Parasitic helminths and the host microbiome – a missing ‘extracellular vesicle-sized’ link?

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Infections by gastrointestinal (GI) helminths have been associated with significant alterations of the structure of microbial communities inhabiting the host gut. However, current understanding of the biological mechanisms that regulate these relationships is still lacking. We propose that helminth-derived extracellular vesicles (EVs) likely represent key players in helminth–microbiota crosstalk. Here, we explore knowledge of helminth EVs with an emphasis on their putative antimicrobial properties, and we argue that (i) an enhanced understanding of the mechanisms governing such interactions might assist the discovery and development of novel strategies of parasite control, and that (ii) the identification and characterisation of helminth molecules with antimicrobial properties might pave the way towards the discovery of novel antibiotics, thus aiding the global fight against antimicrobial resistance.

Helminths and microbes in the vertebrate gut
GI helminths are amongst the most important infectious agents of humans and veterinary species worldwide [1]. Currently, >1.5 billion people are estimated to be infected by GI helminths globally, including hookworms (e.g., Necator americanus and Ancylostoma duodenale), whipworms (e.g., Trichuris trichiura), and roundworms (e.g., Ascaris lumbricoides), resulting in tens of millions of disability-adjusted life years (DALYs) [2]. Similarly, helminths colonising the GI tract of animals, including the ‘barber’s pole’ worm Haemonchus contortus, the ‘brown stomach worm’ Teladorsagia circumcincta, and the liver fluke Fasciola hepatica, as well as the equine tapeworm Anoplocephala perfoliata, are responsible for devastating production and/or performance losses worldwide [3]. Control of infections by GI helminths in both humans and animals currently relies on the administration of antiparasitic drugs, specifically anthelmintics. However, in endemic areas of the world, reinfection rates are often staggeringly high [4], whilst the overuse and overreliance on anthelmintics to control parasites of livestock has led to the emergence of anthelmintic resistance (see Glossary) in most GI helminth species worldwide [5]. Thus, over the last decade, significant efforts have been directed towards the development of alternative strategies for GI parasite control, including anthelmintic vaccines [6]. Whilst several promising vaccine prototypes have been developed against GI helminths of ruminants (e.g., T. circumcincta and H. contortus [7,8]), immunisation studies to date have reported varying efficacy [9,10], thus suggesting that other, yet unexplored, factors might contribute to GI helminth survival within the host. Thus, a thorough understanding of parasite fundamental biology and physiology, and of host–parasite interactions, is urgently needed in order to discover and develop novel, sustainable methods for parasite control in both humans and farmed animals.

Traditionally, research in host–helminth interactions has focused on two players – the vertebrate host and its immune system, and the worm and its excretory/secretory products (ESPs) [11].
Nevertheless, over the last decade, substantial evidence has emerged of the likely role of a third player in the crosstalk between vertebrate hosts and GI helminths, notably the host gut microbiota [12,13]. Indeed, several investigations conducted in helminth-infected humans and animals, under both experimental and natural conditions, have reported significant associations between parasite colonisation and shifts in the composition and/or function of the vertebrate gut microbiota, with likely repercussions on the pathophysiology of helminth infections, host immune responses and disease outcome (reviewed in [14]). Given the key roles that the host gut microbiota plays in nutrient absorption, immune system development and function, and protection against pathogens, including parasites [15], it has been hypothesised that new strategies to control GI helminths and/or minimize pathology associated to parasitic diseases (e.g., in livestock) might focus on the manipulation of the host gut microbial composition and/or function [16]. Nevertheless, an improved understanding of the mechanisms underpinning the interactions between helminths, host and gut microbiota is key to develop translational studies aimed to exploit the latter as means of controlling GI worms.

Thus far, investigations of the ability of GI helminths to modulate the gut environment have mostly focused on parasite ESPs as key mediators of host–parasite interactions [17]. Helminth ESPs comprise a variety of bioactive components [18–20] that participate in a wealth of processes aimed to facilitate host invasion and colonisation, as well as modulation of host immunity (reviewed in [18–20]). Several of them have been localised to the fraction of parasite ESPs containing extracellular vesicles (EVs) [21]. EVs released by parasitic helminths have been implicated in an ever-expanding catalogue of host–parasite relationships, including immunomodulation, and helminth migration and nutrition [22,23]. Interestingly, EVs derived from vertebrates and bacteria exhibit potent antimicrobial properties [24,25]. Thus, it is plausible that the microbiome-modulating properties of GI helminths might be mediated, at least in part, by the activity of helminth-derived EVs (Figure 1). Elucidating the mechanism(s) through which helminth EVs communicate with the host gut microbiota during worm infection and establishment might therefore uncover a wealth of novel targets for the development of sustainable GI parasite control strategies.

In this article, we (i) summarise current knowledge of helminth excretions/secretions, with a particular focus on EVs, in host–parasite–microbiota interactions, (ii) provide an overview of available experimental evidence supporting a likely role of helminth EVs in helminth–microbiota cross-talk, (iii) propose a working framework to investigate mechanisms of helminth EV–microbiota interplay in experimental settings, and (iv) discuss future strategies aimed to develop novel and sustainable approaches for parasite control based on this acquired knowledge.

**Glossary**

**Antimicrobial peptides (AMPs):** small peptides (between 10 and 60 amino acid residues) exerting inhibitory effects against microbes, from bactericidal properties to modulation of host defence systems.

**Antimicrobial/anthelmintic resistance:** the ability of a given pathogen (e.g., helminth) to withstand a drug (e.g., anthelmintic) that once was able to kill, stall, or weaken it.

**Excretory/secretory products (ESPs):** complex mixture of molecules released by live helminths into their hosts either actively, for example, via secretory pathways, or through passive diffusion from the worm soma and tegument or cuticle. ESPs contain proteins, lipids, glycans, nucleic acids, and EVs that participate in a range of biological processes including, but not limited to, host invasion and colonisation, and evasion and modulation of host immune responses.

**Extracellular vesicles (EVs):** membrane-surrounded, nonreplicative particles (30–200 nm size) containing bioactive molecules (e.g., proteins, nucleic acids and metabolites) and released by virtually all cell types as a means of communication with other cells.

**Gram-negative bacteria:** bacteria whose cell wall displays a thin peptidoglycan layer and an outer lipid membrane.

**Gram-positive bacteria:** bacteria whose cell wall displays a thick peptidoglycan layer and no outer lipid membrane.

**Microbiota:** a community of microorganisms inhabiting a given ecosystem.

**Helminth ESPs in helminth–microbiota interactions**

The roles that ESPs from GI helminths play in host–parasite communications have been the subject of intense investigations over the years [17]. For instance, metalloproteases released by *N. americanus* have been shown to cleave the chemokine, eotaxin, both *in vivo* and *in vitro*, thereby preventing recruitment and activation of eosinophils to the site of helminth infection [26]. Similarly, helminth-secreted peroxiredoxin neutralises reactive oxygen species (ROS) released by a number of host immune effector cells, thus limiting worm damage caused by high concentrations of H$_2$O$_2$ [27], whilst a prostaglandin D synthase (FhGST-S1) secreted by *F. hepatica* stimulates anti-inflammatory prostaglandin release in host innate immune cells [28]. In contrast, knowledge of ESP-mediated communication between parasitic helminths and gut bacteria is, thus far, limited. Nevertheless, recent studies have proposed that helminth ESPs may be involved in direct interactions with host GI microbial populations [29]. For instance, Reynolds et al. [29] identified significant compositional alterations within the GI microbiota of...
mice infected with the intestinal-dwelling nematode *Heligmosomoides polygyrus*. Amongst bacterial populations affected by parasite colonisation, members of the family *Lactobacillaceae* were expanded upon *H. polygyrus* infection. Interestingly, mice supplemented with *Lactobacillus taiwanensis* demonstrated increased regulatory T cell (Treg) frequencies in the gut-associated lymphoid tissue that, in turn, were associated with enhanced susceptibility to worm infection [29]. This finding led to the hypothesis that GI helminths may actively promote the rearrangement of the host GI microbiota via the release of ESPs with antimicrobial activity (Figures 1 and 2) [29]. This hypothesis is supported by knowledge that helminth ESPs contain a repertoire of antimicrobial peptides (AMPs) and antimicrobial proteins [29–31]. Indeed, in a seminal
study, Wardlaw et al. [32] reported potent bactericidal activity – against *Bacillus megaterium* and *Staphylococcus aureus* – exerted by components of the pseudocoelomatic fluid of the porcine intestinal nematode, *Ascaris suum*. Subsequently, Midha et al. [30] described several proteins and peptides with known or predicted antimicrobial activity in *A. suum* ESPs – namely, lectins, a cystatin, and members of the antibacterial factor (ASABF) and cecropin AMP families.

In the same study, ESPs from adult *A. suum* induced dose-dependent inhibition of biofilm formation against two biofilm-forming *Escherichia coli* K-12 strains [30]. Moreover, exposure of *E. coli* to adult *A. suum* ESPs, in the presence and absence of CaCl₂, resulted in calcium-dependent bacterial agglutination, thus implicating C-type lectin-domain-containing proteins as potential effectors of ESP–bacteria interactions [30]. Similarly, *H. polygyrus* ESPs were shown to exert antimicrobial activity against several Gram-negative and Gram-positive bacteria, including *E. coli*, *Salmonella enterica* serovar Typhimurium, *Enterococcus faecium*, and *S. aureus* [33]. In a recent proteomics analysis of *A. suum* ESPs, putative AMPs were localised to the EV-rich fraction [31].
thus suggesting a likely role of helminth-secreted EVs in worm–bacteria communication.

**Helminth EVs – mechanisms of biogenesis and putative functions**

EVs of helminths are defined as lipid membrane-enclosed packages, rich in nucleic acids, peptide and protein cargo (reviewed in [21]). Three main subpopulations of EVs have been described based on their size, mechanism of biogenesis, and biochemical composition; these are microvesicles (100–1000 nm), exosomes (30–150 nm), and apoptotic bodies (200–5000 nm). However, to the best of our knowledge, helminth apoptotic bodies remain poorly characterised (cf. [21]) and are therefore not discussed in this article.

Secretion of exosome-like particles has been ascertained in species of nematodes [23], trematodes [34], and cestodes [35], and confirmed using transmission electron microscopy (TEM) and/or nanoparticle tracking analysis (NTA). Exosome formation involves fusion of late endosomes with the plasma membrane and, as such, exosome-like particles are enriched with proteins of the endosomal sorting complexes required for transport (ESCRT) pathway, for instance, Rabs [36], Vps4 [36], Tyro3, Axl, and Mer (TAM)-binding protein, and TSG101 [37]. Conversely, microvesicles have been discovered in secretions from GI helminths, including *A. suum* [31] and *F. hepatica* [34]; these originate from direct outward budding of the plasma membrane and are associated with proteins involved in microvesicle formation, including Rho1, MAPK3, flippase, and/or calpain [38]. The specific function(s) that helminth EVs play in host–parasite communications has/have long been unclear. Nevertheless, evidence that EVs from a range of GI parasitic helminths can be internalized by several host cell types, including intestinal epithelial cells (i.e., the trematode *Echinostoma caproni* and the nematode *H. polygyrus*), colonic and small intestinal organoids (i.e., the whipworm *T. muris* and the hookworm *Nippostrongylus brasiliensis*), and human cholangiocytes (i.e., the liver fluke *Opisthorchis viverrini*) [21] supports the hypothesis of a role in regulating the microenvironment where the parasites reside (reviewed in [21]). Crucially, EVs from several parasitic helminths of public health and veterinary importance, including *F. hepatica*, are internalized by host immune cells, thus suggesting a contribution of EVs to the known immunomodulatory properties of parasitic worms (reviewed in [21]). In addition, more recently, helminth EVs have been implicated in mechanisms of detoxification through drug sequestration via incorporation of anthelmintics [39]. The proposed mechanisms through which helminth EVs may participate in biological processes linked to modulation of host immunity [22], parasite migration through host tissues and feeding [34] and initiation of tumorigenic disease [40], have been discussed extensively elsewhere and are thus beyond the scope of the present article; nevertheless, this knowledge points toward a likely involvement of helminth EVs in the well-documented ability of parasitic helminths to induce qualitative and quantitative alterations in the composition of host gut microbial communities, either directly (i.e., following internalisation by gut bacterial cells) and/or indirectly (i.e., via modulation of the host local and/or systemic immune responses).

**EVs and their role in antimicrobial defence – building the case for helminth EVs as mediators of helminth–host–microbiome interactions**

Internalisation of helminth EVs by bacterial cells residing in the vertebrate host gut is, to the best of our knowledge, yet to be demonstrated. However, the hypothesis of a key role for helminth EVs in worm-mediated alterations in the composition of the vertebrate gut microbiota is supported by evidence that EVs released by both prokaryotes and higher eukaryotes are involved in the trafficking of toxins, including AMPs, that exert bactericidal and/or bacteriostatic functions against microbes residing in the surrounding environment [25]. For instance, *Pseudomonas aeruginosa* produces and secretes outer membrane vesicles (OMVs, a subset of EVs produced solely by Gram-negative bacteria), that contain peptidoglycan hydrolases; these enzymes cleave bonds in peptidoglycan chains and
side-chain branches, thus compromising the viability of other bacterial cells [41]. Building on these findings, Li et al. [42] demonstrated that 15 Gram-negative bacterial strains, including *Escherichia*, *Salmonella*, *Morganella*, *Citrobacter*, *Enterobacter*, *Proteus*, *Klebsiella*, and *Shigella*, release OMVs that exert bacteriolytic activity in culture. EVs released by vertebrate cells have also been shown to have antimicrobial properties. Notably, Hu et al. [43] demonstrated that exosomes carrying AMPs, beta defensin 2 and cathelicidin-37, are released from the GI epithelium of mice. EVs contained in urine from healthy human donors are also enriched with AMPs (e.g., myeloperoxidase, transferrin, galectin-3-binding protein) and induce lysis of *E. coli* [24].

Proteomic investigations of helminth EVs have also led to the detection and characterisation of putative AMPs as cargo [31,37] (cf. Figure 2), for example, cecropins and c-type lectins, and a c-lectin and a peptidoglycan domain-containing protein in *A. suum* and *F. hepatica*, respectively [31,37]. Several lectin-domain containing proteins from humans and plant and animal species have demonstrated both direct and indirect antimicrobial activity (reviewed in [44]). Amongst these, Clec-39 and Clec-49 lectin-domain-containing proteins participate in the defence of the free-living nematode *Caenorhabditis elegans* against infection by pathogenic bacteria [45]. In particular, *C. elegans* strains deficient in Clec-39 and Clec-49 were susceptible to infection by *Serratia marcescens* that led to reduced survival and egg-laying potential compared with wild-type worms. Clec-39 and Clec-49 are thought to function as Ca²⁺-independent pattern-recognition receptors [45]. Amongst mammalian lectins, the human intestinal RegIIIα specifically targets Gram-positive bacteria, oligomerizing on the bacterial membrane to form membrane-penetrating pores, and limiting direct contact between bacteria and the intestinal epithelium [46]. Whilst this evidence supports a direct role of EV-associated lectins (amongst other proteins) from GI helminths in modulating the bacterial communities inhabiting the host gut (cf. Figure 1), such microbiota-altering properties might be plausibly linked to the ability of EVs to regulate the local immune environment (reviewed in [21]).

Indeed, worm EVs are known to contain several proteins with known immunomodulatory functions that include, amongst others, a transforming growth factor β (TGF-β) [47] that is involved in induction of Foxp3⁺ Treg responses and of both innate and adaptive responses to infection [48], and peroxiredoxins (e.g., *E. caproni*, *F. hepatica*, and *T. circumcincta*; [21]) that are able to stimulate Th2 responses via alternative activation of macrophages [27]. The activation of both Foxp3⁺ Treg and Th2 responses has been shown to be intimately linked to modifications of the vertebrate gut microbiome. For example, faecal microbiota transplants from healthy donors to rodent models of inflammatory bowel disease (IBD) lead to the expansion of colonic RORγt⁺ Foxp3⁺ Treg cells that, in turn, are associated with significant increases in microbial density [49]; similarly, administration of the bacterium *Bifidobacterium adolescentis* to mouse models of IBD resulted in expanded populations of Treg and Th2 cells in the colonic lamina propria of diseased mice as well as alterations in the relative abundance of several resident bacterial taxa, such as an increased ratio of *Bacteroides:Firmicutes* and reductions in populations of *Akkermansia* and *Escherichia–Shigella* [50]. Although beyond the scope of the present article, helminths may also utilise small (~22-nucleotide) noncoding RNAs, known as microRNAs (miRNAs), such as let-7 and miR155, to modulate the host immune system and, in turn, the gut microbiota [51]. Indeed, the interplay between miRNAs and the mammalian microbiota is well documented and is hypothesised to contribute to modulation of host pathophysiology, regulation of gene expression and intestinal homeostasis (reviewed in [52]); nonetheless, to date, and to the best of our knowledge, no investigations have been attempted to elucidate the direct and/or indirect implications, if any, of helminth-derived (including EV-associated) miRNAs on the composition and function of the host gut microbiota.

The mechanisms by which helminth EVs induce alterations in host gut microbial composition, the relative abundance of individual microbial species and/or their function(s) are however likely to be
complex and multifaceted, and not limited to the activity of selected cargo molecules with bactericidal/bacteriostatic or immunomodulatory properties. Indeed, it is conceivable that EV-mediated changes in the abundances of specific populations of microorganisms may, in turn, advantage or disadvantage populations of bacteria that are not direct targets of EVs; such effects may involve multiple mechanisms including, but not limited to, alterations in substrate availability, and bacteria cross-communication through bacterial EVs [53] and/or quorum sensing (i.e., regulation of gene expression in response to fluctuations in populations density) [54] (cf. Figure 1). A preliminary study conducted by Allen et al. [55], in which exposure of rumen fluid to EVs isolated from the rumen fluke Calicophoron daubneyi led to a significant overall increase in total bacterial DNA yields, provides support to this hypothesis [55]. However, it is important to note that, while such increase in total bacterial DNA was interpreted as a proxy for increased bacterial species diversity, no statistically significant differences in the relative abundances of Ruminococcus abus, Fibrobacter succinogenes, and Prevotella spp. were detected over time between colonies incubated with C. daubneyi EVs and PBS negative controls [55]. Nevertheless, in a follow-up study, classical colony counting of P. aeruginosa and Bacillus subtilis following incubation with C. daubneyi EVs resulted in 12.4% and 12.1% colony-forming-unit (CFU) reductions, respectively, compared to control colonies (Nathan Allen, PhD Thesis, Aberystwyth University, 2019, https://pure.aber.ac.uk/portal/files/49906429/Allen_Nathan.pdf), which suggests that the observed alterations might be linked, at least in part, to the antimicrobial activity of rumen fluke vesicles. With this in mind, our knowledge of the potential antimicrobial components of C. daubneyi EVs, and indeed other helminths, is limited to reports from proteomic investigations. Although recognised antimicrobial proteins have been identified in EVs from helminths (Figure 2), none have yet been detected within C. daubneyi EVs.

The complex cascade of events that lead to parasite-associated changes in host gut microbiota composition remains, thus far, largely unexplored. Nonetheless, taken together, preliminary data

Box 1. Filling in the EV-sized gap in host–helminth–microbiota interactions: technical considerations and future directions

To date, differential centrifugation (DC) remains the most frequently applied method of isolation of eukaryote EVs, including EVs from parasitic helminths [64]. DC involves the separation of particles from a multicompartment mixture based on their sedimentation rates [65]. However, DC-based EV isolation often results in relatively low recovery yields and suboptimal purity of EV preparations [64]. Alternatively, density gradient isolation, affinity capture, field-flow fractionation and size exclusion chromatography (SEC) represent more profitable methodologies for EV isolation and purification [66]. Further comparative studies on advantages and disadvantages of EV purification methods are required to set a suitable way forward for structural and functional characterisation of helminth EVs. Indeed, according to the Minimal Information for Studies of Extracellular Vesicles (MISEV) statement, the selection of EV-isolation methods must depend on the project aims and expected outcomes [67]. For instance, studies aimed at investigating EV-specific functions rely on the availability of highly purified populations of vesicles, whilst lower EV purity might be acceptable in instances where EV function is presumed to be enhanced by other ‘contaminant’ particles [67].

Following EV isolation, individual vesicles can, and ideally should, be characterised and quantified using single particle analysers, which also allow determination of EV morphometric data (Figure 1). In addition, MISEV guidelines recommend EV characterisation via identification of vesicle surface protein markers using western blotting, flow cytometry and/or proteomics [67]. Morphological and immunohistochemistry studies using transmission electron microscopy (TEM) are recommended to confirm successful isolation of EVs [66].

The standardisation and optimisation of techniques for helminth EV isolation and characterisation represent the necessary basis for subsequent studies of the roles of helminth vesicles in parasite–microbiota interactions. For instance, the direct antimicrobial activity of helminth EVs might be tested through traditional bacterial colony counting. Alternatively, real-time monitoring of luminescent bacterial colonies (i.e., ‘oluminometry’) represents one method that may be applied to the study of the bactericidal and/or bacteriostatic properties of helminth EVs (Figure 1) [24]. Such proof-of-concept studies will precede investigations of functional mechanisms of EV–microbe interactions (Figure 1). In the ever-growing area of helminth genomics and transcriptomics [66], the molecular characterisation of the features of EV-associated peptides/proteins with putative antimicrobial activity; in turn, will represent the necessary basis for functional explorations of these molecules in vivo. The identification of EV-associated antimicrobial peptides/proteins will represent the necessary basis for functional explorations of these molecules via expression in appropriate vectors and in vitro testing of bactericidal and/or bacteriostatic properties.

Downstream functional assays to test the antimicrobial properties of helminth EVs might take advantage of techniques aimed at modifying vesicle structure prior to antimicrobial profiling, for example, EV surface stripping (gentle treatment with proteases to digest EV surface proteins while maintaining the integrity of luminal proteins [70]), Antibodies can then be obtained against surface proteins of interest and utilised in further antibody neutralisation experiments to assess mechanisms of EV–bacteria interactions (Figure 1).
collected to date (e.g., [55]) serve as proof-of-concept of the direct and/or immune-mediated involvement of helminth EVs in host–parasite–microbiota interactions; mechanistic studies investigating such crosstalk are urgently needed in order to shed light on the relative contribution(s) of worm EVs in host–pathogen relationships and dynamics of helminth infection and establishment in the vertebrate hosts. Inevitably, such studies rely on the availability of standardised techniques to isolate, purify, and characterise populations of EVs often from minute amounts of parasite material (Box 1).

Figure I. Unveiling the roles of helminth extracellular vesicles (EVs) in worm–microbiota interactions. Overview of the principal methods and technologies currently applied to the isolation and characterisation of helminth-derived EVs, and functional assays that might assist investigations into mechanisms of worm–microbiota crosstalk. Abbreviations: SEC, size exclusion chromatography; NTA, nanoparticle tracking analysis; TEM, transmission electron microscopy. Figure created with BioRender.com.
Concluding remarks
Helminths have cohabited with their host GI microbiome for hundreds of millions of years (cf. [56]). Hence, it is highly conceivable that, besides mechanisms to communicate with host epithelial and immune cells [57], parasitic worms have also developed strategies to modulate the populations of microorganisms that share their niche inside the vertebrate host. Whilst substantial efforts have been directed towards understanding the impact that host microbiome alterations exert on helminth fitness and survival [12,13,58–60], current knowledge of the consequences of worm establishment on the microbiome structure and function, as well as on the pathophysiology of helminth disease, remains scarce. Here, we propose that decoding the role(s) that helminth excretions/secretions, including EVs and their cargo molecules, play in modulating the host gut microbiota composition will assist elucidating the intricacies of helminth–host interactions. In particular, identifying the biological mechanisms underpinning helminth-associated alterations of host gut microbial composition will provide the essential basis for investigations aimed to discover and develop novel therapeutics and/or vaccines targeting such interactions. Such studies should primarily focus on elucidating the spectrum of antimicrobial activity exerted by ESP- and EV-associated candidate molecules, and on investigating similarities between bacterial targets of antimicrobials secreted by a variety of GI helminth species. Determining the parasite burden necessary to generate ESP/EV quantities able to induce detectable modifications in host gut microbiota composition will also be crucial, as will the characterisation of the exact mechanism(s) of helminth EV internalisation by bacterial cells. Such studies will inevitably require the integration of sophisticated microbiome-engineering technologies [61] coupled with organoids and/or gut-on-chip systems [62,63]. Furthermore, the newly discovered catalogue of helminth EV-derived AMPs might represent a gold mine for antibiotic research, thus aiding the global fight against rapidly spreading antimicrobial resistance (see Outstanding questions).

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Declaration of interests
The authors declare no competing interests.

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Outstanding questions
Are helminth extracellular vesicles internalised by vertebrate gut bacteria and via what mechanism?

What impact do helminth–microbiome interactions exert on the overall pathophysiology of helminth disease?

Can AMPs in excretory/secretory products and EVs of helminths be exploited in the search for new antimicrobials?

How can knowledge of helminth–microbiome interactions assist the development of novel and sustainable parasiticides?
Ascaris suum worms secrete extracellular vesicles derived from their excretory/secretory proteins. These vesicles can be internalized by host immune cells, possibly contributing to the regulation of the host immune response. For example, vesicles derived from Ascaris suum contain C-type lectins that can bind to host cells and modulate immune responses. These vesicles may also contain miRNAs that can regulate gene expression in the host.

Teladorsagia circumcincta, another parasitic nematode, also secretes extracellular vesicles that can interact with host cells. These vesicles contain immunoregulatory molecules that can modulate the host immune response, potentially shifting it towards a more protective state.

Inflammation and immune modulation are key aspects of the host-parasite interaction. Helminth parasites, such as Ascaris suum and Teladorsagia circumcincta, secrete extracellular vesicles that can interact with host immune cells, modulating immune responses and influencing the host's ability to clear the infection. These vesicles can also play a role in the development of chronic infections and immune tolerance, which are important factors in the pathogenesis of helminthic infections.
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