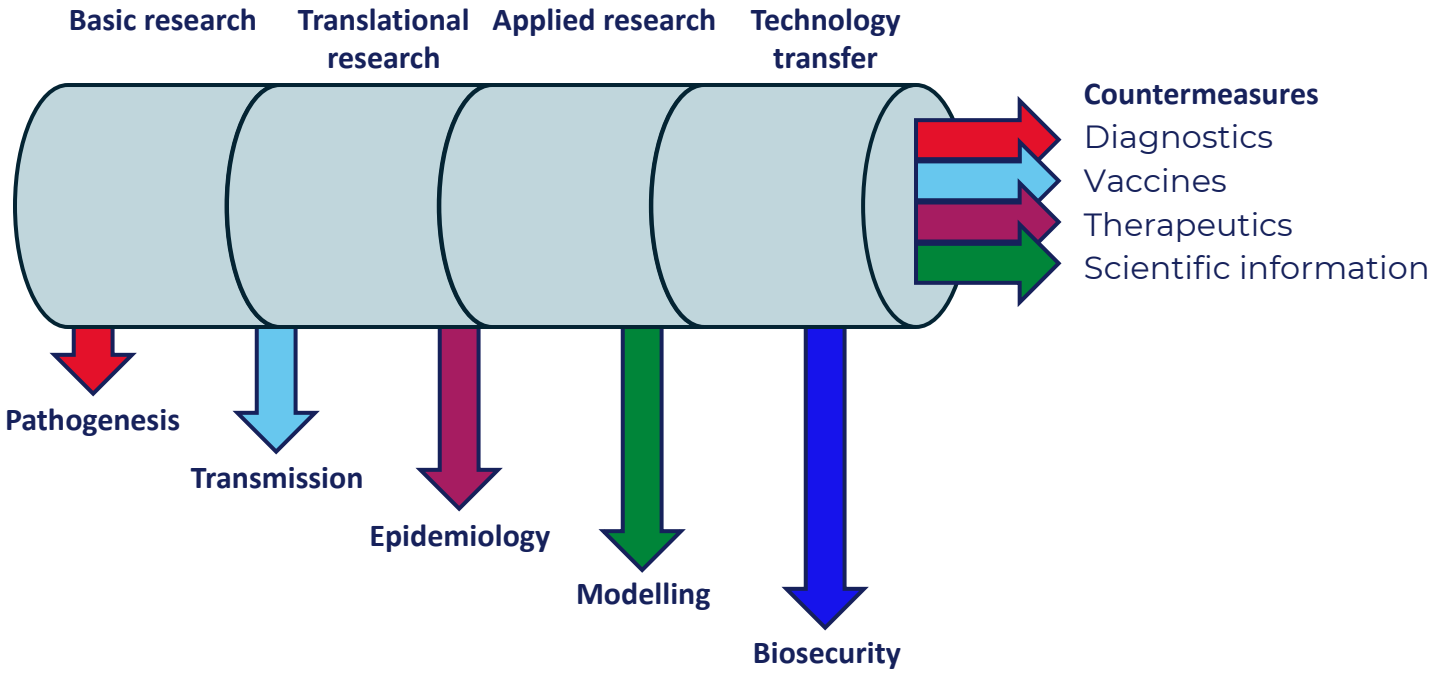
Objectives and deliverables

The overall objective of STAR-IDAZ IRC is to coordinate research at international level to accelerate the delivery of new tools and improved animal health strategies

Deliverables include:

- Candidate vaccines
- Diagnostics
- Therapeutics
- Other animal health products and procedures
- Key scientific information/tools to support risk analysis and disease control



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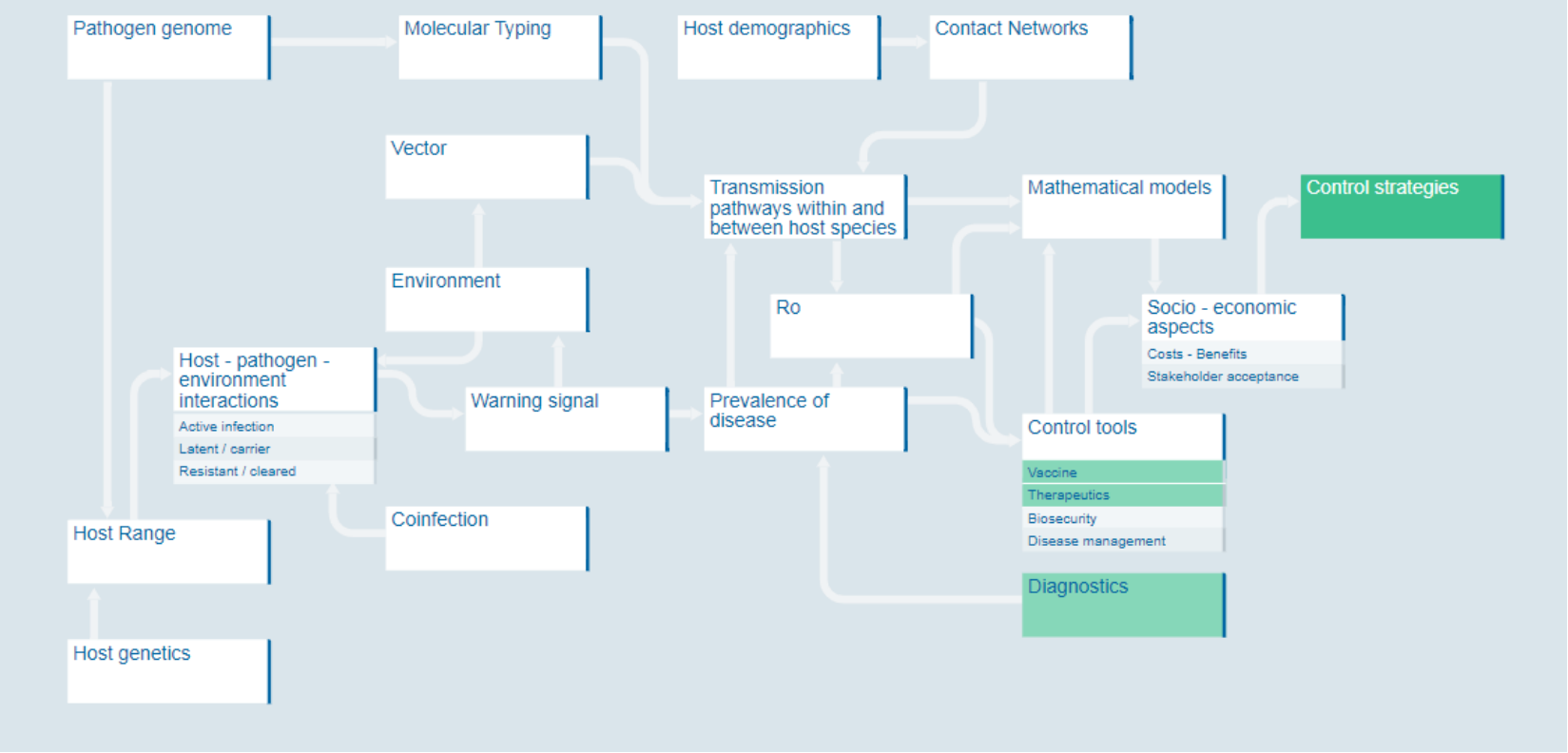
Research Roadmaps

Development pathway of the significant steps that have to be taken and problems that have to be solved based on the gaps identified by the WGs



- Provide a structure and focus on where research is most needed, identifying bottlenecks and critical gaps
- Way of visualizing a complex problem
- Provide a valuable resource for the research community, including funders
- Interactive, 'living' tool publicly available online at www.star-idaz.net

•Vector Borne Diseases

ector

Vector Transmission and Control

Vector-borne diseases pose a significant risk to animal and human health.

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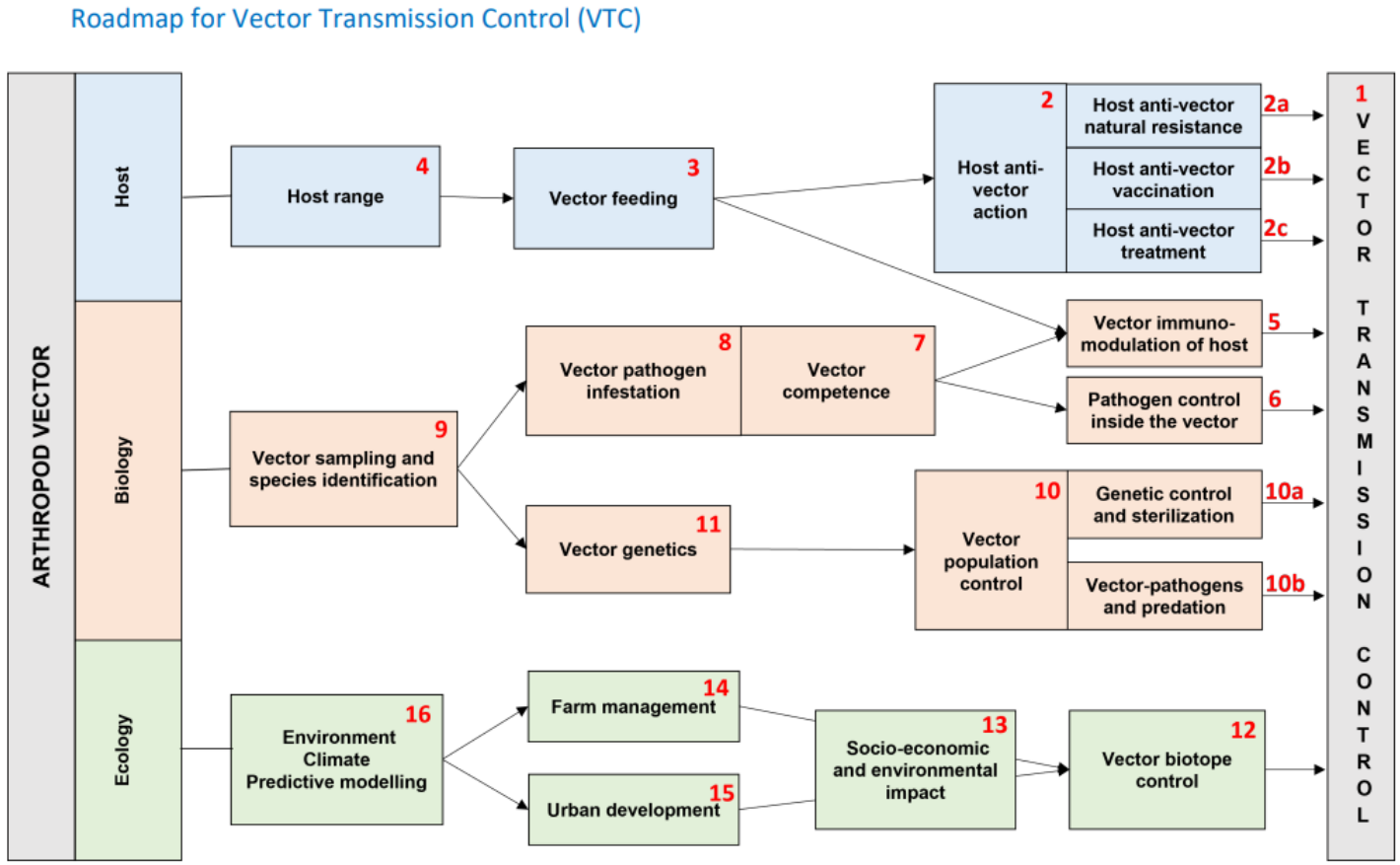
Research Roadmap (1)

The generic roadmap for Control of Vectors and of Transmission of Vector-borne Diseases considers the control through three routes:

- Control on the host (blue)
- Control on the vector (orange)
- Control on the ecology or biotope of vector and host (green).

The generic roadmap can be used in conjunction with STAR-IDAZ roadmaps for specific vector-transmitted diseases.



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Tick Vaccine Workshop (2)

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Short Summary of the STAR IDAZ Tick Vaccine Workshop

17 June 2024
Sala Coral, Rebouças Convention Centre, São Paulo, Brazil

Workshop Objectives

- Discuss recent advances in development of vaccines for cattle ticks
- Evaluate existing experimental designs in tick vaccine research
- Discuss the development of a Scientific Target Product Profile (S-TPP) for cattle tick vaccines
- Integrate expert insights and contributions to ensure relevance and applicability

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Tick Vaccine Article (3)

IMMUNOBIOLOGICAL CONTROL OF CATTLE TICKS

ADDRESSING GAPS IN KNOWLEDGE IN THE CONTEXT OF A SCIENTIFIC TARGET PRODUCT PROFILE FOR A TICK VACCINE

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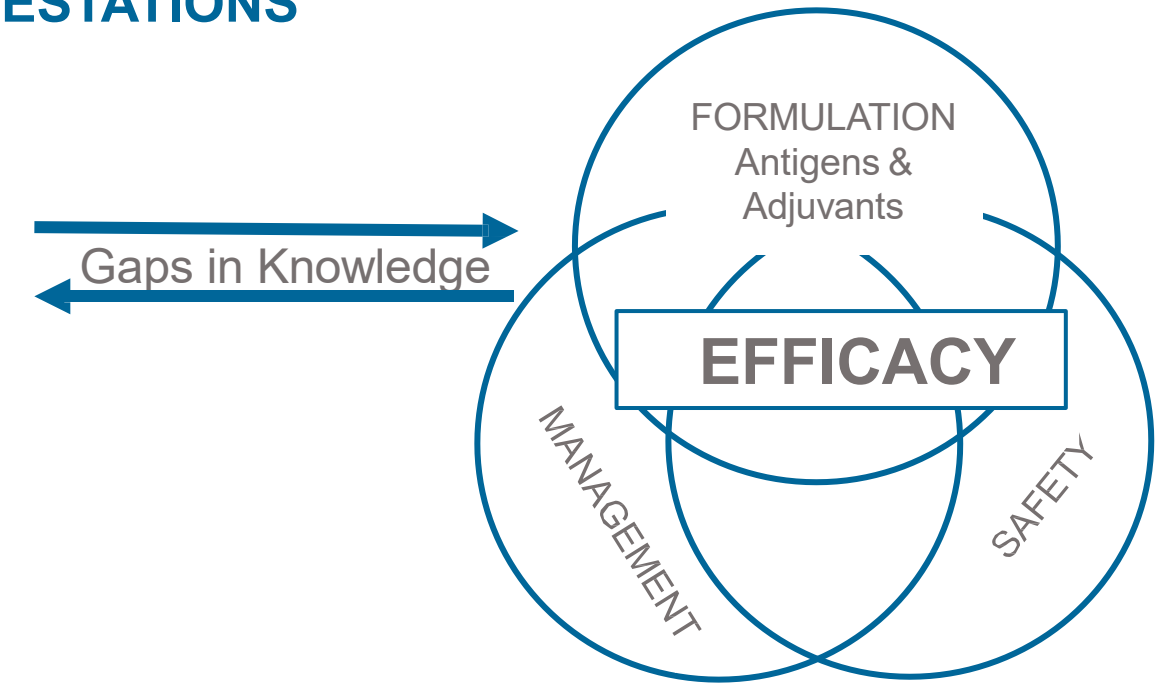
ADRESSING GAPS IN R&D IN THE CONTEXT OF A TPP

COMPONENTS OF A TARGET PRODUCT PROFILE FOR VACCINES TO CONTROL TICK INFESTATIONS

1. Target Population
2. Antiparasitic Modality
3. Level of Efficacy
4. Safety
5. Dosing, Administration & Management
6. Approach
7. Mechanism of Action
8. Biological Activity



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TPP – 1. Target Population

- **Essential Profile**
- **Ideal Profile**
- **Filling gaps in knowledge**

•Do past infestations reduce vaccine effectiveness?
  - e.g. blocking antibodies, antigen imprinting

•Can maternal antibodies (via colostrum) impact protection of calf?
  - Age at 1st vaccination

•Is the vaccine effective across different tick species?

•Do antigens match/cover the MHC diversity in commercial cattle breeds?
  - MHC variability limits efficacy of subunit vaccines.
  - Challenge is worsened by small genetic pools in commercial cattle breeds.

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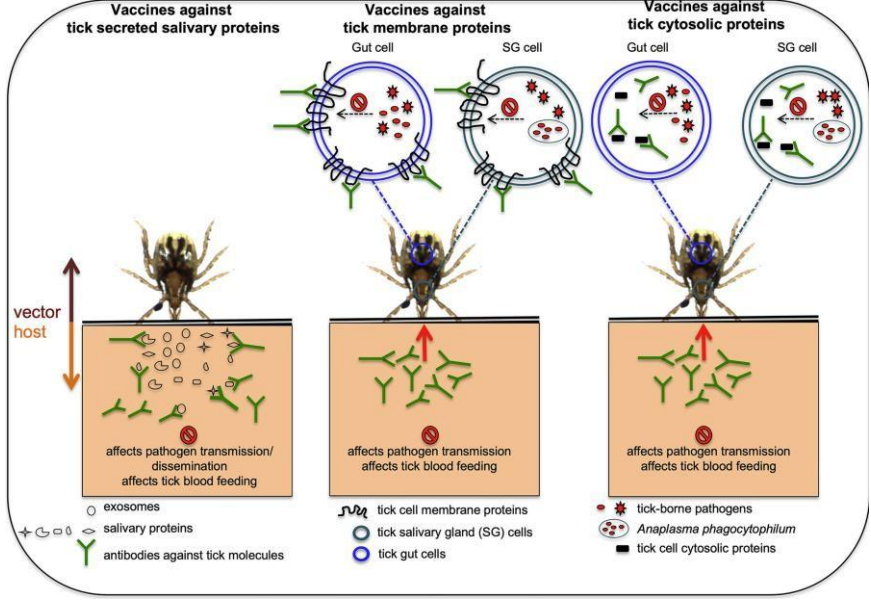
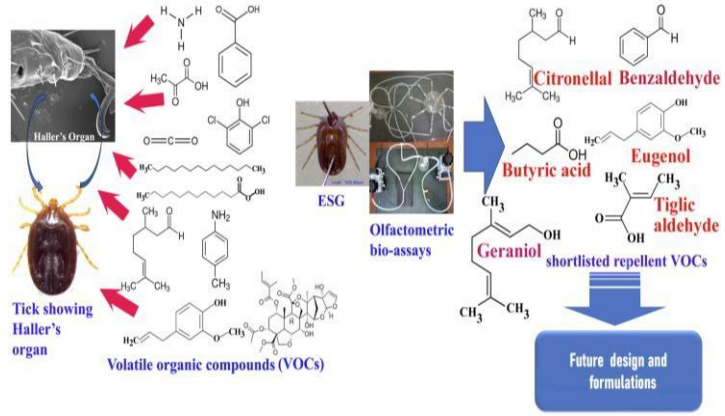
TPP – 2. Anti-parasitic Modality

- **Essential Profile**
  - Immunobiological
- **Ideal profile**
  - Immunobiological integrated with other technologies
- **Knowledge gaps**
  - Do antibodies truly neutralize targets in the tick?
  - Can vaccines modulate tick immunity or semiochemicals?





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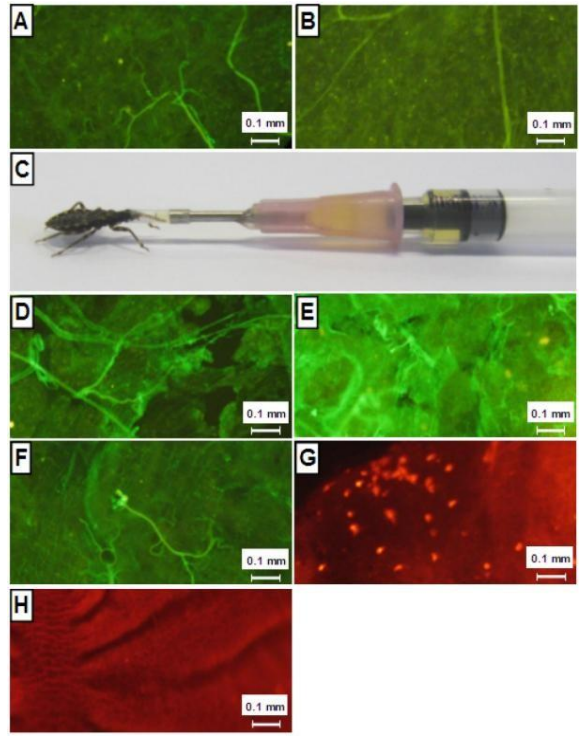
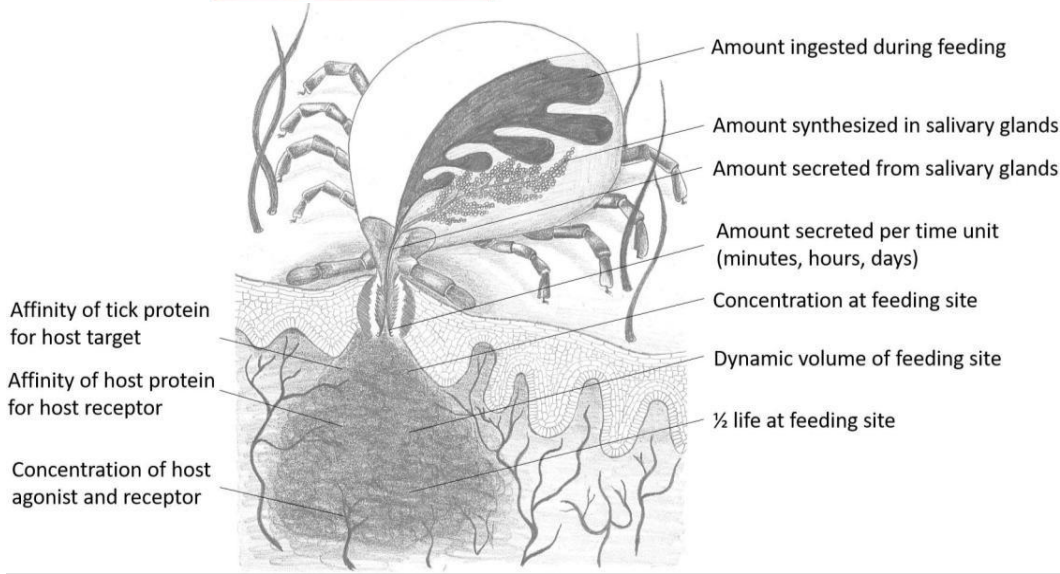
TPP – 3. Level of Efficacy

- **Efficacy Goals**
- **Key Points**
- **Critical Gaps**

- Define efficacy thresholds
- Standardize trial design
- Clarify host vs. pasture impact
- Understand direct vs. indirect efficacy
- Investigate tick immune evasion
- Assess role / Define potency of neutralizing antibodies
- Ensure sustained antibody levels





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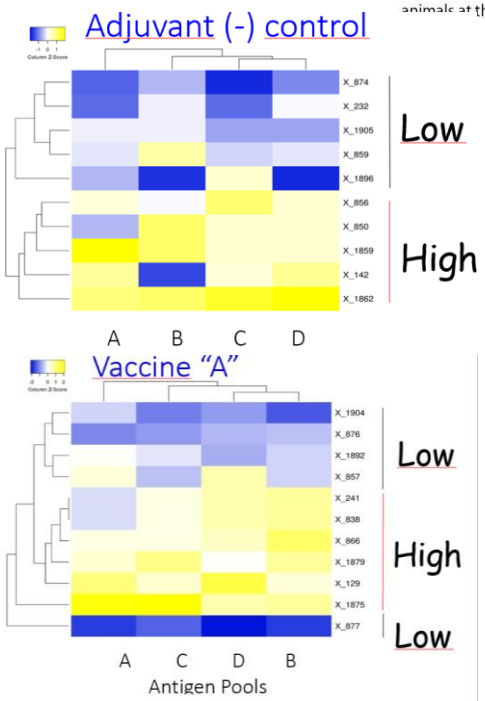
TPP – 4. Safety

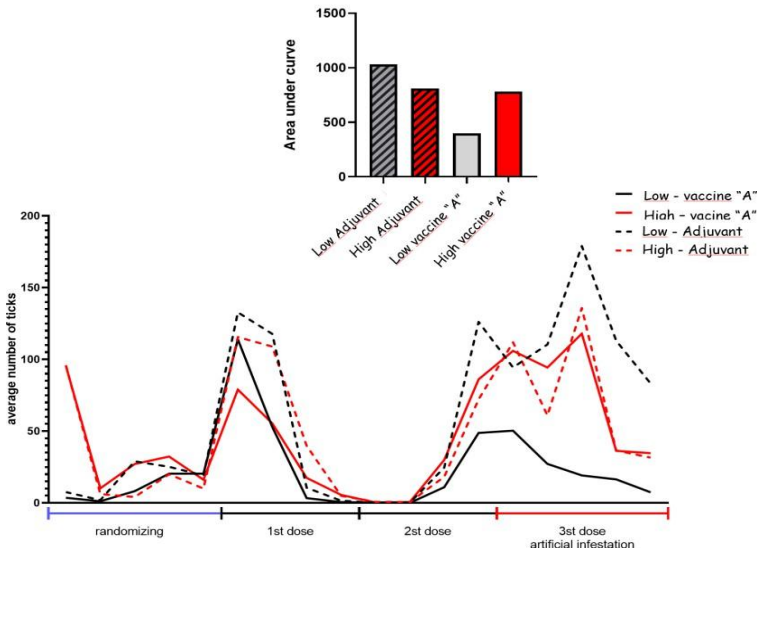
TPP – 5. Dosing, Administration & Management

- **Essential**
- **Ideal**
  - All animals, regardless of diet, previous exposure and of concomitant infestations
- **Critical Gaps**
  - Distribution of dosage & interval between boosts
  - Are infestations and/or feed antibiotics immunosuppressive?
  - Should vaccination occur before the Spring Rise?

37% of 19 antigens are histamine-binding proteins; too much free histamine in skin of vaccinated animals?

Fig. 2. Tick challenge of 19ISP mRNA-LNP immunized guinea pigs induces erythema. Guinea pigs were immunized with 19ISP or control (IL-21) mRNA, and 25 *I. scapularis* nymphs were allowed to engorge on their shaved backs. All animals were monitored for the development of erythema as a cardinal initial sign of acquired tick resistance over a period of 6 days or until all ticks detached. The images show representative (**A**) 19ISP-immunized or (**B**) control animals at the indicated time points.





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TPP– 6-8. Approach, Mechanism of Action & Biological Activity

- **Essential**
  - Prevention – neutralizing antibodies decrease parasite's fertility and tick loads on "vaccine-eligible" hosts
- **Ideal**
  - Prevention – all animals, regardless of diet, previous exposure and of concomitant infestations; clean pastures
  - Decrease vectorial capacity; increase susceptibility of tick to entomopathogens; decrease attractiveness of host
- **Critical Gaps**
  - Distribution of dosage & interval between boosts for optimal vaccine performance
  - Are infestations and/or feed antibiotics immunosuppressive?
  - Can vaccination generally be applied before the Spring Rise *versus* need for marker of vaccine readiness of herds?
  - How to target tick's vectorial capacity and immunity? Host's attractiveness?

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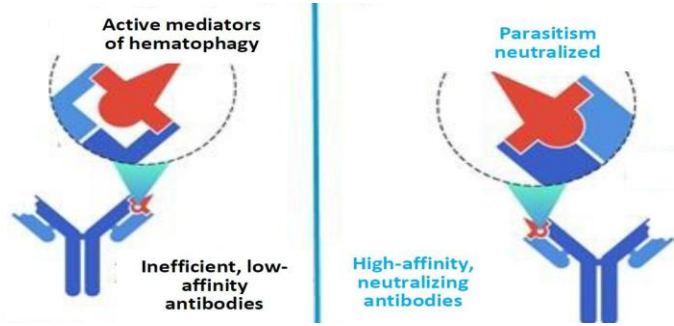
REASSESSMENT OF VACCINE FORMULATIONS



Antigens

Are we testing the best antigens?

Are we testing antigens correctly?

Will vaccines be standalone or is integrated control necessary?

Do we need more antigens per vaccine?

Do subunit (peptide-based or protein-based) vaccines provide coverage of MHC in small effective populations (N_e)?

Adjuvants

>10 different adjuvants have been assessed for tick vaccines

Adjuvants determine antibody affinities

Tick vaccines need to elicit high affinity Abs that neutralize functions of tick proteins

- No studies measure antibody affinities induced by tick vaccines
- No studies evaluate impact of specific antibodies on function of target protein of tick (possible exception: Bm86)

Target Tick Species

Antigens – Description HIDDEN (not so hidden) X EXPOSED – eccrine, apocrine and holocrine secretion mechanisms

Expression System

Effect on Ticks – parameters evaluated; N of larvae and viability; time to clean pasture

Overall Vaccine Efficacy Single Antigen

Overall Vaccine Efficacy Antigen Cocktail

Animal Model – **Complementarity of biologies**

Survey of 173 published trials for tick vaccines

If cattle, breed of cattle - BoLA and HTLs

Size of experimental groups - Randomization for innate tick burden when using outbred animals

Age of bovines/sheep - Impact of maternal antibodies and of previous exposures - vaccination calender

Naive before immunization and challenge? LN fibrosis; regulatory Antibodies

Adjuvant – Antibody affinity and neutralization of functions of Ags

Dose (per animal) – overcoming blocking antibodies

Administration route – ipsi and contralateral boosts and affinity maturation

Intervals between doses - increasing intervals can enhance affinity maturation

Animals tick-free during immunization? Tick saliva is immunosuprressive. Should acaricides be employed to prepare hosts for vaccination? (for ANY vaccine?)

Interval between last dose and challenge – Is efficacy an artifact due to Immune Complexes? Wikel & Allen study

Challenge System (adults, nymphs, larvae) and N of each challenge – What is the “surrogate number” of natural infestations? What is the minimum reduction of females and/or larvae to clean pastures with same interval as acarides (i.e., ~180 days)

Strain of tick for challenge - Acaricide-resistant? Infected with hemoparasites?

Season of trial – impact of photoperiod on immunity and on coat thickness and hair follicle physiology

Impact of ABX in feed: inflammasome; microbiota of host and tick

Impact of concomitant immunizations – convenient vaccination calender that producers want or calender that is effective?

MEMORY evaluated? – How is memory achieved without re-exposure to (hidden) antigens?

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Thank you for your attention

For more information on STAR-IDAZ IRC, how to become an IRC partner or join the regional networks:

- www.star-idaz.net
- www.linkedin.com/company/star-idaz-irc/
- Twitter.com/StarIdaz

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