

GLOBAL HEALTH AND TROPICAL MEDICINE



GHTM



**Omic studies on *Rhipicephalus bursa*- *Babesia ovis*.
development of tick-borne diseases alternative
control methods**

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FCT

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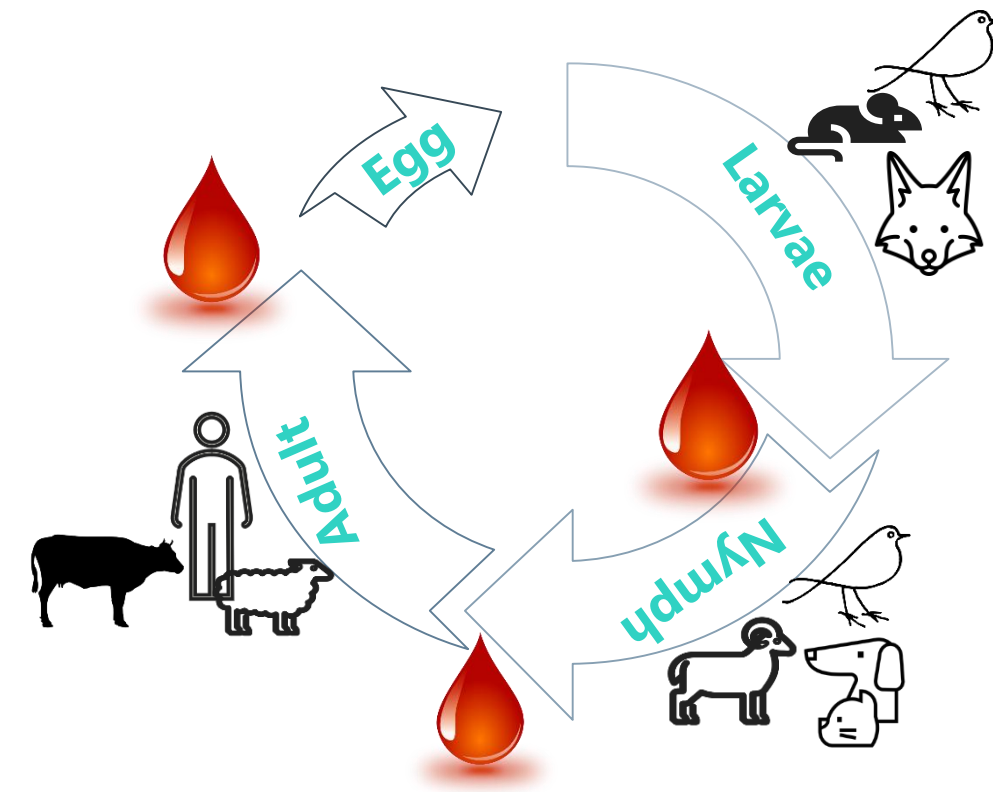
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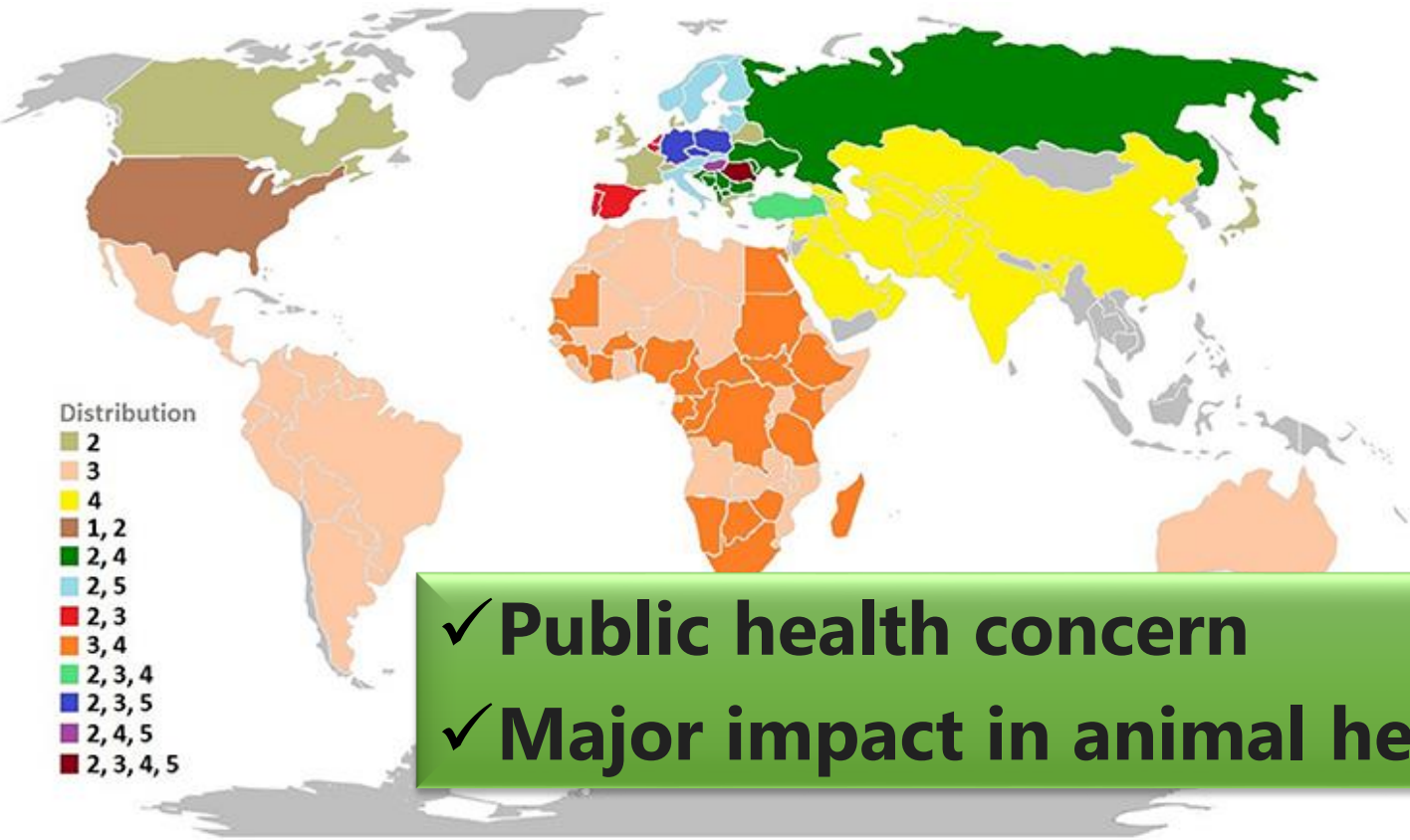
Ticks

- Main vector of disease in animals and second in humans
- About 900 species identified & distributed worldwide
- At least 10% are competent vectors of pathogens
- Different blood meals to complete life cycle



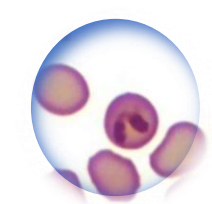
Tick-borne diseases

Diseases	Pathogens	Main tick vector
1 Human granulocytic anaplasmosis	<i>Anaplasma phagocytophilum</i>	<i>Ixodes</i>
2 Lyme disease	<i>Borrelia burgdorferi</i>	<i>Ixodes</i>
3 Babesiosis	<i>Babesia</i> spp.	<i>Rhipicephalus</i> <i>Ixodes</i>
4 Crimean-congo hemorrhagic fever	CCSFV	<i>Hyalomma</i>
5 Tick-borne encephalitis	TBEV	<i>Ixodes</i>



✓ Public health concern
 ✓ Major impact in animal health

Prevention and control



Pathogen

- Chemotherapy
- Vaccination



Vector

- Ecological approaches
- Biological control
- Genetic control
- **Acaricides**

Safer & Sustainable Methods Needed

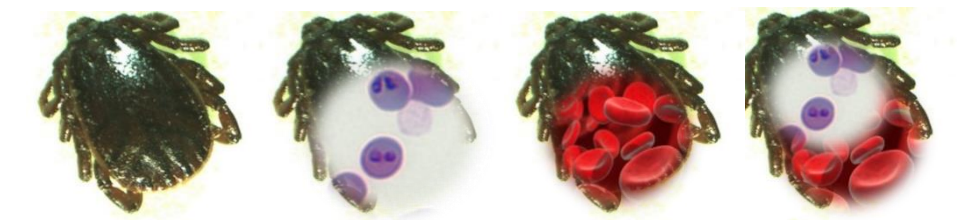
Anti-TTBD vaccines

de la Fuente J, Antunes S, et al. (2017) Tick-Pathogen Interactions and Vector Competence: Identification of Molecular Drivers for Tick-Borne Diseases. Front Cell Infect Microbiol. 7:114 doi: 10.3389/fcimb.2017.00114.



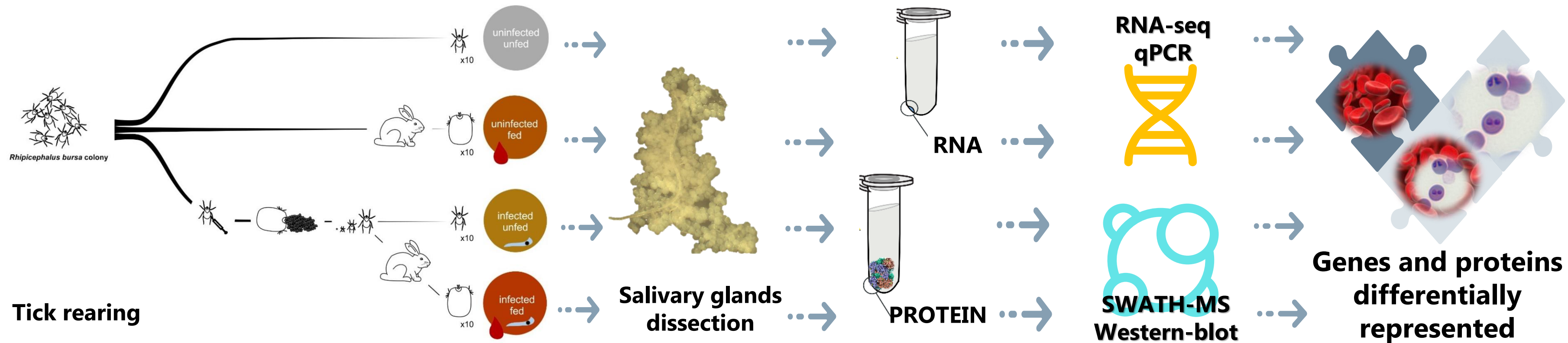
Anti-TTBD Vaccines

Strategies for tick protective antigens discovery



Model : *Rhipicephalus bursa- Babesia ovis*

Comparative transcriptomics and proteomics



Potential candidates

- Fold change
- Putative function
- Response to both feeding and infection



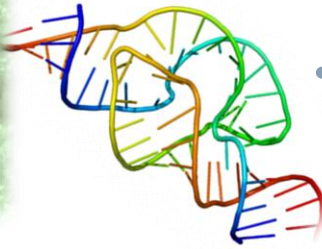


Potential protective antigens

Model : *Rhipicephalus bursa- Babesia ovis*

Selection by gene functional analysis *via* RNA interference

dsRNA synthesis of targets



qPCR for gene silencing and infection + Evaluation of biological parameters



A

Group	Gene silencing (% Ave ± S.D.)	<i>B. ovis</i> infection levels (Ave ± S.D.)	Infection rate (Ave ± S.D.) (N)
<i>vitellogenin-3</i>	92 ± 2*	4.67e ⁻⁰⁴ ± 3.05e ⁻⁰⁴	314 ± 255.17(4) ^a
<i>achacin</i>	51 ± 9*	4.48e ⁻⁰⁷ ± 1.20e ⁻⁰⁷	0.30 ± 0.09(8)*
<i>glycine-rich</i>	ND	-	-
<i>secreted cement</i>	65 ± 11**	2.97e ⁻⁰⁶ ± 2.68e ⁻⁰⁶	1.99 ± 2.18
Control	-	1.49e ⁻⁰⁶ ± 1.09e ⁻⁰⁶	-

Vitellogenin

Gene Knockdown: 100% increase in tick mortality population and infection rate

Secreted cement

Gene Knockdown: 40% increase in tick mortality, 46% of failure in attachment Influence on *Babesia* infection in adult SCS and ovaries

- Antunes, S., Couto, J., ... Domingos, A., 2018. *Frontiers in Cellular and Infection Microbiology*. DOI: 10.3389/fcimb.2018.00116.
- Couto J,....., Antunes S, de la Fuente J., 2020. *Vaccines*. DOI: 10.3390/vaccines8010091

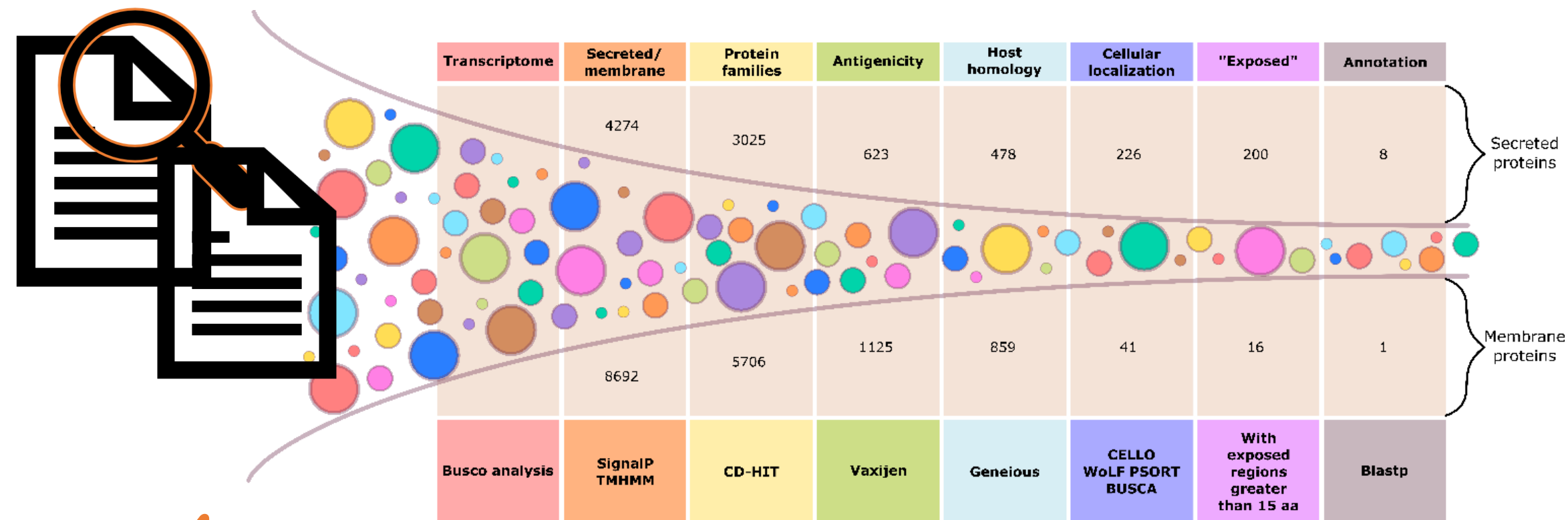




Potential protective antigens

Model : *Rhipicephalus bursa*- *Babesia ovis*

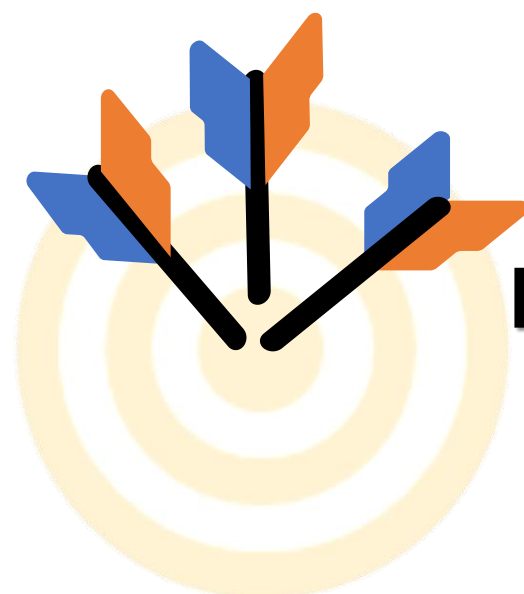
Selection by reverse vaccinology using the *R. bursa* sialomes



Identify antigens capable of inducing a **protective, robust, and long-lasting immune response** with no allergenic or toxic effects in vivo.



➤ **exposed regions** screened for overlapping coincident epitope groups (**CEGs**), structure, exposure, and the presence of **B and T cell epitopes**.



MARVEL, EVASIN and **RICIN** like proteins.
(peptide-based therapeutics)



Pilot vaccination trials with the **Seven candidate protective antigens** identified