



Review

Multi-Omics Technologies Applied to Improve Tick Research

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Abstract: The advancement of multi-omics technologies is crucial to deepen knowledge on tick biology. These approaches, used to study diverse phenomena, are applied to experiments that aim to understand changes in gene transcription, protein function, cellular processes, and prediction of systems at global biological levels. This review addressed the application of omics data to investigate and elucidate tick physiological processes, such as feeding, digestion, reproduction, neuronal, endocrine systems, understanding population dynamics, transmitted pathogens, control, and identifying new vaccine targets. Furthermore, new therapeutic perspectives using tick bioactive molecules, such as anti-inflammatory, analgesic, and antitumor, were summarized. Taken together, the application of omics technologies can help to understand the protein functions and biological behavior of ticks, as well as the identification of potential new antigens influencing the development of alternative control strategies and, consequently, the tick-borne disease prevention in veterinary and public health contexts. Finally, tick population dynamics have been determined through a combination of environmental factors, host availability, and genetic adaptations, and recent advances in omics technologies have improved our understanding of their ecological resilience and resistance mechanisms. Future directions point to the integration of spatial omics and artificial intelligence to further unravel tick biology and improve control strategies.

Keywords: Argasidae; biology; control; Ixodidae; microbiota; physiology; vaccine



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1. Introduction

The mapping and sequencing of the human genome stimulated the development of new technologies for DNA sequencing, improving the characterization and identification of the composition and function of gene products of various living organisms [1]. In this sense, molecular tools were developed and/or improved to expand knowledge of

proteomics, transcriptomics, genomics, metabolomics, lipidomics, and epigenomics, which correspond to global analysis of proteins, RNA, genes, metabolites, lipids, and methylated DNA or modified histone proteins in the chromosomes and are designated by the suffix “omics” [2,3].

In recent years, new tools for molecular analysis have been developed that allow for a comprehensive characterization of the spatial organization of molecules, cells within tissues, or transcriptomes of a set of cells, which has allowed for a better understanding of the biology of different organisms [4]. An example of the application of these technologies has been in the study of ticks, which are the first vector of pathogens in animals and the second vector in humans [5]. This has facilitated the sequencing and assembly of genomes of different tick species around the world [6,7].

These tools have improved the quality of tick genomic analyses, allowing for progress in the biological science of these arthropods. These high-quality genomes (at chromosome-level genome assembly) have allowed for the elucidation of new epigenetic functions, the expansion of gene families, and the deciphering of genetic variations between tick species. In addition, the relationship with their microbiota and the pathogens they transmit, among other findings, allows for a deeper understanding of these vectors [8–10]. Therefore, this review summarizes and discusses multi-omics information that can provide deeper insight into the coordination of various and intricate host–tick–pathogen interactions, tick population spread dynamics, and the development of new therapeutic drugs.

2. Methods

2.1. Information Search Strategy

The previously proposed methodologies by Moher et al. [11], Aromataris et al. [12], and Page et al. [13] were used to collect the information used in this review. Data were extracted from the PubMed, Scopus, SciELO, ScienceDirect, and Redalyc databases using the search terms “omics” and “tick”. The search was conducted between May 2024 and January 2025.

2.2. Inclusion and Exclusion Criteria

Studies providing omics data to investigate and elucidate the physiological and biological processes of ticks, such as feeding, digestion, reproduction, and neural and endocrine systems, population dynamics, transmitted pathogens, control strategies, and identification of new vaccine targets were included. In addition, studies published in English, Portuguese, or Spanish were selected. Studies not published in indexed journals, books, or non-peer-reviewed sources were not included in the review. The publication year of the studies was not restricted, as the use of omics tools in tick research spans less than 30 years.

2.3. Number of Studies

Based on the search strategy and the proposed criteria, a total of 541 results were identified, of which 244 were eligible for evaluation. Of these, information from 181 studies stored across the five databases was used (see the overlap rate between sources in Figure S1).

3. Recent Omics Studies That Improved Knowledge About Tick Biology

3.1. Embryonic Development

Embryogenesis is the process of embryo development, during which it forms and matures into a larva and, more rarely, a nymph depending on the tick’s species [14]. Transcriptomic studies have allowed for more detailed transcript profiles for each stage of embryonic development in *Rhipicephalus turanicus*, *Haemaphysalis flava*, and *Rhipicephalus microplus* (Table 1) [15–17]. For example, for *R. turanicus*, more differentially expressed

genes (DEGs) were observed at early embryonic stages compared to later stages, showing stage-specific characteristics [15]. Understanding gene expression profiles could be used in the future to disrupt embryonic development in ticks, which in turn could also affect the transovarial transmission of some pathogens carried by these arthropods during embryogenesis [17].

Table 1. Application of omics to improve tick research.

Area	Omics	Technology ¹	Tick	Highlights	Ref.
Feeding and Digestion					
	Proteomic	LC-MS/MS	<i>Amblyomma americanum</i>	Profile of tick saliva proteins during different phases of the tick feeding process	[18]
	Transcriptomics	RNA-seq	<i>Ixodes scapularis</i>	Morphological changes in tick midgut are accomplished through transcriptional changes	[19]
	Transcriptomics	RNA-seq	<i>Ornithodoros hermsi</i>	Unfed soft ticks intensify the transcription of genes related to blood feeding/digestion prior to the blood meal	[20]
	Transcriptomics	sc-RNA-seq	<i>A. americanum</i>	Hemocyte heterogeneity in blood-feeding tick and changes in <i>Ehrlichia</i> -infected hemocytes	[21]
Reproduction and Embryology					
	Proteomic	LC-MS/MS	<i>R. microplus</i>	Protein profile during ovary maturation	[22,23]
	Transcriptomic	RNA-seq	<i>Ixodes ricinus</i>	Importance of ovaries as molting regulators	[24]
	Transcriptomic	RNA-seq	<i>R. turanicus</i>	Gene expression profiles at different stages in embryonic development	[15]
Neural and Endocrine Regulation					
	Transcriptomic		<i>I. ricinus</i>	Evolution of the cys-loop ion-ligand channel family	[25]
Tick Control					
	Transcriptomic and proteomic	RNA-seq and LC-MS	<i>R. microplus</i>	Transcripts and protein profile of salivary glands are affected by developmental stage and the source of blood	[26]
	Transcriptomic	RNA-seq	<i>Dermacentor nuttalli</i>	Transcriptome composition shows variation through the life cycle	[27]
Bacterial Microbiota					
	Metagenomic	WGS	<i>Rhipicephalus sanguineus</i> s.l. and <i>R. turanicus</i>	Implications of tick microbiota in rickettsial diseases	[28]
	Transcriptomics	RNA-seq	<i>Amblyomma maculatum</i>	<i>Rickettsia parkeri</i> infects hemocytes to modify tick cellular immune response	[29]
Changes in Tick Populations					
	Genomics	NGS	<i>I. ricinus</i> , <i>Ixodes persulcatus</i> , <i>Ixodes pacificus</i> , and <i>Ixodes hexagonus</i>	Improve the understand of gene evolution in tick biology	[30]

¹ Liquid chromatography: LC. Mass spectrometry: MS. RNA sequencing: RNA-seq. Longitudinal single-cell RNA-seq: sc-RNA-seq. Next-generation sequencing: NGS. Whole Genome Sequencing: WGS.

Likewise, through the use of sequencing techniques, differential transcription profiles during embryogenesis have been identified for *glutathione S-transferases* (GSTs) and

ferritins (*Fers*). Proteins from these genes participate in the detoxification of xenobiotic compounds and oxidative stress, respectively, in ticks [31–33]. In *Haemaphysalis longicornis*, high transcription levels of *GST* genes have been identified in eggs, particularly during the first day after oviposition and in the early stage of embryogenesis. In contrast, *Fers* gene transcriptions increase on day 10, reaching a peak on day 15 of embryogenesis [32]. On the other hand, in studies conducted in *Hyalomma rufipes*, high relative transcription of *Fers* in the ovary was found, suggesting that *Fers* may have a more prominent role in ovary function in this tick species [33].

Other functional omics studies using RNA interference (RNAi) techniques have been able to describe glycogen used by *R. microplus* during vitellogenesis and embryogenesis [34–37]. The results obtained in the characterization of the role of AKT (protein kinase B) and GSK-3 (glycogen synthase kinase-3) in glycogen metabolism and cell viability during embryonic development in the tick species *R. microplus* and *H. longicornis* have shown a conserved role of the AKT/GSK-3 axis in cell survival and glycogen metabolism [37,38]. For example, in *R. microplus*, silencing the *GSK-3* gene using RNAi leads to a reduction in oviposition and hatching of fully engorged female larvae in this tick species [39].

Additionally, the RNAi technique has allowed researchers to describe the function of proteins, such as THAP (Tick Heme-binding Aspartic Protease) [40], phospholipase A₂ [41], BYC (*Boophilus* yolk cathepsin) [42], poly P (polyphosphate P) [43], NPC1 (Niemann-Pick C1) [44], VTDCE (Vitellin-Degrading Cysteine endopeptidase) [45,46], Bm05br (Brazil *Rhipicephalus microplus* protein 05) [47], PERK (Kinase R-like endoplasmic reticulum) [48], TOR (Rapamycin) [49], PEPCK (Phosphoenolpyruvate carboxykinase enzyme) [50], Salp12 (*Ixodes scapularis* salivary gland protein of 12 kDa) [51], and RmVgR (*Rhipicephalus microplus* vitellogenin receptor) [52]. These genes are associated with functions like vitellogenesis, embryogenesis, transport, metabolism, and important signaling pathways related to reproduction in ticks.

3.2. Feeding Process

The increase in tick omics data in recent years has allowed for improving knowledge of the physiological processes of these parasites, especially during feeding (Table 1) [44,53–56]. These analyses are showing, for example, that several proteins are differentially expressed in the midgut of fed and unfed ticks as enzymes involved in digestion, iron metabolism, and oxidative stress [57,58]. This represents another step towards identifying distinct midgut pathways and metabolic activities, as shown for *A. americanum*, *I. ricinus*, *H. flava*, and *Ornithodoros erraticus* [59–61]. Furthermore, the discrimination of different levels of midgut gene transcription during pathogen acquisition, persistence, or transmission is improving the understanding of tick vector competence [62–64].

Another organ related to the feeding process is the salivary glands [65,66]. The use of high-throughput RNA sequencing (RNA-seq) for salivary glands allowed for the description of sialomes in an increasing number of tick species today, revealing the abundance and complexity of salivary gland transcriptomes and proteomes [67–69]. Omics analyses are very helpful to identify the role of components of saliva, which allows blood uptake through antihemostatic and immunomodulatory activities, in the tick–host interface [70–72]. Many protein families involved in the hematophagic processes, such as peptidases or transporter proteins, can be characterized through such an analysis [64]. For example, Jia et al. [64] identified the expansion of the transmembrane protease serine 6 family of matrilysin 2, which helps counteract oxidative stress; the serine carboxypeptidase, which is involved in nutrient acquisition; and the alcohol dehydrogenase, which plays a role in nutrient metabolism. As a consequence, the differential expression of salivary and midgut proteins

during the hematophagic process allows for the adaptation of ticks against different host and/or host defense mechanisms.

Additionally, omics technologies can improve the understanding of diseases caused by tick molecules injected into the hosts during blood feeding. For example, one host allergic reaction developed during *A. americanum* or *I. ricinus* feeding is known as alpha-Gal syndrome (AGS), where IgE antibodies are produced against glycan galactose-alpha-1-3-galactose (alpha-Gal), resulting in skin redness and allergy in more severe cases [73,74]. The exact nature of tick molecules that result in AGS is not fully characterized, but it was proposed that glycolipids with bound alpha-Gal can result in AGS [62]. In this way, by performing a tick salivary proteome and lipidome, it was shown that proteins and lipids lacking alpha-Gal can also be related to AGS [75], improving knowledge about sensitization development.

Finally, new tick saliva proteins that are essential for the feeding and transmission of pathogens are being described by applying methods like liquid chromatography (LC) and mass spectrometry (MS), techniques in the study of proteomics, which have allowed for the analysis of the sialoma of the species *A. americanum*, *Argas monolakensis*, *I. ricinus*, *R. microplus*, and *R. sanguineus* s.l. [18,59,76–80]. Recently, it was observed that the bacterium *Borrelia burgdorferi* (which causes Lyme disease), in order to survive in the species *I. scapularis*, makes modifications to the protein content in the saliva to promote its survival at the tick feeding site [81]. For example, the enzymes copper/zinc superoxide dismutase, which lead to the production of H_2O_2 , which is toxic to *B. burgdorferi*, were suppressed, while catalase and thioredoxin, which neutralize H_2O_2 , and pyruvate kinase, which produces pyruvate that protects *B. burgdorferi* from death by H_2O_2 , were increased [82].

3.3. Neural and Endocrine Regulation

G protein-coupled receptors (GPCRs) are transmembrane proteins that mediate signal transduction and biological processes [83]. Omics have provided a wide range of information about the nucleotide and protein or peptide sequences that are necessary for understanding their roles [83]. In humans, GPCRome-wide homology models containing structural and biological activity information are available in a GPCRdb database, allowing for the prediction of six classes of these receptors [84–86].

In ticks, GPCRs have already been annotated, and it has been shown that the interaction between these receptors and hormones, neuropeptides, peptide hormones, and lipoglicoproteins, among other ligands, leads to signal transduction, which influences most of the physiological processes [63,83]. A combination of structural-based and alignment-free methods based on sequence similarity allowed for the identification of 112 GPCR candidates in the synganglion of *R. microplus* that were distributed in different families: secretin, glutamate, and rhodopsin [87]. In addition, it has been shown that for every 20 GPCRs, five biogenic amines were identified, a pattern similar across different arthropods. In insects, each neuropeptide can interact with one or two receptors, but, in *I. scapularis*, this number increases 10-fold [63,88], suggesting potential targets for tick control [89].

Previous work has been able to provide identification and characterization of neuropeptide sequences. The presence of these signaling molecules was observed in different hard tick species, with the highest abundance of transcripts encoding neuropeptides being identified in the *R. microplus* synganglion (Table 1) [90]. Corazonin is a conserved neuropeptide involved in arthropod ecdysis [91]. Using a bioinformatic approach, two splice variants of the corazonin receptor were identified in *I. scapularis* [88]. In general, GPCRs do not present an N-terminal signal sequence; however, this signal sequence is present in one of these splice variants, which could aid in the insertion of the receptor into the rough endoplasmic reticulum membrane [88,91].

It must be taken into account that GPCRs as well as their ligands can be duplicated or lose their function throughout evolution [92]. Allatostatin C is a neuropeptide that was first described in *Manduca sexta* and plays a role in inhibiting hormone juvenile synthesis [93,94]. Like the vertebrate neuropeptide somatostatin, allatostatin C acts on GPCR, and both neuropeptide sequences were considered orthologous [94,95]. The alignment of allatostatin sequences from different arthropods showed that these neuropeptides present important structural differences, which allowed them to be grouped into three groups of paralogous peptides: allatostatin C, allatostatin CC, and allatostatin CCC [94,96]. Interestingly, allatostatin C was not identified in the genomic and transcriptomic analysis of tick sequences, suggesting the loss of this peptide during evolution [90]. Thus, understanding new physiological processes that describe the involvement of endocrine regulation, GPCRs, and their ligands may help in the identification of new targets and in the development of alternative tick control strategies.

4. Omics Analysis for Tick Bacterial Microbiota

The application of meta-omics through the integration of metatranscriptomics and metaproteomics of some tick species studied worldwide (Table 1) has allowed us to improve our knowledge about the species, abundances, co-occurrences, or associations of the different taxa of bacteria that are part of the microbiota of these arthropods [8,97–99]. Advances in next-generation sequencing (NGS) technology have enabled individual analysis of networks that describe the complexity and broader role that bacteria play in tick biology [100–102], as well as host/tick–pathogen and host/tick–microbiome interactions [99,101].

Also, by sequencing the microbiome of the 16S rRNA gene in ticks and applying bioinformatics tools, researchers have been able to identify microbial variation in zoonotic pathogens in *I. scapularis* [10], such as *B. burgdorferi* and *Streptococcus* spp. Similarly, the interaction between ticks and their hosts can lead to changes in the tick's microbiota, as ticks acquire new bacterial genera from their host [103,104]. This fact has been confirmed through RNA sequencing of skin tissues in mice infested with *Dermacentor marginatus* and *Haemaphysalis montgomeryi*, which demonstrated that certain bacterial genera in the skin microbiome of the mice were also found in these tick species [105,106].

Deep sequencing methodologies have played a key role in this accumulation of knowledge, being able to identify and classify different molecules from the tick microbiota. With this information, it has been possible to phylogenetically group bacterial species as endosymbionts, pathogens, clade differentiation, regulation of functions or adaptation, and tick immunity [107–109]. For example, bacterial metabolic barcoding targeting the 16S rRNA locus demonstrated that Australian tick species *Amblyomma triguttatum*, *Ixodes antechini*, *Ixodes australiensis*, *Ixodes holocyclus*, *Ixodes tasmani*, and *Ixodes trichosuri* harbor unique and diverse bacterial communities [110,111]. In addition, it reveals taxa of health interest, such as *Anaplasmataceae*, *Bartonella*, *Borrelia*, *Coxiellaceae*, *Francisella*, *Midichloria*, *Mycoplasma*, and *Rickettsia* [112].

By applying metagenomics, it was possible to find out that the microbiome varies between tissues of different tick species. In a study of the microbiome of the midgut and ovaries of the ticks *I. ricinus* and *R. microplus* before, during, and after blood feeding, it was possible to establish that the number of copies of the 16S rDNA of the bacterial species present in the ovarian microbiome of both tick species was higher compared to the copies of 16S rDNA of the midgut microbiome [113,114]. Also, it was possible to demonstrate the instability and deficiency of the midgut microbiome in contrast to the abundant and stable monospecific microbiome of the ovaries in these two tick species [113].

The use of omics technologies allowed us to understand the diversity and variety of the microbiota that exist in the different stages of development of tick species belonging to the Ixodidae and Argasidae families [115–119]. In *Dermacentor silvarum* (Ixodidae), specific bacterial species associated with each stage of development were shown, with the bacterial phylum Actinobacteria being more abundant in nymphs and Proteobacteria in adults [120]. In studies carried out in *Argas persicus* (Argasidae), the bacterial diversity was different, recording the bacterial phylum Actinobacteria in all stages and Proteobacteria only in larvae and nymphs [118].

As omics technology advances, our knowledge of the tick microbiome is improving, as well as our knowledge of how it can affect the acquisition, maintenance, and transmission of pathogens according to different factors, such as the geographic area where the ticks develop [118]. In a study of the microbiome of different populations of the tick species *Dermacentor variabilis* from four regions of the United States (West, Midwest, South, and Northeast), it was found that the geographic location of each tick population consistently influenced bacterial species richness. Specifically, 18 bacterial genera were specific to each region studied [120].

The application of multi-omics strategies in the last decade allowed for developing deeper knowledge of the bacterial microbiota found in ticks by identifying and better understanding the interactions with this arthropod and the pathogens they transmit [99,121,122]. This information could open up new control strategies by generating potential targets for the development of, for example, anti-tick microbiota vaccines [123–128], resulting in poor tick fitness through microbiota dysregulation. However, it is still necessary to identify a series of standard marker genes and reference databases that can identify new groups or discover their interaction with this arthropod. Rapidly evolving molecular techniques are expected to help make this understanding a reality in the coming years.

5. Therapeutic Advances Through Omics Using Tick Molecules

Utilizing omics technologies, it has been found that specific proteins in ticks could be used as pharmacological candidates in the future [129]. For example, proteomic analysis of salivary glands from partially engorged females of *Haemaphysalis qinghaiensis* allowed for the identification of the protein Hq023 (*Haemaphysalis qinghaiensis* 023). When tested in laboratory mice as an experimental model, this protein demonstrated an analgesic effect [130]. The discovery of this protein could open a new avenue for the development of tick-derived analgesics. Likewise, in the study of the transcriptome of the salivary gland of *Amblyomma cajennense*, using expressed sequence tags (EST), the protein Amblyomin-X (*Amblyomma cajennense* s.l. factor X inhibitory protein) was identified, an inhibitor of the Kunitz-type serine protease, and it was described with cytotoxic functions in various tumor cells [131,132]. A study conducted by Chudzinski-Tavassi et al. [133] on the antitumor activity of Amblyomin-X showed a regression of tumor mass and a decrease in the number of metastatic events in a B16F10 murine melanoma model, observing alterations in the expression of genes related to the cell cycle when two tumor cell lines were treated with Amblyomin-X, indicating that this protein acts selectively on tumor cells, inducing apoptotic cell death, possibly by targeting the ubiquitin–proteasome system [133].

Furthermore, the use of genomics has allowed for the identification and use of peptide sequences from scorpion and *I. ricinus* defenses (Scorpions-Ticks Defensins Ancestor, STiDA), which showed antimicrobial activities against distant pathogens related to fungal species, Gram-negative and Gram-positive bacteria, or the apicomplexan parasite *Plasmodium falciparum* [134].

As omics technologies, especially transcriptomics and proteomics, advance, other doors will open to the discovery of a wide variety of bioactive tick molecule applicable

to the treatment of different diseases in animals or humans [135–137]. In vitro assays performed with the recombinant protein Coversin (*Ornithodoros moubata* complement inhibitor OmCI) showed that it binds to complement component 5 (C5), selectively preventing proteolytic activation of the terminal lytic pathway of the complement, making it an alternative for use in primary immunodeficiency diseases, such as inappropriate complement activation [138]. This same protein was used in a porcine model of myocardial infarction (*Sus scrofa*), obtaining a reduction in infarct size, improved ventricular function, and attenuated interleukin-1 β and E-selectin by inhibiting C5 [139].

Recently, next-generation sequencing technologies have discovered different microRNA (miRNA) profiles conserved in the saliva of *O. erraticus* and *O. moubata* and different life stages of *H. longicornis* that could serve as biomarkers or genes with interesting therapeutic functions for some diseases [140,141]. These miRNAs could help delineate the regulatory signaling networks involved between pathogens and ticks or guide the development of tick vaccine candidates [122,140].

6. Omics to Analyze Changes in Tick Populations

Tick population changes are mainly influenced by various factors affected by climatic changes, such as host availability, habitat modifications, and the presence of human activities [142,143]. Recent advances in omics technologies have improved knowledge about the biology and genetics of ticks worldwide by being able to understand the mechanisms through which these arthropods adapt to the climatic conditions of the different areas where they are distributed (Table 1) [144,145].

Several studies have identified specific genetic markers associated with host preferences, acaricide resistances, and environmental tolerances [146–149]. For instance, genomic analysis of both *I. scapularis* and *I. ricinus* has revealed key features of their evolutionary adaptation and ecological dynamics [147–151]. In the case of *I. ricinus*, migratory birds enable the flow of genes through the European population and introduce new variants into the existing diversity [152].

Proteomics has served to expand information on the function of heat shock proteins (HSPs), which are used by ticks to prevent cell damage and restore normal cellular and physiological processes caused by the temperature fluctuations to which ticks are exposed [153–155]. Metabolomics obtained from HSPs has been able to demonstrate how the species *A. americanum*, *Dermacentor reticulatus*, *D. variabilis*, and *I. scapularis* manage energy, produce metabolites, increase different types of genes, and mitigate oxidative damage caused by temperature variations [155–158].

Likewise, the microRNAs miR-2a and miR-279, which are functionally associated with cold tolerance, have been identified in *D. silvarum*, providing insights into the mechanisms that enable such ecological adaptation [159–161]. In this same tick species, in the study of the genome of heat shock proteins, the genes *Dshsp70* (Hsp gene 70 of *Dermacentor silvarum*) and tubulin were identified as playing an essential role in the adaptation of *D. silvarum* to low temperatures [161–164]. Furthermore, DNA methylation is a reversible, heritable epigenetic modification some arthropods use to adapt to environmental stress [159,165]. The analysis of DNA methylation mediated by DNA methyltransferases (*Dnmts*) in *D. silvarum* and *H. longicornis* showed that the genes *DsDnmt* and *DsDnmt1* in *D. silvarum* and *HlDnmt1* and *HlDnmt* in *H. longicornis* played an important role in cold tolerance [166]. The above results contribute to understanding the survival and acclimatization of hibernating ticks.

Another important cofactor in understanding changes in tick populations is the link between the pathogens they transmit [167]. Infections with *B. burgdorferi* in *I. scapularis* affect gene expressions, influencing vector competence and immune response, demonstrating the multilayered relationship between pathogens and their host [168–170]. A huge number of

transcripts encoding numerous distinct protein families has been identified through recent investigations of the hard tick transcriptome [74,171,172]. This demonstrated hard tick dynamic gene expression patterns in response to blood feeding, exhibiting host immune evasion, or feeding on various hosts [66,173].

On the other hand, the use of omics has allowed for the identification of specific genetic markers associated with host preferences and resistance to chemical acaricides by ticks, which has contributed to the quicker establishment of these arthropods in previously described regions [174–176]. For example, the use of the high-resolution quantitative polymerase chain reaction–fusion technique to identify single nucleotide polymorphisms (SNPs) of the para-sodium channel gene identified the T2134C mutation, which causes an amino acid change from phenylalanine to leucine at position 712, which may be associated with deltamethrin resistance by *R. microplus* [177,178].

7. Omics to Improve Tick Control

High-throughput discovery and characterization of tick antigens and tick-borne pathogens using vaccinomics technology combined with other analytical techniques, such as Big Data, have allowed for important recent advances in this area of research [179–181]. These methodologies can be used to potentially contribute to a comprehensive analysis of large datasets, which could be crucial for the selection of potential vaccine targets with high efficacy potential, resulting in the development of next-generation vaccines [179,182]. However, challenges remain, including the complexity of large omics datasets and the few immunoinformatics tools for non-model hosts, which makes challenging the analysis of the complex interactions between different tick–host–pathogen species.

Despite these obstacles, vaccinomics is allowing for the analysis and use of genome data from different tick species that have helped in the development of vaccines [179], as demonstrated by reverse vaccinology studies in *O. erraticus*, *O. moubata*, *R. microplus*, or *Rhipicephalus bursa* [183–185]. Through in silico analysis of tick proteins from different tissues, researchers can identify new potential antigens that can elicit strong immune responses [184,186], which need validation through in vivo vaccination assays in different conditions, such as specific host breeds and tick populations, as well as vaccine formulations. In this regard, rabbit vaccination using *O. moubata* midgut membrane proteins selected using reverse vaccinology was tested to determine their potential as vaccine targets against *O. moubata* and *O. erraticus* infestations [183,187]. Interestingly, protection was higher against *O. erraticus*, showing the potential of this strategy to support the reach of antigens against cross tick species.

One interesting use of omics technology involves the functional implication analyses of already well-characterized antigens, such as subolesin, a highly conserved tick transcription factor protein [188]. For example, transcriptomic, proteomics, and graph theory data were used in tick cells where subolesin transcripts were silenced [188]. This approach provided critical insights into the mechanisms of subolesin vaccine protection, shedding light on the gene expression regulation of specific proteins involved in intracellular transport, oxidative stress, metabolic processes and proteolysis, signal transduction, microbicidal activity, water channels, and cell stress response that can impact tick infestation efficacy.

For high-efficacy anti-tick vaccines, select conserved antigenic epitopes are crucial to minimize vaccine escape in ticks from distinct geographic areas. Through DNA sequencing and bioinformatic tools, a study analyzed the conservation of 14 tick proteins used in vaccination trials, including subolesin, from different *R. microplus* populations collected across the Americas and Pakistan [189]. The results showed significant variation in amino acid conservation across these proteins, identifying RmAQP1 (recombinant aquaporin

1 protein of *Rhipicephalus microplus*), vitellogenin receptor, serpin-1, subolesin, and the voltage-dependent anion channel as potential vaccine antigens [189].

Moreover, immunoinformatics were applied to find potential *R. microplus* and *Anaplasma marginale* protective antigens against bovine anaplasmosis [190]. This analysis identified two *A. marginale* proteins and one *R. microplus* peroxinectin, a protein involved in immunological processes that can be targeted to elicit protective immune responses to control pathogen infection. Moreover, omics analysis of the modulation of tick regulatory components in response to pathogen infections by *Anaplasma phagocytophilum* can be used for the identification of new control targets [191]. Characterizing ticks to alter their gene expression in response to pathogen infection (e.g., *A. marginale* or *A. phagocytophilum*) could help to identify vulnerabilities that could be exploited to develop new protective antigens.

8. Perspectives

The recent advances described in this revision highlight the potential of omics analysis as a tool to uncover gaps in different aspects of tick knowledge [192,193]. The single-cell analysis represents a new technology that can enable further high-throughput molecular profiling of tick cells. For example, using this technology, it has been possible to identify clusters of hemocyte signatures in immunity and fitness in the tick species *A. americanum* and *Ixodes dammini* [70,109]. Furthermore, the role of tick extracellular vesicles was characterized in disturbing host tissue repair via the $\gamma\delta$ T cell–keratinocyte axis during hematophagy [194], as well as host immune responses against tick-borne diseases, such as severe fever with thrombocytopenia syndrome or Lyme disease [195,196]. In this way, single-cell technology represents a disruptive tool to understand the intricate biology of ticks, offering unprecedented insights at the cellular level that were previously inaccessible.

Likewise, multi-omics have unveiled a novel reservoir of target biomolecules that have been discovered in different tick species with immunomodulation, antimicrobial, anticoagulant, anti-inflammatory, and antitumor functions in different tumor cell lines. These molecular biology technologies have opened new lines of research at the pharmacological level, analyzing ticks not only as ectoparasites and vectors of pathogens but as an excellent source of new molecules with a variety of functions and therapeutic properties. However, despite the fact that a variety of possible therapies using biomolecules from ticks have been identified, no studies have been continued that could lead to the approval of any type of new drug by federal health agencies, such as the Food and Drug Administration (FDA) in the United States [137].

It is expected that in the coming years, other types of technologies, such as spatial omics and holo-omics, can be used, combined with advances in single-cell omics that allow for a better understanding of the interactions between different cells and molecular distributions or their relationship with the tick microbiota [197,198]. Finally, the development of faster, high-performance, and lower-cost sequencing technologies can be integrated with already advanced artificial intelligence tools for data analysis, opening new avenues for research on this critical pathogen vector in both animal and human health.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/microorganisms13040795/s1>, Figure S1: PRISMA flowchart used to collect data and select reports in this study.

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References

1. Welch, J.; Kozareva, V.; Ferreira, A.; Vanderburg, C.; Martin, C.; Macosko, Z. Single-Cell Multi-Omic Integration Compares and Contrasts Features of Brain Cell Identity. *Cell* **2019**, *177*, 1873–1887. [\[CrossRef\]](#) [\[PubMed\]](#)
2. Shendure, J.; Ji, H. Next-Generation DNA Sequencing. *Nat. Biotechnol.* **2008**, *26*, 1135–1145. [\[CrossRef\]](#) [\[PubMed\]](#)
3. Dai, X.; Li, S. Advances and Trends in Omics Technology Development. *Front. Med.* **2022**, *9*, 911861. [\[CrossRef\]](#)
4. Bressan, D.; Battistoni, G.; Hannon, G. The Dawn of Spatial Omics. *Science* **2023**, *381*, eabq4964. [\[CrossRef\]](#)
5. De la Fuente, J.; Estrada-Pena, A.; Venzal, J.; Kocan, K.; Sonenshine, D. Overview: Ticks as vectors of pathogens that cause disease in humans and animals. *Front. Biosci.* **2007**, *13*, 6938–6946. [\[CrossRef\]](#)
6. Singh, K.; Kumar, S.; Sharma, A.; Jacob, S.; RamVerma, M.; Singh, N.; Shakya, M.; Sankar, M.; Ghosh, S. Economic Impact of Predominant Ticks and Tick-Borne Diseases on Indian Dairy Production Systems. *Exp. Parasitol.* **2022**, *243*, 108408. [\[CrossRef\]](#)
7. Murgia, M.V.; Bell-Sakyi, L.; De La Fuente, J.; Kurtti, T.J.; Makepeace, B.L.; Mans, B.; McCoy, K.D.; Munderloh, U.; Plantard, O.; Rispe, C.; et al. Meeting the Challenge of Tick-Borne Disease Control: A Proposal for 1000 *Ixodes* Genomes. *Ticks Tick Borne Dis.* **2019**, *10*, 213–218. [\[CrossRef\]](#)
8. Ribeiro, J.M.; Bayona-Vásquez, N.J.; Budachetri, K.; Kumar, D.; Frederick, J.C.; Tahir, F.; Faircloth, B.C.; Glenn, T.C.; Karim, S.A. Draft of the Genome of the Gulf Coast Tick *Amblyomma maculatum*. *Ticks Tick Borne Dis.* **2022**, *14*, 102090. [\[CrossRef\]](#)
9. Rosani, U.; Sollitto, M.; Fogal, N.; Salata, C. Comparative Analysis of Presence-Absence Gene Variations in Five Hard Tick Species: Impact and Functional Considerations. *Int. J. Parasitol.* **2024**, *54*, 147–156. [\[CrossRef\]](#)
10. Hernández-Jarguín, A.; Díaz-Sánchez, S.; Villar, M.; de la Fuente, J. Integrated Metatranscriptomics and Metaproteomics for the Characterization of Bacterial Microbiota in Unfed *Ixodes ricinus*. *Ticks Tick Borne Dis.* **2018**, *9*, 1241–1251. [\[CrossRef\]](#)
11. Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med.* **2009**, *6*, e1000097. [\[CrossRef\]](#)
12. Aromataris, E.; Lockwood, C.; Porritt, K.; Pilla, B.; Jordan, Z. JBI Manual for Evidence Synthesis. *JBI Evid Synth.* **2024**, 2106–2107. [\[CrossRef\]](#)
13. Page, M.; McKenzie, J.; Bossuyt, P.; Boutron, I.; Hoffmann, T.; Mulrow, C.; Shamseer, L.; Tetzlaff, J.; Akl, E.; Brennan, S.; et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* **2021**, *372*, 71. [\[CrossRef\]](#)
14. Santos, V.T.; Ribeiro, L.; Fraga, A.; De Barros, C.M.; Campos, E.; Moraes, J.; Fontenele, M.R.; Araújo, H.M.; Feitosa, N.M.; Logullo, C.; et al. The Embryogenesis of the Tick *Rhipicephalus (Boophilus) microplus*: The Establishment of a New Chelicerate Model System. *Genesis* **2013**, *51*, 803–818. [\[CrossRef\]](#) [\[PubMed\]](#)
15. Ruiling, Z.; Wenjuan, L.; Kexin, Z.; Xuejun, W.; Zhong, Z. Developmental Transcriptomics Throughout the Embryonic Developmental Process of *Rhipicephalus turanicus* Reveals Stage-Specific Gene Expression Profiles. *Parasit. Vectors* **2022**, *15*, 89. [\[CrossRef\]](#) [\[PubMed\]](#)
16. Cheng, R.; Li, D.; Duan, D.Y.; Parry, R.; Cheng, T.Y.; Liu, L. Egg Protein Profile and Dynamics During Embryogenesis in *Haemaphysalis flava* ticks. *Ticks Tick Borne Dis.* **2023**, *14*, 102180. [\[CrossRef\]](#)
17. Kim, T.K.; Waldman, J.; Ibanez-Carrasco, F.; Tirloni, L.; Waltero, C.; Calixto, C.; Braz, G.R.; Mulenga, A.; Da Soçva Vaz, I.; Logullo, C. Stable Internal Reference Genes for Quantitative RT-PCR Analyses in *Rhipicephalus microplus* During Embryogenesis. *Ticks Tick Borne Dis.* **2023**, *14*, 102251. [\[CrossRef\]](#)
18. Kim, T.K.; Tirloni, L.; Pinto, A.F.M.; Diedrich, J.K.; Moresco, J.J.; Yates, J.R.; Da Silva Vaz, I.; Mulenga, A. Time-Resolved Proteomic Profile of *Amblyomma americanum* Tick Saliva During Feeding. *PLoS Negl. Trop. Dis.* **2020**, *14*, e0007758. [\[CrossRef\]](#)
19. Lu, S.; Martins, L.A.; Kotál, J.; Ribeiro, J.M.C.; Tirloni, L. A Longitudinal Transcriptomic Analysis from Unfed to Post-Engorgement Midguts of Adult Female *Ixodes scapularis*. *Sci. Rep.* **2023**, *13*, 11360. [\[CrossRef\]](#)

20. De Sousa-Paula, L.C.; Berger, M.; Talyuli, O.a.C.; Schwartz, C.L.; Saturday, G.A.; Ribeiro, J.M.C.; Tirloni, L. Exploring the Transcriptome of Immature Stages of *Ornithodoros hermsi*, the Soft-Tick Vector of Tick-Borne Relapsing Fever. *Sci. Rep.* **2024**, *14*, 12466. [\[CrossRef\]](#)
21. Adegoke, A.; Hanson, J.; Smith, R.C.; Karim, S. Ehrlichia chaffeensis Co-opts Phagocytic Hemocytes for Systemic Dissemination in the Lone Star Tick, *Amblyomma americanum*. *J. Innate Immun.* **2024**, *16*, 66–79. [\[CrossRef\]](#)
22. Xavier, M.A.; Tirloni, L.; Pinto, A.F.M.; Diedrich, J.K.; Yates, J.R.; Mulenga, A.; Logullo, C.; Da Silva Vaz, I.; Seixas, A.; Termignoni, C. A Proteomic Insight into Vitellogenesis During Tick Ovary Maturation. *Sci. Rep.* **2018**, *8*, 4698. [\[CrossRef\]](#) [\[PubMed\]](#)
23. Barrero, R.A.; Guerrero, F.D.; Black, M.; McCooke, J.; Chapman, B.; Schilkey, F.; De León, A.A.P.; Miller, R.J.; Bruns, S.; Dobry, J.; et al. Gene-Enriched Draft Genome of the Cattle Tick *Rhipicephalus microplus*: Assembly by the Hybrid Pacific Biosciences/Illumina Approach Enabled Analysis of the Highly Repetitive Genome. *Int. J. Parasitol.* **2017**, *47*, 569–583. [\[CrossRef\]](#) [\[PubMed\]](#)
24. Vechtova, P.; Fussy, Z.; Cegan, R.; Sterba, J.; Erhart, J.; Benes, V.; Grubhoffer, L. Catalogue of Stage-Specific Transcripts in *Ixodes ricinus* and Their Potential Functions During the Tick Life-Cycle. *Parasites Vectors* **2020**, *13*, 311. [\[CrossRef\]](#)
25. Rispe, C.; Hervet, C.; De La Cotte, N.; Daveu, R.; Labadie, K.; Noel, B.; Aury, J.; Thany, S.; Taillebois, E.; Cartereau, A.; et al. Transcriptome of the Synganglion in the Tick *Ixodes ricinus* and Evolution of the Cys-Loop Ligand-Gated Ion Channel Family in Ticks. *BMC Genom.* **2022**, *23*, 463. [\[CrossRef\]](#)
26. Garcia, G.R.; Ribeiro, J.M.C.; Maruyama, S.R.; Gardinassi, L.G.; Nelson, K.; Ferreira, B.R.; Andrade, T.G.; De Miranda Santos, I.K.F. A Transcriptome and Proteome of the Tick *Rhipicephalus microplus* Shaped by the Genetic Composition of Its Hosts and Developmental Stage. *Sci. Rep.* **2020**, *10*, 12857. [\[CrossRef\]](#)
27. Ma, H.; Lao, Y.; Liu, S.; Ai, J.; Sun, X.; Zhang, W.; Kang, M.; Li, J.; Sun, Y. The Diurnal Salivary Glands Transcriptome of *Dermacentor nuttalli* from the First Four Days of Blood Feeding. *Ticks Tick Borne Dis.* **2023**, *14*, 102178. [\[CrossRef\]](#)
28. Maitre, A.; Kratou, M.; Corona-Guerrero, I.; Abuin-Denis, L.; Mateos-Hernández, L.; Mosqueda, J.; Almazan, C.; Said, M.B.; Piloto-Sardiñas, E.; Obregon, D.; et al. Differential Interactions of *Rickettsia* Species with Tick Microbiota in *Rhipicephalus sanguineus* and *Rhipicephalus turanicus*. *Sci. Rep.* **2024**, *14*, 20674. [\[CrossRef\]](#)
29. Adegoke, A.; Ribeiro, J.M.C.; Brown, S.; Smith, R.C.; Karim, S. *Rickettsia parkeri* Hijacks Tick Hemocytes to Manipulate Cellular and Humoral Transcriptional Responses. *Front. Immunol.* **2023**, *14*, 1094326. [\[CrossRef\]](#)
30. Guizzo, M.; Neupane, S.; Kucera, M.; Perner, J.; Frantová, H.; da Silva Vaz, I.; Oliveira, P.; Kopacek, P.; Zurek, L. Poor Unstable Midgut Microbiome of Hard Ticks Contrasts with Abundant and Stable Monospecific Microbiome in Ovaries. *Front. Cell. Infect. Microbiol.* **2020**, *10*, 211. [\[CrossRef\]](#)
31. Freitas, D.R.J.; Rosa, R.M.; Moraes, J.; Campos, E.; Logullo, C.; Da Silva Vaz, I.; Masuda, A. Relationship Between Glutathione S-Transferase, Catalase, Oxygen Consumption, Lipid Peroxidation and Oxidative Stress in Eggs and Larvae of *Boophilus microplus* (Acarina: Ixodidae). *Comp. Biochem. Physiol. A Mol. Integr. Physiol.* **2007**, *146*, 688–694. [\[CrossRef\]](#) [\[PubMed\]](#)
32. Hernandez, E.P.; Shimazaki, K.; Niihara, H.; Umemiya-Shirafuji, R.; Fujisaki, K.; Tanaka, T. Expression Analysis of Glutathione S-Transferases and Ferritins During the Embryogenesis of the Tick *Haemaphysalis longicornis*. *Heliyon* **2020**, *6*, e03644. [\[CrossRef\]](#) [\[PubMed\]](#)
33. Gao, Z.; Zheng, P.; Wang, K.; Ji, X.; Shi, Y.; Song, X.; Liu, J.; Yu, Z.; Yang, X. The Molecular and Functional Characterization of Ferritins in the Hard Tick *Hyalomma rufipes*. *Parasit. Vectors* **2022**, *15*, 368. [\[CrossRef\]](#)
34. Tang, X.; Huang, Y.; Lei, J.; Luo, H.; Zhu, X. The Single-Cell Sequencing: New Developments and Medical Applications. *Cell Biosci.* **2019**, *9*, 53. [\[CrossRef\]](#)
35. De La Fuente, J.; Kocan, K.M.; Almazán, C.; Blouin, E.F. RNA Interference for the Study and Genetic Manipulation of Ticks. *Trends Parasitol.* **2007**, *23*, 427–433. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Moraes, J.; Galina, A.; Alvarenga, P.H.; Rezende, G.L.; Masuda, A.; Da Silva Vaz, I.; Logullo, C. Glucose Metabolism During Embryogenesis of the Hard Tick *Boophilus microplus*. *Comp. Biochem. Physiol. A Mol. Integr. Physiol.* **2007**, *146*, 528–533. [\[CrossRef\]](#)
37. Logullo, C.; Witola, W.H.; Andrade, C.; Abreu, L.; Gomes, J.; Da Silva Vaz, I.; Imamura, S.; Konnai, S.; Ohashi, K.; Onuma, M. Expression and Activity of Glycogen Synthase Kinase During Vitellogenesis and Embryogenesis of *Rhipicephalus (Boophilus) microplus*. *Vet. Parasitol.* **2009**, *161*, 261–269. [\[CrossRef\]](#)
38. De Abreu, L.A.; Calixto, C.; Walthero, C.F.; Noce, B.P.D.; Githaka, N.W.; Seixas, A.; Parizi, L.F.; Konnai, S.; da Silva Vaz, I.; Ohashi, K.; et al. The Conserved Role of the AKT/GSK3 Axis in Cell Survival and Glycogen Metabolism in *Rhipicephalus (Boophilus) microplus* Embryo Tick Cell Line BME26. *Biochim. Biophys. Acta Gen. Subj.* **2013**, *1830*, 2574–2582. [\[CrossRef\]](#)
39. Fabres, A.; De Andrade, C.P.; Guizzo, M.; Sorgine, M.H.F.; Paiva-Silva, G.O.; Masuda, A.; da Silva Vaz, I.; Logullo, C. Effect of GSK-3 Activity, Enzymatic Inhibition and Gene Silencing by RNAi on Tick Oviposition and Egg Hatching. *Parasitology* **2010**, *137*, 1537–1546. [\[CrossRef\]](#)
40. Pohl, P.C.; Sorgine, M.H.F.; Leal, A.T.; Logullo, C.; Oliveira, P.L.; Da Silva Vaz, I.; Masuda, A. An Extraovarian Aspartic Protease Accumulated in Tick Oocytes with Vitellin-Degradation Activity. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.* **2008**, *151*, 392–399. [\[CrossRef\]](#)

41. Lyu, B.; Li, J.; Niemeyer, B.; Anderson, D.; Beerntsen, B.; Song, Q. Identification, Structural Modeling, Gene Expression Analysis and RNAi Effect of Putative Phospholipase A₂ in the Lone Star Tick *Amblyomma americanum*. *Ticks Tick Borne Dis.* **2024**, *15*, 102256. [[CrossRef](#)] [[PubMed](#)]
42. Nascimento-Silva, M.C.L.; Leal, A.T.; Daffre, S.; Juliano, L.; Da Silva Vaz, I.; Paiva-Silva, G.O.; Oliveira, P.L.; Sorgine, M.H.F. BYC, an Atypical Aspartic Endopeptidase from *Rhipicephalus (Boophilus) microplus* Eggs. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.* **2008**, *149*, 599–607. [[CrossRef](#)] [[PubMed](#)]
43. Campos, E.; Façanha, A.R.; Costa, E.P.; Da Silva Vaz, I.; Masuda, A.; Logullo, C. Exopolyphosphatases in Nuclear and Mitochondrial Fractions During Embryogenesis of the Hard Tick *Rhipicephalus (Boophilus) microplus*. *Comp. Biochem. Physiol. B Biochem. Mol. Biol.* **2008**, *151*, 311–316. [[CrossRef](#)]
44. De Dios-Blázquez, L.; Cano-Argüelles, A.L.; Pérez-Sánchez, R.; González-Sánchez, M.; Oleaga, A. First Data on Cholesterol Metabolism in *Ornithodoros* Argasid Ticks: Molecular and Functional Characterization of the N-Terminal Domain of Niemann-Pick C1 proteins. *Ticks Tick Borne Dis.* **2024**, *15*, 102382. [[CrossRef](#)] [[PubMed](#)]
45. Seixas, A.; Dos Santos, P.C.; Velloso, F.F.; Da Silva Vaz, I.; Masuda, A.; Horn, F.; Termignoni, C. A *Boophilus microplus* Vitellin-Degrading Cysteine Endopeptidase. *Parasitology* **2003**, *126*, 155–163. [[CrossRef](#)]
46. Seixas, A.; Oliveira, P.; Termignoni, C.; Logullo, C.; Masuda, A.; da Silva Vaz, I. *Rhipicephalus (Boophilus) microplus* Embryo Proteins as Target for Tick Vaccine. *Vet. Immunol. Immunopathol.* **2012**, *148*, 149–156. [[CrossRef](#)]
47. Alzugaray, M.F.; Parizi, L.F.; Seixas, A.; Benavides, U.; da Silva Vaz, I. Molecular and Functional Characterization of Bm05br Antigen from *Rhipicephalus microplus*. *Ticks Tick Borne Dis.* **2017**, *8*, 320–329. [[CrossRef](#)]
48. Rosche, K.L.; Hurtado, J.; Fisk, E.A.; Vosbigian, K.A.; Warren, A.L.; Sidak-Loftis, L.C.; Wright, S.J.; Ramirez-Zepp, E.; Park, J.M.; Shaw, D.K. PERK-Mediated Antioxidant Response is Key for Pathogen Persistence in Ticks. *mSphere* **2023**, *8*, e00321-23. [[CrossRef](#)]
49. Waltero, C.; de Abreu, L.A.; Alonso, T.; Nunes-da-Fonseca, R.; da Silva Vaz, I., Jr.; Logullo, C. TOR as a Regulatory Target in *Rhipicephalus microplus* Embryogenesis. *Front. Physiol.* **2019**, *10*, 965. [[CrossRef](#)]
50. Da Silva, R.M.; Daumas Filho, C.R.O.; Calixto, C.; da Silva, J.N.; Lopes, C.; da Silva Vaz, I., Jr.; Logullo, C. PEPCCK and Glucose Metabolism Homeostasis in Arthropods. *Insect Biochem. Mol. Biol.* **2023**, *160*, 103986. [[CrossRef](#)]
51. Murfin, K.E.; Kleinbard, R.; Aydin, M.; Salazar, S.A.; Fikrig, E. *Borrelia burgdorferi* Chemotaxis Toward Tick Protein Salp12 Contributes to Acquisition. *Ticks Tick Borne Dis.* **2019**, *10*, 1124–1134. [[CrossRef](#)]
52. Seixas, A.; Alzugaray, M.F.; Tirloni, L.; Parizi, L.F.; Pinto, A.F.M.; Githaka, N.W.; Konnai, S.; Ohashi, K.; Yates, J.R., III; Termignoni, C.; et al. Expression Profile of *Rhipicephalus microplus* Vitellogenin Receptor During Oogenesis. *Ticks Tick Borne Dis.* **2018**, *9*, 72–81. [[CrossRef](#)]
53. Tarazona, S.; Balzano-Nogueira, L.; Gómez-Cabrero, D.; Schmidt, A.; Imhof, A.; Hankemeier, T.; Tegnér, J.; Westerhuis, J.A.; Conesa, A. Harmonization of Quality Metrics and Power Calculation in Multi-Omic Studies. *Nat. Commun.* **2020**, *11*, 3092. [[CrossRef](#)]
54. Micheel, C.M.; Nass, S.J.; Omenn, G.S. *Evolution of Translational Omics: Lessons Learned and the Path Forward*. Institute of Medicine; The National Academies Press: Washington, DC, USA, 2012; p. 354.
55. Xiao, J.; Yao, X.; Guan, X.; Xiong, J.; Fang, Y.; Zhang, Y.; Zhang, Y.; Moming, A.; Su, Z.; Jin, J.; et al. Viromes of *Haemaphysalis longicornis* Reveal Different Viral Abundance and Diversity in Free and Engorged Ticks. *Virol. Sin.* **2024**, *39*, 194–204. [[CrossRef](#)] [[PubMed](#)]
56. Reyes, J.B.; McVicar, M.; Beniwal, S.; Sharma, A.; Tillett, R.; Petereit, J.; Nuss, A.; Gulia-Nuss, M. A Multi-Omics Approach for Understanding Blood Digestion Dynamics in *Ixodes scapularis* and Identification of Anti-Tick Vaccine Targets. *Ticks Tick Borne Dis.* **2024**, *15*, 102379. [[CrossRef](#)] [[PubMed](#)]
57. Sojka, D.; Franta, Z.; Horn, M.; Caffrey, C.R.; Mareš, M.; Kopáček, P. New Insights into the Machinery of Blood Digestion by Ticks. *Trends Parasitol.* **2013**, *29*, 276–285. [[CrossRef](#)] [[PubMed](#)]
58. Oleaga, A.; Obolo-Mvoulouga, P.; Manzano-Román, R.; Pérez-Sánchez, R. Midgut Proteome of an Argasid Tick, *Ornithodoros erraticus*: A Comparison between Unfed and Engorged Females. *Parasites Vectors* **2015**, *8*, 525. [[CrossRef](#)]
59. Cramaro, W.J.; Revets, D.; Hunewald, O.E.; Sinner, R.; Reye, A.L.; Muller, C.P. Integration of *Ixodes ricinus* Genome Sequencing with Transcriptome and Proteome Annotation of the Naïve Midgut. *BMC Genom.* **2015**, *16*, 871. [[CrossRef](#)]
60. Lu, S.; De Sousa, L.C.; Ribeiro, J.; Tirloni, L. Exploring Midgut Expression Dynamics: Longitudinal Transcriptomic Analysis of Adult Female *Amblyomma americanum* Midgut and Comparative Insights with Other Hard Tick Species. *bioRxiv* **2024**. [[CrossRef](#)]
61. Liu, L.; Cheng, T.; He, X. Proteomic Profiling of the Midgut Contents of *Haemaphysalis flava*. *Ticks Tick Borne Dis.* **2018**, *9*, 490–495. [[CrossRef](#)]
62. Mahmood, S.; Sima, R.; Urbanova, V.; Trentelman, J.J.A.; Krezdorn, N.; Winter, P.; Kopacek, P.; Hovius, J.W.; Hajdusek, O. Identification of Tick *Ixodes ricinus* Midgut Genes Differentially Expressed During the Transmission of *Borrelia afzelii* Spirochetes Using a Transcriptomic Approach. *Front. Immunol.* **2021**, *11*, 612412. [[CrossRef](#)]

63. Gulia-Nuss, M.; Nuss, A.B.; Meyer, J.M.; Sonenshine, D.E.; Roe, R.M.; Waterhouse, R.M.; Sattelle, D.B.; De La Fuente, J.; Ribeiro, J.M.; Megy, K.; et al. Genomic Insights into the *Ixodes scapularis* Tick Vector of Lyme Disease. *Nat. Commun.* **2016**, *7*, 10507. [\[CrossRef\]](#) [\[PubMed\]](#)
64. Jia, N.; Wang, J.; Shi, W.; Du, L.; Sun, Y.; Zhan, W.; Jiang, J.F.; Wang, Q.; Zhang, B.; Ji, P.; et al. Large-Scale Comparative Analyses of Tick Genomes Elucidate Their Genetic Diversity and Vector Capacities. *Cell* **2020**, *182*, 1328–1340.e13. [\[CrossRef\]](#) [\[PubMed\]](#)
65. Tirloni, L.; Lu, S.; Calvo, E.; Sabadin, G.; Di Maggio, L.; Suzuki, M.; Nardone, G.; Da Silva Vaz, I.; Ribeiro, J. Integrated Analysis of Sialotranscriptome and Sialoproteome of the Brown Dog Tick *Rhipicephalus sanguineus* (s.l.): Insights into Gene Expression During Blood Feeding. *J. Proteom.* **2020**, *229*, 103899. [\[CrossRef\]](#)
66. Da Silva Vaz, I.; Lu, S.; Pinto, A.F.M.; Diedrich, J.K.; Yates, J.R.; Mulenga, A.; Termignoni, C.; Ribeiro, J.M.; Tirloni, L. Changes in Saliva Protein Profile Throughout *Rhipicephalus microplus* Blood Feeding. *Parasites Vectors* **2024**, *17*, 36. [\[CrossRef\]](#)
67. Perner, J.; Kropáčková, S.; Kopáček, P.; Ribeiro, J.M.C. Sialome Diversity of Ticks Revealed by RNAseq of Single Tick Salivary Glands. *PLoS Negl. Trop. Dis.* **2018**, *12*, e0006410. [\[CrossRef\]](#)
68. Liu, L.; Cheng, R.; Mao, S.Q.; Duan, D.Y.; Feng, L.L.; Cheng, T.Y. Saliva Proteome of Partially- and Fully-Engorged Adult Female *Haemaphysalis flava* Ticks. *Vet. Parasitol.* **2023**, *318*, 109933. [\[CrossRef\]](#)
69. Tirloni, L.; Kim, T.K.; Coutinho, M.L.; Ali, A.; Seixas, A.; Termignoni, C.; Mulenga, A.; Da Silva Vaz, I. The Putative Role of *Rhipicephalus microplus* Salivary Serpins in the Tick-Host Relationship. *Insect Biochem. Mol. Biol.* **2016**, *71*, 12–28. [\[CrossRef\]](#)
70. Ribeiro, J.M.; Makoul, G.T.; Levine, J.; Robinson, D.R.; Spielman, A. Antihemostatic, Antiinflammatory, and Immunosuppressive Properties of the Saliva of a Tick, *Ixodes dammini*. *J. Exp. Med.* **1985**, *161*, 332–344. [\[CrossRef\]](#)
71. Šimo, L.; Kazimirova, M.; Richardson, J.; Bonnet, S.I. The Essential Role of Tick Salivary Glands and Saliva in Tick Feeding and Pathogen Transmission. *Front. Cell. Infect. Microbiol.* **2017**, *7*, 281. [\[CrossRef\]](#)
72. Ali, A.; Zeb, I.; Alouffi, A.; Zahid, H.; Almutairi, M.M.; Alshammari, F.A.; Alrouji, M.; Termignoni, C.; Da Silva Vaz, I.; Tanaka, T. Host Immune Responses to Salivary Components—A Critical Facet of Tick-Host Interactions. *Front. Cell. Infect. Microbiol.* **2022**, *12*, 809052. [\[CrossRef\]](#)
73. Hamsten, C.; Starkhammar, M.; Tran, T.; Johansson, M.; Bengtsson, U.; Ahlén, G.; Sällberg, M.; Grönlund, M.; van Hage, M. Identification of Galactose- α -1,3-Galactose in the Gastrointestinal Tract of the Tick *Ixodes ricinus*; Possible Relationship With Red Meat Allergy. *Allergy* **2013**, *68*, 549–552. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Sharma, S.; Crispell, G.; Mohamed, A.; Cox, C.; Lange, J.; Choudhary, S.; Commings, S.; Karim, S. Alpha-Gal Syndrome: Involvement of *Amblyomma americanum* α -D-Galactosidase and β -1,4 Galactosyltransferase Enzymes in α -Gal Metabolism. *Front. Cell. Infect. Microbiol.* **2021**, *11*, 775371. [\[CrossRef\]](#)
75. McGill, S.K.; Hashash, J.G.; Platts-Mills, T.A. AGA Clinical Practice Update on Alpha-Gal Syndrome for the GI Clinician: Commentary. *Clin. Gastroenterol. Hepatol.* **2023**, *21*, 891–896. [\[CrossRef\]](#)
76. Román-Carrasco, P.; Lieder, B.; Somoza, V.; Ponce, M.; Szépfalusi, Z.; Martin, D.; Hemmer, W.; Swoboda, I. Only α -Gal Bound to Lipids, but not to Proteins, is Transported Across Enterocytes as an IgE-Reactive Molecule that Can Induce Effector Cell Activation. *Allergy* **2019**, *74*, 1956–1968. [\[CrossRef\]](#)
77. Vaz-Rodrigues, R.; Mazuecos, L.; Villar, M.; Contreras, M.; González-García, A.; Bonini, P.; Scimeca, R.C.; Mulenga, A.; De La Fuente, J. Tick Salivary Proteome and Lipidome with Low Glycan Content Correlate with Allergic Type Reactions in the Zebrafish Model. *Int. J. Parasitol.* **2024**, *54*, 649–659. [\[CrossRef\]](#)
78. Mans, B.J.; Andersen, J.F.; Francischetti, I.M.B.; Valenzuela, J.G.; Schwan, T.G.; Pham, V.M.; Garfield, M.K.; Hammer, C.H.; Ribeiro, J.M.C. Comparative Sialomics Between Hard and Soft Ticks: Implications for the Evolution of Blood-Feeding Behavior. *Insect Biochem. Mol. Biol.* **2008**, *38*, 42–58. [\[CrossRef\]](#)
79. Chmelař, J.; Anderson, J.M.; Mu, J.; Jochim, R.C.; Valenzuela, J.G.; Kopecký, J. Insight into the Sialome of the Castor Bean Tick, *Ixodes ricinus*. *BMC Genom.* **2008**, *9*, 233. [\[CrossRef\]](#)
80. Tirloni, L.; Reck, J.; Terra, R.M.S.; Martins, J.R.; Mulenga, A.; Sherman, N.E.; Fox, J.W.; Yates, J.R.; Termignoni, C.; Pinto, A.F.M.; et al. Proteomic Analysis of Cattle Tick *Rhipicephalus (Boophilus) microplus* Saliva: A Comparison Between Partially and Fully Engorged Females. *PLoS ONE* **2014**, *9*, e94831. [\[CrossRef\]](#)
81. Kim, T.K.; Tirloni, L.; Bencosme-Cuevas, E.; Kim, T.H.; Diedrich, J.K.; Yates, J.R.; Mulenga, A. *Borrelia burgdorferi* Infection Modifies Protein Content in Saliva of *Ixodes scapularis* Nymphs. *BMC Genom.* **2021**, *22*, 152. [\[CrossRef\]](#)
82. Troxell, B.; Zhang, J.J.; Bourret, T.J.; Zeng, M.Y.; Blum, J.; Gherardini, F.; Hassan, H.M.; Yang, X.F. Pyruvate Protects Pathogenic Spirochetes from H₂O₂ Killing. *PLoS ONE* **2014**, *9*, e84625. [\[CrossRef\]](#)
83. Pietrantonio, P.V.; Xiong, C.; Nachman, R.J.; Shen, Y. G Protein-Coupled Receptors in Arthropod Vectors: Omics and Pharmacological Approaches to Elucidate Ligand-Receptor Interactions and Novel Organismal Functions. *Curr. Opin. Insect Sci.* **2018**, *29*, 12–20. [\[CrossRef\]](#) [\[PubMed\]](#)
84. Fredriksson, R.; Lagerström, M.C.; Lundin, L.G.; Schiöth, H.B. The G-protein-Coupled Receptors in the Human Genome Form Five Main Families. Phylogenetic Analysis, Paralogon Groups, and Fingerprints. *Mol. Pharmacol.* **2003**, *63*, 1256–1272. [\[CrossRef\]](#) [\[PubMed\]](#)

85. Kolakowski, L.F., Jr. GCRDb: A G-Protein-Coupled Receptor Database. *Recept. Channels* **1994**, *2*, 1–7. [\[PubMed\]](#)
86. Pándy-Szekeres, G.; Munk, C.; Tsonkov, T.M.; Mordalski, S.; Harpsøe, K.; Hauser, A.S.; Bojarski, A.J.; Gloriam, D.E. GPCRdb in 2018: Adding GPCR Structure Models and Ligands. *Nucleic Acids Res.* **2018**, *46*, D440–D446. [\[CrossRef\]](#)
87. Guerrero, F.D.; Kellogg, A.; Ogrey, A.N.; Heekin, A.M.; Barrero, R.; Bellgard, M.I.; Dowd, S.E.; Leung, M.Y. Prediction of G Protein-Coupled Receptor Encoding Sequences from the Synganglion Transcriptome of the Cattle Tick, *Rhipicephalus microplus*. *Ticks Tick Borne Dis.* **2016**, *7*, 670–677. [\[CrossRef\]](#)
88. Hauser, F.; Pallesen, M.; Lehnhoff, J.; Li, S.; Lind, A.; Grimmelikhuijzen, C.J. A Corazonin G Protein-Coupled Receptor Gene in the Tick *Ixodes scapularis* Yields Two Splice Variants, Each Coding for a Specific Corazonin Receptor. *Biochem. Biophys. Res. Commun.* **2023**, *666*, 162–169. [\[CrossRef\]](#)
89. Waldman, J.; Klafke, G.M.; Tirloni, L.; Logullo, C.; da Silva Vaz, I., Jr. Putative Target Sites in Synganglion for Novel Ixodid Tick Control Strategies. *Ticks Tick Borne Dis.* **2023**, *14*, 102123. [\[CrossRef\]](#)
90. Waldman, J.; Xavier, M.A.; Vieira, L.R.; Logullo, R.; Braz, G.R.C.; Tirloni, L.; Ribeiro, J.M.C.; Veenstra, J.A.; Silva Vaz, I.D. Neuropeptides in *Rhipicephalus microplus* and Other Hard Ticks. *Ticks Tick Borne Dis.* **2022**, *13*, 101910. [\[CrossRef\]](#)
91. Rutz, C.; Klein, W.; Schüle, R. N-Terminal Signal Peptides of G Protein-Coupled Receptors: Significance for Receptor Biosynthesis, Trafficking, and Signal Transduction. *Prog. Mol. Biol. Transl. Sci.* **2015**, *132*, 267–287. [\[CrossRef\]](#)
92. Hauser, F.; Cazzamali, G.; Williamson, M.; Park, Y.; Li, B.; Tanaka, Y.; Predel, R.; Neupert, S.; Schachtner, J.; Verleyen, P.; et al. A Genome-Wide Inventory of Neurohormone GPCRs in the Red Flour Beetle *Tribolium castaneum*. *Front. Neuroendocrinol.* **2008**, *29*, 142–165. [\[CrossRef\]](#) [\[PubMed\]](#)
93. Kramer, S.J.; Toschi, A.; Miller, C.A.; Kataoka, H.; Quistad, G.B.; Li, J.P.; Carney, R.L.; Schooley, D.A. Identification of an Allatostatin from the Tobacco Hornworm *Manduca sexta*. *Proc. Natl. Acad. Sci. USA* **1991**, *88*, 9458–9462. [\[CrossRef\]](#)
94. Veenstra, J.A. Allatostatins C, Double C and Triple C: The Result of a Local Gene Triplication in an Ancestral Arthropod. *Gen. Comp. Endocrinol.* **2016**, *230–231*, 153–157. [\[CrossRef\]](#)
95. Kreienkamp, H.J.; Larusson, H.J.; Witte, I.; Roeder, T.; Birgul, N.; Honck, H.H.; Harder, S.; Ellinghausen, G.; Buck, F.; Richter, D. Functional Annotation of Two Orphan G-Protein-Coupled Receptors, Drostar1 and -2, from *Drosophila melanogaster* and Their Ligands by Reverse Pharmacology. *J. Biol. Chem.* **2002**, *277*, 39937–39943. [\[CrossRef\]](#) [\[PubMed\]](#)
96. Veenstra, J.A. Allatostatin C and Its Paralog Allatostatin Double C: The Arthropod Somatostatins. *Insect Biochem. Mol. Biol.* **2009**, *39*, 161–170. [\[CrossRef\]](#)
97. Debnath, M.; Prasad, G.B.; Bisen, P.S. Omics Technology. In *Molecular Diagnostics: Promises and Possibilities*; Springer eBook: Dordrecht, The Netherlands, 2010; pp. 11–31. [\[CrossRef\]](#)
98. De Araujo, A.C.; Noël, B.; Bretaudeau, A.; Labadie, K.; Boudet, M.; Tadrent, N.; Istace, B.; Kritli, S.; Cruaud, C.; Olasso, R.; et al. Genome Sequences of Four *Ixodes* Species Expands Understanding of Tick Evolution. *BMC Biol.* **2024**, *23*, 17. [\[CrossRef\]](#)
99. Narasimhan, S.; Fikrig, E. Tick Microbiome: The Force Within. *Trends Parasitol.* **2015**, *31*, 315–323. [\[CrossRef\]](#)
100. De, S.; Kingan, S.; Kitsou, C.; Portik, D.; Foor, S.; Frederick, C.; Rana, V.; Paulat, N.; Ray, D.; Wang, Y.; et al. A high-quality *Ixodes scapularis* genome advances tick science. *Nat. Genet.* **2023**, *55*, 301–311. [\[CrossRef\]](#)
101. Duron, O.; Morel, O.; Noël, V.; Buysse, M.; Binetruy, F.; Lancelot, R.; Loire, E.; Ménard, C.; Bouchez, O.; Vavre, F.; et al. Tick-Bacteria Mutualism Depends on B Vitamin Synthesis Pathways. *Curr. Biol.* **2018**, *28*, 1896–1902.e5. [\[CrossRef\]](#)
102. Xu, Z.; Li, W.; Dong, X.; Chen, Y.; Zhang, D.; Wang, J.; Zhou, L.; He, G. Precision Medicine in Colorectal Cancer: Leveraging Multi-Omics, Spatial Omics, and Artificial Intelligence. *Clin. Chim. Acta* **2024**, *559*, 119686. [\[CrossRef\]](#)
103. Fountain-Jones, N.M.; Khoo, B.S.; Rau, A.; Berman, J.D.; Burton, E.N.; Oliver, J.D. Positive Associations Matter: Microbial Relationships Drive Tick Microbiome Composition. *Mol. Ecol.* **2023**, *32*, 4078–4092. [\[CrossRef\]](#) [\[PubMed\]](#)
104. Swee, A.; Kwan, J.Y. Tick Microbiome and Pathogen Acquisition Altered by Host Blood Meal. *ISME J.* **2017**, *11*, 813–816. [\[CrossRef\]](#) [\[PubMed\]](#)
105. Du, L.F.; Zhang, M.Z.; Yuan, T.T.; Ni, X.B.; Wei, W.; Cui, X.M.; Wang, N.; Xiong, T.; Zhang, J.; Pan, Y.S.; et al. New Insights Into the Impact of Microbiome on Horizontal and Vertical Transmission of a Tick-Borne Pathogen. *Microbiome* **2023**, *11*, 50. [\[CrossRef\]](#)
106. Kocan, K.M.; De La Fuente, J.; Blouin, E.F.; Coetzee, J.F.; Ewing, S.A. The Natural History of *Anaplasma marginale*. *Vet. Parasitol.* **2010**, *167*, 95–107. [\[CrossRef\]](#) [\[PubMed\]](#)
107. Aguilar-Díaz, H.; Quiroz-Castañeda, R.E.; Salazar-Morales, K.; Cossío-Bayúgar, R.; Miranda-Miranda, E. Tick Immunobiology and Extracellular Traps: An Integrative Vision to Control of Vectors. *Pathogens* **2021**, *10*, 1511. [\[CrossRef\]](#)
108. Bonnet, S.I.; Pollet, T. Update on the Intricate Tango Between Tick Microbiomes and Tick-Borne Pathogens. *Parasite Immunol.* **2021**, *43*, e12813. [\[CrossRef\]](#)
109. Adegoke, A.; Ribeiro, J.M.C.; Smith, R.C.; Karim, S. Tick Innate Immune Responses to Hematophagy and *Ehrlichia* Infection at Single-Cell Resolution. *Front. Immunol.* **2024**, *14*, 1305976. [\[CrossRef\]](#)
110. Egan, S.L.; Loh, S.M.; Banks, P.B.; Gillett, A.; Ahlstrom, L.; Ryan, U.M.; Irwin, P.J.; Oskam, C.L. Bacterial Community Profiling Highlights Complex Diversity and Novel Organisms in Wildlife Ticks. *Ticks Tick Borne Dis.* **2020**, *11*, 101407. [\[CrossRef\]](#)

111. Gofton, A.W.; Doggett, S.; Ratchford, A.; Ryan, U.; Irwin, P. Phylogenetic Characterisation of Two Novel Anaplasmataceae From Australian *Ixodes holocyclus* Ticks: 'Candidatus Neoehrlichia australis' and 'Candidatus Neoehrlichia arcana'. *Int. J. Syst. Evol. Microbiol.* **2016**, *66*, 4256–4261. [\[CrossRef\]](#)
112. Egan, S.L.; Taylor, C.L.; Banks, P.B.; Northover, A.S.; Ahlstrom, L.A.; Ryan, U.M.; Irwin, P.J.; Oskam, C.L. The Bacterial Biome of Ticks and Their Wildlife Hosts at the Urban-Wildland Interface. *Microb. Genom.* **2021**, *7*, 000730. [\[CrossRef\]](#)
113. Guizzo, M.G.; Dolezelikova, K.; Neupane, S.; Frantova, H.; Hrbatova, A.; Pafco, B.; Fiorotti, J.; Kopacek, P.; Zurek, L. Characterization and Manipulation of the Bacterial Community in the Midgut of *Ixodes ricinus*. *Parasites Vectors* **2022**, *15*, 248. [\[CrossRef\]](#) [\[PubMed\]](#)
114. Moreno, C.X.; Moy, F.; Daniels, T.J.; Godfrey, H.P.; Cabello, F.C. Molecular Analysis of Microbial Communities Identified in Different Developmental Stages of *Ixodes scapularis* Ticks from Westchester and Dutchess Counties, New York. *Environ. Microbiol.* **2006**, *8*, 761–772. [\[CrossRef\]](#)
115. Duan, D.; Cheng, T. Determination of the Microbial Community Features of *Haemaphysalis flava* in Different Developmental Stages by High-Throughput Sequencing. *J. Basic Microbiol.* **2017**, *57*, 302–308. [\[CrossRef\]](#) [\[PubMed\]](#)
116. Umemiya-Shirafuji, R.; Xuan, X.; Fujisaki, K.; Yamagishi, J. Draft Genome Sequence Data of *Haemaphysalis longicornis* Oita Strain. *Data Brief.* **2023**, *49*, 109352. [\[CrossRef\]](#)
117. Duan, D.Y.; Liu, Y.K.; Liu, L.; Liu, G.H.; Cheng, T.Y. Microbiome Analysis of the Midguts of Different Developmental Stages of *Argas persicus* in China. *Ticks Tick Borne Dis.* **2022**, *13*, 101868. [\[CrossRef\]](#) [\[PubMed\]](#)
118. Li, L.F.; Wei, R.; Liu, H.B.; Jiang, B.G.; Cui, X.M.; Wei, W.; Hu, Y.L. Characterization of Microbial Communities in *Ixodes persulcatus* (Ixodida: Ixodidae), A Veterinary and Medical Important Tick Species in Northeastern China. *J. Med. Entomol.* **2020**, *57*, 1270–1276. [\[CrossRef\]](#) [\[PubMed\]](#)
119. Zhang, R.; Yu, G.; Huang, Z.; Zhang, Z. Microbiota Assessment Across Different Developmental Stages of *Dermacentor silvarum* (Acari: Ixodidae) Revealed Stage-Specific Signatures. *Ticks Tick Borne Dis.* **2020**, *11*, 101321. [\[CrossRef\]](#)
120. Wilson, J.M.; Breitschwerdt, E.B.; Juhasz, N.B.; Marr, H.S.; de Brito Galvão, J.F.; Pratt, C.L.; Qurollo, B.A. Novel *Rickettsia* Species Infecting Dogs, United States. *Emerg. Infect. Dis.* **2020**, *12*, 3011–3015. [\[CrossRef\]](#)
121. Duncan, K.T.; Elshahed, M.S.; Sundstrom, K.D.; Little, S.E.; Youssef, N.H. Influence of Tick Sex and Geographic Region on the Microbiome of *Dermacentor variabilis* Collected from Dogs and Cats Across the United States. *Ticks Tick Borne Dis.* **2022**, *13*, 102002. [\[CrossRef\]](#)
122. Wu-Chuang, A.; Mateos-Hernandez, L.; Maitre, A.; Rego, R.O.M.; Šíma, R.; Porcelli, S.; Rakotobe, S.; Foucault-Simonin, A.; Moutailler, S.; Palinauskas, V.; et al. Microbiota Perturbation by Anti-Microbiota Vaccine Reduces the Colonization of *Borrelia afzelii* in *Ixodes ricinus*. *Microbiome* **2023**, *11*, 151. [\[CrossRef\]](#)
123. Lew-Tabor, A.E.; Valle, M.R. A Review of Reverse Vaccinology Approaches for the Development of Vaccines Against Ticks and Tick Borne Diseases. *Ticks Tick Borne Dis.* **2016**, *7*, 573–585. [\[CrossRef\]](#) [\[PubMed\]](#)
124. Zhang, B.; Zhang, N.; Zheng, T.; Lu, M.; Baoli, B.; Jie, R.; Wang, X.; Li, K. Tick-borne bacterial agents in *Hyalomma asiaticum* ticks from Xinjiang Uygur Autonomous Region, Northwest China. *Parasites Vectors* **2024**, *17*, 167. [\[CrossRef\]](#) [\[PubMed\]](#)
125. Mateos-Hernández, L.; Obregón, D.; Maye, J.; Borneres, J.; Versille, N.; de la Fuente, J.; Estrada-Peña, A.; Hodžić, A.; Šimo, L.; Cabezas-Cruz, A. Anti-Tick Microbiota Vaccine Impacts *Ixodes ricinus* Performance During Feeding. *Vaccines* **2020**, *8*, 702. [\[CrossRef\]](#) [\[PubMed\]](#)
126. Mateos-Hernández, L.; Obregón, D.; Wu-Chuang, A.; Maye, J.; Bornères, J.; Versillé, N.; de la Fuente, J.; Díaz-Sánchez, S.; Bermúdez-Humarán, L.G.; Torres-Maravilla, E.; et al. Anti-Microbiota Vaccines Modulate the Tick Microbiome in a Taxon-Specific Manner. *Front. Immunol.* **2021**, *12*, 704621. [\[CrossRef\]](#)
127. Cano-Argüelles, A.L.; Piloto-Sardiñas, E.; Maitre, A.; Mateos-Hernández, L.; Maye, J.; Wu-Chuang, A.; Abuin-Denis, L.; Obregón, D.; Bamgbose, T.; Oleaga, A.; et al. Microbiota-Driven Vaccination in Soft Ticks: Implications for Survival, Fitness and Reproductive Capabilities in *Ornithodoros moubata*. *Mol. Ecol.* **2024**, *33*, e17506. [\[CrossRef\]](#)
128. Kim, D.; Li, R.; Dudek, S.; Ritchie, M. Identifying Interactions Between Different Levels of Genomic Data Associated with Cancer Clinical Outcomes Using Grammatical Evolution Neural Network. *BioData Min.* **2013**, *6*, 23. [\[CrossRef\]](#)
129. Xian, T.; Cao, M.; Chen, K.; Zhao, W.; Liu, Y.; Yao, W.; Guang, H.; Yang, Y.; Su, M.; Zhang, R.; et al. Identification of a Novel Protein Hq023 of the Hard Tick *Haemaphysalis qinghaiensis* and Preliminary Evaluation of Its Analgesic Effect in Mice Model. *Parasitol. Int.* **2024**, *103*, 102933. [\[CrossRef\]](#)
130. Batista, I.F.; Chudzinski-Tavassi, A.M.; Faria, F.; Simons, S.M.; Barros-Batestti, D.M.; Labruna, M.B.; Leão, L.I.; Ho, P.L.; Junqueira-De-Azevedo, I.L.M. Expressed Sequence Tags (ESTs) from the Salivary Glands of the Tick *Amblyomma cajennense* (Acari: Ixodidae). *Toxicon* **2007**, *51*, 823–834. [\[CrossRef\]](#)
131. Batista, I.F.C.; Ramos, O.H.P.; Ventura, J.S.; Junqueira-De-Azevedo, I.L.M.; Ho, P.L.; Chudzinski-Tavassi, A.M. A New Factor Xa Inhibitor from *Amblyomma cajennense* with a Unique Domain Composition. *Arch. Biochem. Biophys.* **2009**, *493*, 151–156. [\[CrossRef\]](#)

132. Chudzinski-Tavassi, A.M.; De-Sá-Júnior, P.L.; Simons, S.M.; Maria, D.A.; De Souza Ventura, J.; De Fátima Correia Batista, I.; Faria, F.; Durães, E.; Reis, E.M.; Demasi, M. A New Tick Kunitz Type Inhibitor, Amblyomin-X, Induces Tumor Cell Death by Modulating Genes Related to the Cell Cycle and Targeting the Ubiquitin-Proteasome System. *Toxicon* **2010**, *56*, 1145–1154. [\[CrossRef\]](#)
133. Cabezas-Cruz, A.; Tonk, M.; Bouchut, A.; Pierrot, C.; Pierce, R.J.; Kotsyfakis, M.; Rahnamaeian, M.; Vilcinskis, A.; Khalife, J.; Valdés, J.J. Antiplasmodial Activity Is an Ancient and Conserved Feature of Tick Defensins. *Front. Microbiol.* **2016**, *7*, 1682. [\[CrossRef\]](#)
134. Aljamali, M.N.; Hern, L.; Kupfer, D.; Downard, S.; So, S.; Roe, B.A.; Sauer, J.R.; Essenberg, R.C. Transcriptome Analysis of the Salivary Glands of the Female Tick *Amblyomma americanum* (Acari: Ixodidae). *Insect Mol. Biol.* **2009**, *18*, 129–154. [\[CrossRef\]](#) [\[PubMed\]](#)
135. Bullard, R.L.; Williams, J.; Karim, S. Temporal Gene Expression Analysis and RNA Silencing of Single and Multiple Members of Gene Family in the Lone Star Tick *Amblyomma americanum*. *PLoS ONE* **2016**, *11*, e0147966. [\[CrossRef\]](#)
136. Murfin, K.E.; Fikrig, E. Tick Bioactive Molecules as Novel Therapeutics: Beyond Vaccine Targets. *Front. Cell. Infect. Microbiol.* **2017**, *7*, 222. [\[CrossRef\]](#)
137. Kuhn, N.; Schmidt, C.Q.; Schlapschy, M.; Skerra, A. PASylated Coversin, a C5-Specific Complement Inhibitor with Extended Pharmacokinetics, Shows Enhanced Anti-Hemolytic Activity in Vitro. *Bioconjugate Chem.* **2016**, *27*, 2359–2371. [\[CrossRef\]](#)
138. Pischke, S.E.; Gustavsen, A.; Orrem, H.L.; Egge, K.H.; Courivaud, F.; Fontenelle, H.; Despont, A.; Bongoni, A.K.; Rieben, R.; Tønnessen, T.I.; et al. Complement Factor 5 Blockade Reduces Porcine Myocardial Infarction Size and Improves Immediate Cardiac Function. *Basic Res. Cardiol.* **2017**, *112*, 20. [\[CrossRef\]](#) [\[PubMed\]](#)
139. Cano-Argüelles, A.L.; Pérez-Sánchez, R.; Oleaga, A. A microRNA Profile of the Saliva in the Argasid Ticks *Ornithodoros erraticus* and *Ornithodoros moubata* and Prediction of Specific Target Genes. *Ticks Tick Borne Dis.* **2023**, *14*, 102249. [\[CrossRef\]](#)
140. Luo, J.; Tan, Y.; Zhao, S.; Ren, Q.; Guan, G.; Luo, J.; Yin, H.; Liu, G. Role of Recognition MicroRNAs in *Haemaphysalis longicornis* and *Theileria orientalis* Interactions. *Pathogens* **2024**, *13*, 288. [\[CrossRef\]](#)
141. Léger, E.; Vourc'h, G.; Vial, L.; Chevillon, C.; McCoy, K.D. Changing Distributions of Ticks: Causes and Consequences. *Exp. Appl. Acarol.* **2013**, *59*, 219–244. [\[CrossRef\]](#) [\[PubMed\]](#)
142. Makwarela, T.G.; Nyangiwe, N.; Masebe, T.; Mbizeni, S.; Nesengani, L.T.; Djikeng, A.; Mapholi, N.O. Tick Diversity and Distribution of Hard (Ixodidae) Cattle Ticks in South Africa. *Microbiol. Res.* **2023**, *14*, 42–59. [\[CrossRef\]](#)
143. Agwunobi, D.; Pei, T.; Bai, R.; Wang, Z.; Shi, X.; Zhang, M.; Yu, Z.; Liu, J. miR-2a and miR-279 are Functionally Associated with Cold Tolerance in *Dermacentor silvarum* (Acari: Ixodidae). *Comp. Biochem. Physiol. D Genom. Proteom.* **2022**, *41*, 100946. [\[CrossRef\]](#)
144. De Rouck, S.; İnak, E.; Dermauw, W.; Van Leeuwen, T. A Review of the Molecular Mechanisms of Acaricide Resistance in Mites and Ticks. *Insect Biochem. Mol. Biol.* **2023**, *159*, 103981. [\[CrossRef\]](#)
145. Kunz, S.E.; Kemp, D.H. Insecticides and Acaricides: Resistance and Environmental Impact. *Rev. Sci. Tech. (Int. Off. Epizoot.)* **1994**, *13*, 1249–1286. [\[CrossRef\]](#)
146. Araya-Anchetta, A.; Busch, J.D.; Scoles, G.A.; Wagner, D.M. Thirty Years of Tick Population Genetics: A Comprehensive Review. *Infect. Genet. Evol.* **2015**, *29*, 164–179. [\[CrossRef\]](#)
147. Robbertse, L.; Baron, S.; van der Merwe, N.A.; Madder, M.; Stoltz, W.H.; Maritz-Olivier, C. Genetic Diversity, Acaricide Resistance Status and Evolutionary Potential of a *Rhipicephalus microplus* Population from a Disease-Controlled Cattle Farming Area in South Africa. *Ticks Tick Borne Dis.* **2016**, *7*, 595–603. [\[CrossRef\]](#)
148. Kumar, R. Molecular Markers and Their Application in the Monitoring of Acaricide Resistance in *Rhipicephalus microplus*. *Exp. Appl. Acarol.* **2019**, *78*, 149–172. [\[CrossRef\]](#)
149. Templeton, A.R. Nested Clade Analyses of Phylogeographic Data: Testing Hypotheses about Gene Flow and Population History. *Mol. Ecol.* **1998**, *7*, 381–397. [\[CrossRef\]](#)
150. Avise, J.C. *Phylogeography: The History and Formation of Species*; Harvard University Press: Cambridge, MA, USA, 2000; Volume 447. [\[CrossRef\]](#)
151. Røed, K.H.; Kvie, K.S.; Hasle, G.; Gilbert, L.; Leinaas, H.P. Phylogenetic Lineages and Postglacial Dispersal Dynamics Characterize the Genetic Structure of the Tick, *Ixodes ricinus*, in Northwest Europe. *PLoS ONE* **2016**, *11*, e0167450. [\[CrossRef\]](#)
152. Wu, C. Heat Shock Transcription Factors: Structure and Regulation. *Annu. Rev. Cell Dev. Biol.* **1995**, *11*, 441–469. [\[CrossRef\]](#)
153. Tutar, L.; Tutar, Y. Heat Shock Proteins; An Overview. *Curr. Pharm. Biotechnol.* **2010**, *11*, 216–222. [\[CrossRef\]](#) [\[PubMed\]](#)
154. Villar, M.; Ayllón, N.; Busby, A.T.; Galindo, R.C.; Blouin, E.F.; Kocan, K.M.; de la Fuente, J. Expression of Heat Shock and Other Stress Response Proteins in Ticks and Cultured Tick Cells in Response to *Anaplasma* spp. Infection and Heat Shock. *Int. J. Proteom.* **2010**, *2010*, 657261. [\[CrossRef\]](#)
155. Bullard, R.; Sharma, S.R.; Das, P.K.; Morgan, S.E.; Karim, S. Repurposing of Glycine-Rich Proteins in Abiotic and Biotic Stresses in the Lone-Star Tick (*Amblyomma americanum*). *Front. Physiol.* **2019**, *10*, 744. [\[CrossRef\]](#)
156. Yunik, M.E.; Chilton, N.B. Supercooling Points of Adult *Dermacentor variabilis* (Acari: Ixodidae) from a Population Near the Northern Distribution Limit. *J. Med. Entomol.* **2021**, *58*, 961–964. [\[CrossRef\]](#)

157. Maldonado-Ruiz, L.P.; Urban, J.; Davis, B.N.; Park, J.J.; Zurek, L.; Park, Y. Dermal Secretion Physiology and Thermoregulation in the Lone Star Tick, *Amblyomma americanum*. *Ticks Tick Borne Dis.* **2022**, *13*, 101962. [\[CrossRef\]](#)
158. Toxopeus, J.; Sinclair, B.J. Mechanisms Underlying Insect Freeze Tolerance. *Biol. Rev.* **2018**, *93*, 1891–1914. [\[CrossRef\]](#)
159. Zhou, X.; Zhang, H.; He, L.; Wu, X.; Yin, Y. Long-Term L-Serine Administration Reduces Food Intake and Improves Oxidative Stress and Sirt1/NFκB Signaling in the Hypothalamus of Aging Mice. *Front. Endocrinol.* **2018**, *9*, 476. [\[CrossRef\]](#)
160. Agwunobi, D.O.; Wang, T.; Zhang, M. Functional Implication of Heat Shock Protein 70/90 and Tubulin in Cold Stress of *Dermacentor silvarum*. *Parasites Vectors* **2021**, *14*, 542. [\[CrossRef\]](#)
161. Wang, H.; Lei, Z.; Li, X.; Oetting, R.D. Rapid Cold Hardening and Expression of Heat Shock Protein Genes in the B-Biotype *Bemisia tabaci*. *Environ. Entomol.* **2011**, *40*, 132–139. [\[CrossRef\]](#)
162. Ji, H.; Wu, Y.K.; Guo, J.R.; Wang, J.F.; Li, S.Z.; Yang, H.M.; Liu, J.X. Effects of Cold Stress on Expression of *Hsp70* Gene in Blood Lymphocyte of Piglets. *Int. J. Anim. Vet. Adv.* **2012**, *11*, 3914–3920.
163. Garbuz, D.G. Regulation of Heat Shock Gene Expression in Response to Stress. *Mol. Biol.* **2017**, *51*, 352–367. [\[CrossRef\]](#)
164. Reinders, J.; Wulff, B.B.; Mirouze, M.; Marí-Ordóñez, A.; Dapp, M.; Rozhon, W. Compromised Stability of DNA Methylation and Transposon Immobilization in Mosaic Arabidopsis Epigenomes. *Genes Dev.* **2009**, *23*, 939–950. [\[CrossRef\]](#) [\[PubMed\]](#)
165. Agwunobi, D.O.; Zhang, M.; Shi, X.; Zhang, S.; Zhang, M.; Wang, T.; Masoudi, A.; Yu, Z.; Liu, J. DNA Methyltransferases Contribute to Cold Tolerance in Ticks *Dermacentor silvarum* and *Haemaphysalis longicornis* (Acari: Ixodidae). *Front. Vet. Sci.* **2021**, *8*, 726731. [\[CrossRef\]](#) [\[PubMed\]](#)
166. Eisen, R.J.; Eisen, L.; Ogden, N.H.; Beard, C.B. Linkages of Weather and Climate with *Ixodes scapularis* and *Ixodes pacificus* (Acari: Ixodidae), Enzootic Transmission of *Borrelia burgdorferi*, and Lyme Disease in North America. *J. Med. Entomol.* **2016**, *53*, 250–261. [\[CrossRef\]](#)
167. De Silva, A.M.; Fikrig, E. Growth and Migration of *Borrelia burgdorferi* in *Ixodes* Ticks During Blood Feeding. *Am. J. Trop. Med. Hyg.* **1995**, *53*, 397–404. [\[CrossRef\]](#)
168. De la Fuente, J.; Antunes, S.; Bonnet, S.; Cabezas-Cruz, A.; Domingos, A.G.; Estrada-Peña, A.; Rego, R.O. Tick-Pathogen Interactions and Vector Competence: Identification of Molecular Drivers for Tick-Borne Diseases. *Front. Cell. Infect. Microbiol.* **2017**, *7*, 114. [\[CrossRef\]](#)
169. Kurokawa, C.; Lynn, G.E.; Pedra, J.H.; Pal, U.; Narasimhan, S.; Fikrig, E. Interactions between *Borrelia burgdorferi* and ticks. *Nat. Rev. Microbiol.* **2020**, *18*, 587–600. [\[CrossRef\]](#)
170. De Castro, M.H.; De Klerk, D.; Pienaar, R.; Rees, D.J.G.; Mans, B.J. Sialotranscriptomics of *Rhipicephalus zambeziensis* Reveals Intricate Expression Profiles of Secretory Proteins and Suggests Tight Temporal Transcriptional Regulation During Blood-Feeding. *Parasites Vectors* **2017**, *10*, 384. [\[CrossRef\]](#)
171. Rodríguez-Valle, M.; Moolhuijzen, P.; Barrero, R.A.; Ong, C.T.; Busch, G.; Karbanowicz, T.; Tabor, A.E. Transcriptome and Toxin Family Analysis of the Paralysis Tick, *Ixodes holocyclus*. *Int. J. Parasitol.* **2018**, *48*, 71–82. [\[CrossRef\]](#) [\[PubMed\]](#)
172. Narasimhan, S.; Booth, C.J.; DePonte, K.; Wu, M.J.; Liang, X.; Mohanty, S.; Fikrig, E. Host-Specific Expression of *Ixodes scapularis* Salivary Genes. *Ticks Tick Borne Dis.* **2019**, *10*, 386–397. [\[CrossRef\]](#)
173. Corley, S.W.; Jonsson, N.N.; Piper, E.K.; Cutullé, C.; Stear, M.J.; Seddon, J.M. Mutation in the *RmβAOR* Gene Is Associated with Amitraz Resistance in the Cattle Tick *Rhipicephalus microplus*. *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 16772–16777. [\[CrossRef\]](#)
174. Margos, G.; Hepner, S.; Mang, C.; Marosevic, D.; Reynolds, S.E.; Krebs, S.; Fingerle, V. Lost in Plasmids: Next Generation Sequencing and the Complex Genome of the Tick-Borne Pathogen *Borrelia burgdorferi*. *BMC Genom.* **2017**, *18*, 422. [\[CrossRef\]](#)
175. De la Canal, L.H.; Dall'Agnol, B.; Webster, A.; Reck, J.; Martins, J.R.; Klafke, G.M. Mechanisms of Amitraz Resistance in a *Rhipicephalus microplus* Strain from Southern Brazil. *Ticks Tick Borne Dis.* **2021**, *12*, 101764. [\[CrossRef\]](#)
176. Villar, D.; Klafke, G.M.; Rodríguez-Durán, A.; Bossio, F.; Miller, R.; Perez de Leon, A.A.; Chaparro-Gutiérrez, J.J. Resistance Profile and Molecular Characterization of Pyrethroid Resistance in a *Rhipicephalus microplus* Strain from Colombia. *Med. Vet. Entomol.* **2020**, *34*, 105–115. [\[CrossRef\]](#)
177. Obaid, M.K.; Almutairi, M.M.; Alouffi, A.; Safi, S.Z.; Tanaka, T.; Ali, A. Assessment of Cypermethrin and Amitraz Resistance and Molecular Profiling of Voltage-Gated Sodium Channel and Octopamine Tyramine Genes of *Rhipicephalus microplus*. *Front. Cell. Infect. Microbiol.* **2023**, *13*, 1176013. [\[CrossRef\]](#)
178. Kanampalliwar, A.; Soni, R.; Girdhar, A.; Tiwari, A. Reverse Vaccinology: Basics and Applications. *Open Vaccine J.* **2013**, *4*, 1–5. [\[CrossRef\]](#)
179. Abbas, M.N.; Jmel, M.A.; Mekki, I.; Dijkgraaf, I.; Kotsyfakis, M. Recent Advances in Tick Antigen Discovery and Anti-Tick Vaccine Development. *Int. J. Mol. Sci.* **2023**, *24*, 4969. [\[CrossRef\]](#)
180. De La Fuente, J.; Ghosh, S. Evolution of Tick Vaccinology. *Parasitology* **2024**, *151*, 1045–1052. [\[CrossRef\]](#)
181. Sobrino, I.; Villar, M.; De La Fuente, J. The Path to Anti-Vector Vaccines: Current Advances and Limitations in Proteomics and Bioinformatics. *Expert Rev. Proteom.* **2024**, *21*, 497–500. [\[CrossRef\]](#)
182. Díaz-Martín, V.; Manzano-Román, R.; Obolo-Mvoulouga, P.; Oleaga, A.; Pérez-Sánchez, R. Development of Vaccines against *Ornithodoros* Soft Ticks: An Update. *Ticks Tick Borne Dis.* **2015**, *6*, 211–220. [\[CrossRef\]](#)

183. Domingues, L.N.; Bendele, K.G.; Bodine, D.M.; Halos, L.; Cutolo, A.A.; Liebshtein, M.; Widener, J.; Figueiredo, M.; Moreno, Y.; Epe, C.; et al. A Reverse Vaccinology Approach Identified Novel Recombinant Tick Proteins with Protective Efficacy against *Rhipicephalus Microplus* Infestation. *Ticks Tick Borne Dis.* **2024**, *15*, 102403. [\[CrossRef\]](#)
184. Ndekezi, C.; Nkamwesiga, J.; Ochwo, S.; Kimuda, M.P.; Mwiine, F.N.; Twayongyere, R.; Amanyire, W.; Muhanguzi, D. *In Silico* Analysis of Ixodid Tick Aquaporin-1 Protein as a Candidate Anti-Tick Vaccine Antigen. *BioRxiv* **2019**. [\[CrossRef\]](#)
185. Couto, J.; Seixas, G.; Stutzer, C.; Olivier, N.A.; Maritz-Olivier, C.; Antunes, S.; Domingos, A. Probing the *Rhipicephalus bursa* Sialomes in Potential Anti-Tick Vaccine Candidates: A Reverse Vaccinology Approach. *Biomedicines* **2021**, *9*, 363. [\[CrossRef\]](#)
186. Obolo-Mvoulouga, P.; Oleaga, A.; Manzano-Román, R.; Pérez-Sánchez, R. Evaluation of the Protective Efficacy of *Ornithodoros Moubata* Midgut Membrane Antigens Selected Using Omics and *In Silico* Prediction Algorithms. *Ticks Tick Borne Dis.* **2018**, *9*, 1158–1172. [\[CrossRef\]](#)
187. Naranjo, V.; Ayllón, N.; Pérez de la Lastra, J.M.; Galindo, R.C.; Kocan, K.M.; Blouin, E.F.; Mitra, R.; Alberdi, P.; Villar, M.; de la Fuente, J. Reciprocal Regulation of NF- κ B (Relish) and Subolesin in the Tick Vector, *Ixodes scapularis*. *PLoS ONE* **2013**, *8*, e65915. [\[CrossRef\]](#)
188. Busch, J.D.; Stone, N.E.; Pemberton, G.L.; Roberts, M.L.; Turner, R.E.; Thornton, N.B.; Sahl, J.W.; Lemmer, D.; Buckmeier, G.; Davis, S.K.; et al. Leading Anti-Tick Vaccine Targets Are Variably Conserved in Cattle Fever Ticks. *Res. Sq.* **2024**. [\[CrossRef\]](#)
189. Rodríguez-Camarillo, S.D.; Quiroz-Castañeda, R.E.; Aguilar-Díaz, H.; Vara-Pastrana, J.E.; Pescador-Pérez, D.; Amaro-Estrada, I.; Martínez-Ocampo, F. Immunoinformatic Analysis to Identify Proteins to Be Used as Potential Targets to Control Bovine Anaplasmosis. *Int. J. Microbiol.* **2020**, *2020*, 8882031. [\[CrossRef\]](#)
190. Artigas-Jerónimo, S.; Estrada-Peña, A.; Cabezas-Cruz, A.; Alberdi, P.; Villar, M.; de la Fuente, J. Modeling Modulation of the Tick Regulome in Response to *Anaplasma phagocytophilum* for the Identification of New Control Targets. *Front. Physiol.* **2019**, *10*, 462. [\[CrossRef\]](#)
191. Wen, L.; Tang, F. Boosting the Power of Single-Cell Analysis. *Nat. Biotechnol.* **2018**, *36*, 408–409. [\[CrossRef\]](#)
192. Purushothaman, S.; Meola, M.; Egli, A. Combination of Whole Genome Sequencing and Metagenomics for Microbiological Diagnostics. *Int. J. Mol. Sci.* **2022**, *23*, 9834. [\[CrossRef\]](#)
193. Marnin, L.; Bogale, H.N.; Laukaitis-Yousey, H.J.; Valencia, L.M.; Rolandelli, A.; O'Neal, A.J.; Ferraz, C.R.; Schmitter-Sánchez, A.D.; Cuevas, E.B.; Nguyen, T.T.; et al. Tick Extracellular Vesicles Impair Epidermal Homeostasis Through Immune-Epithelial Networks During Hematophagy. *BioRxiv* **2023**. [\[CrossRef\]](#)
194. Jiang, R.; Meng, H.; Raddassi, K.; Fleming, I.; Hoehn, K.B.; Dardick, K.R.; Belperron, A.A.; Montgomery, R.R.; Shalek, A.K.; Hafler, D.A.; et al. Single-cell Immunophenotyping of the Skin Lesion Erythema Migrans Identifies IgM Memory B cells. *JCI Insight* **2021**, *6*, e148035. [\[CrossRef\]](#) [\[PubMed\]](#)
195. Kumaresan, V.; Ingle, T.M.; Kilgore, N.; Zhang, G.; Hermann, B.P.; Seshu, J. Cellular and Transcriptome Signatures Unveiled by Single-cell RNA-Seq Following *Ex Vivo* Infection of Murine Splenocytes with *Borrelia burgdorferi*. *Front. Immunol.* **2023**, *14*, 1296580. [\[CrossRef\]](#)
196. Han, Z.; Quan, Z.; Zeng, S.; Wen, L.; Wang, H. Utilizing Omics Technologies in the Investigation of Depsis-Induced Cardiomyopathy. *IJC Heart Vasc.* **2024**, *54*, 101477. [\[CrossRef\]](#)
197. Liu, L.; Chen, A.; Li, Y.; Mulder, J.; Heyn, H.; Xu, X. Spatiotemporal Omics for Biology and Medicine. *Cell* **2024**, *187*, 4488–4519. [\[CrossRef\]](#)
198. Odriozola, I.; Rasmussen, J.A.; Gilbert, M.T.P.; Limborg, M.T.; Alberdi, A. A Practical Introduction to Holo-omics. *Cell Rep. Methods* **2024**, *4*, 100820. [\[CrossRef\]](#)

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