Trends in
Parasitology

CellPress

Forum

Beyond genomics: a multiomics future for parasitology

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Parasitology has long relied on genomics and transcriptomics to explore gene function, diversity, and host–parasite interactions, yet functional insight often requires deeper molecular resolution. This forum highlights advances in proteomics, metabolomics, lipidomics, and emerging technologies. We advocate an integrative multiomics approach to better understand parasite biology in context.

A broader molecular lens

High-throughput genomics and transcriptomics have profoundly reshaped biology, enabling insights into evolution, gene function, and disease mechanisms across life forms [1,2]. Despite their importance, parasites account for only a small fraction of this molecular research effort, with most studies understandably focused on a handful of medically relevant species where funding and resources are concentrated [3]. That fraction is likely even smaller when considering large-scale studies of proteins and their functional intermediates. Indeed, over the past 25 years, genomics and transcriptomics have dominated parasitological research (Box 1), comprising nearly three-quarters of all published '-omics' studies. Outside a few well-resourced model systems, we still lack the breadth of data needed to reflect the vast molecular diversity of parasites. Fortunately, new technologies, made feasible by foundational work on medically prioritised species, are now lowering barriers for studying neglected parasites.

This limited scope constrains our understanding of parasite biology. Gene expression data alone often fail to reflect functional outcomes, especially given the well-established disconnect between mRNA and protein abundance [4]. Post-transcriptional regulation, metabolic rewiring, and lipid-mediated signalling are all critical for parasite development, survival, and manipulation of host systems, yet remain underexplored.

This forum highlights emerging -omics technologies that can fill these gaps (Resources organised by application in Table S1 in the supplemental information online). Historically limited by technical and analytical barriers, proteomics, metabolomics, and lipidomics are becoming more accessible and scalable, offering new opportunities for functional insight. Single-cell and spatial techniques promise to revolutionise resolution, and integrative multiomics workflows are bringing holistic perspectives to parasite biology [5] (Figure 1). By focusing on these tools, we aim to encourage a broader, more functional molecular view of parasitology that meets the complexity of host–parasite systems with equally sophisticated methods.

Comprehensive proteomics is now within reach

Proteomics enables the large-scale identification and quantification of proteins and their regulation across conditions, typically through liquid chromatography-mass spectrometry (LC-MS) (Figure 1). This versatile platform allows researchers to tailor experiments toward specific protein groups or broader proteome-wide changes [6]. After decades of development, proteomic instrumentation[i,ii] and workflows are now widely used across all life sciences, often as discovery tools for disease phenotype biomarkers or to provide insight into life cycle and transmission mechanisms of biological systems. In parasites, proteomics is increasingly used to study proteome-wide expression in hosts and parasites across infection stages, pathway changes, infection mechanisms, and links between molecular and phenotypic alterations such as host behaviour and immunity. Modern proteomics has allowed researchers to identify critical factors related to transmission, immune modulation or evasion, and development in several important human parasites [7]. Proteomics could also be used to identify parasite-derived antigens, characterise stage-specific secretomes, or monitor post-translational modifications linked to drug resistance.

Importantly, modern genomics techniques facilitate proteomic analysis of non-model species and poorly annotated systems by building protein databases from transcriptomes, making it more accessible to any life science researcher. With recent advances in proteomic analyses, many tools are readily available for data processing[iii–vii], data analysis[viii–x], and data visualisation[xi,xii], both open source and for purchase (Figure 1). Advances in high-throughput sample preparation (Evosep One[xiii], PreOmics[xiv], and TMT[xv]), detection sensitivity, and instrument speed have improved the quality and robustness of analysis while bringing costs down, making this technology suitable for answering various biological questions [6].

Metabolomics and lipidomics enter the field

Metabolomics and lipidomics focus on profiling the small-molecule metabolites

Box 1. Parasite -omics research trends

To understand how -omics research has progressed in parasitology, we searched for papers on helminths (nematodes, trematodes, cestodes, and acanthocephalans), focusing on single- and multiomics. Aside from a few key disease-causing protists, helminths are the most extensively studied parasites and likely reflect broader trends in parasite -omics research. We searched Web of Science (title, abstract, keywords) for primary research articles from 2000 to 2024 inclusively using search terms covering helminths and five -omics fields (see Box S1 in the supplemental information online for search terms). To separate single- from multiomics categories, we excluded studies mentioning additional -omics types using Boolean logic. We identified 1559 relevant publications (Figure IA), over 60% of which involved genomics either alone or in combination (Figure IB). No multiomics study combined more than three -omics, with ~17% combining two -omics, and 1% combining three – most of the latter being conceptual papers. Genomics has dominated research output over the past 25 years (~50% annually), followed by transcriptomics and proteomics. While multiomics proportions have remained stable at ~10% yearly since 2010, transcriptomics has overtaken the early lead of proteomics. Most multiomics studies focus on plant-parasitic nematodes (e.g., *Bursaphelenchus xylophilus* and *Meloidogyne incognita*) and key human helminths such as *Echinococcus* (cestode), *Schistosoma* (trematode), and *Strongyloides* (nematode).

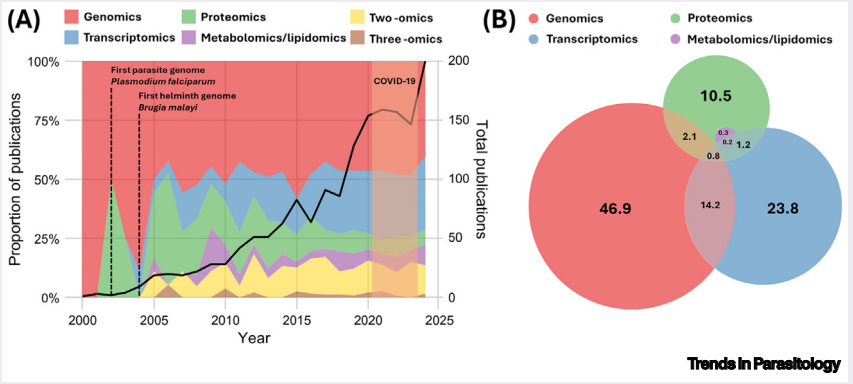

Figure I. Trends in single- and multiomics research on helminths from 2000 to 2024. (A) Stacked area chart showing the yearly number of publications in single- and multiomics research. The black line indicates the total number of publications per year. Notable milestones, such as the first published parasite and helminth genomes, are highlighted with broken lines. The coronavirus disease 2019 (COVID-19) period is shaded to indicate its potential impact on research trends. (B) Euler diagram depicting the percentages of total publications focused on individual -omics and their overlaps (multiomics). Note: metabolomics and lipidomics are grouped together due to the low representation of lipidomics (less than 1% of total publications).

and lipids that constitute the actual biochemical phenotype of cells, providing a real-time snapshot of metabolic activity. Unlike genomics or transcriptomics, which reveal genetic potential or expression, metabolomic profiling directly reports the end-products and intermediates of enzymatic pathways at any chosen time. These -omics can elucidate the developmental stages of parasites, including lipid remodelling for host adaptation and membrane biogenesis, allowing for the identification of potential drug targets. However, due to their complex life cycles, a major challenge in host–parasite metabolomics is attributing each metabolite to parasite or host origin. This is further compounded by the absence of comprehensive, parasite-specific reference databases, hindering accurate annotation and biological interpretation, particularly of bioactive lipids. That said, several publicly funded resources such as VEuPathDB, the NIAID BRCs, and GenDB (Wellcome Sanger Institute) are helping to close this gap by providing parasite and vector genomic and transcriptomic data. Nevertheless, attributing each metabolite may be less important than understanding how metabolic profiles shift over the course of infection, particularly given the cross-compartmental nature of many host–parasite–microbiome metabolic pathways. While the presence of host material has traditionally been viewed as a contaminant, modern multiomics approaches such as dual RNA-seq and plasma proteomics now turn this complexity into a strength, enabling insights into both host and parasite components of infection.

Despite these inherent challenges, experimental workflows have become increasingly refined, with established one-step sample preparation protocols and method development in LIPID MAPS[xvi] and recent reviews [8]. Coupled with high-resolution mass spectrometry and novel chromatographic methods (Figure 1), these platforms can now resolve thousands of metabolites and lipids. Data processing barriers are being overcome by the continuous development of publicly and commercially available software[xvii–xxi], and a growing number of spectral libraries and databases[xxii–xviii], collectively facilitating more robust analysis and interpretation.

For example, recent advances in metabolomics workflows have enabled detailed analysis of *Plasmodium falciparum* life stages, validating genome-predicted pathways and identifying novel lipid and metabolic ones [9]. Furthermore, cutting-edge lipidomics has revealed novel classes of bioactive lipids and lipid-like signalling molecules, including pheromones [10] that may mediate parasite communication. Integrating these -omics into parasitology not only fills functional gaps but opens new avenues for biomarker discovery, drug target validation, and ecological insight across parasite life cycles. These approaches could also help define nutrient dependencies, uncover metabolic signatures of parasite development, and monitor host metabolic reprogramming during infection.

The challenges and promise of multiomics integration

Although multiomics studies in parasitology are still emerging (Box 1), integrative

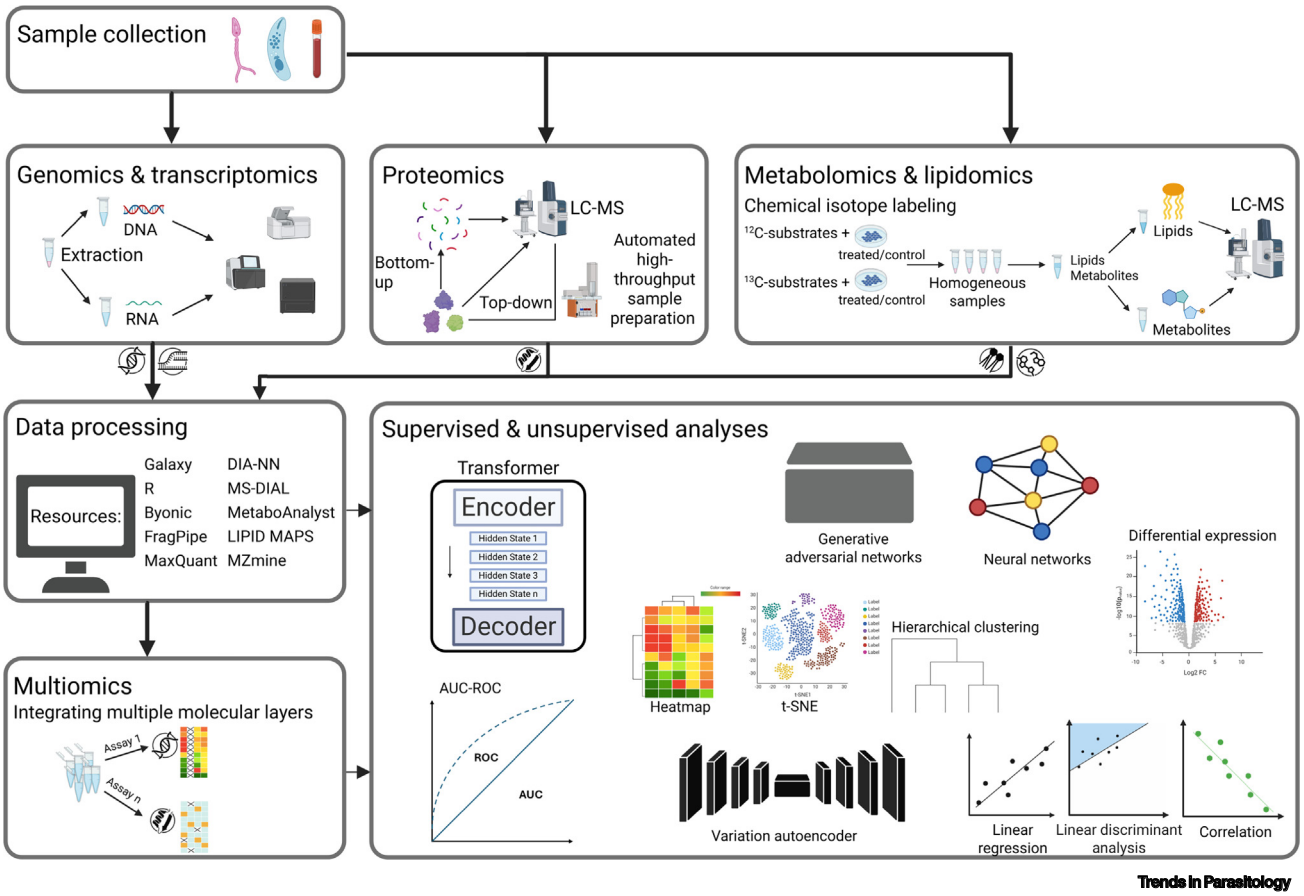

Figure 1. Multiomics workflows and integration in parasitology. Key -omics workflows used to study parasite biology. Genomics and transcriptomics are well established, while proteomics, metabolomics, and lipidomics offer functional insights into protein abundance, metabolism, and lipid signalling. These layers are increasingly accessible through advances in sample preparation, mass spectrometry, and analysis platforms. Tools such as MaxQuant[iv], DIA-NN[v], MS-DIAL[xvii], and MetaboAnalyst[xix] support data processing for specific -omics modalities. Integrated multiomics analyses enable deeper biological interpretation through clustering, network modelling, and machine learning. Together, these approaches support a systems-level understanding of host–parasite interactions and the complex molecular mechanisms driving parasitic life cycles. This figure was created using BioRender.

metabolomics analysis of *Plasmodium*, for example, has already identified actionable metabolomic targets [5]. Current wet lab workflows typically involve parallel sample processing for each -omics layer, which increases time and resource demands. Future directions aim to develop integrated, automated platforms that enable simultaneous multiomics data collection, improving scalability and reproducibility. Integrative multiomics could reveal coordinated changes in gene expression, protein activity, and metabolite output that drive virulence, life cycle transitions (transmission), or parasite-driven changes in host phenotype (host manipulation).

Integrating data from various molecular layers requires harmonisation of their respective standardised workflows. Normalisation reduces technical variation, but methods vary by -omics (methods used in DESeq2[xxix] for transcriptomics; proteiNorm[xxx] for proteomics; Pareto scaling in IMIFA[xxxi] for metabolomics). Imputation tools[xxxii,xxxiii] can address missing data, while regression tools like limma[ix] adjust for confounders to focus on the biological question. After transformation, data can be analysed statistically with specialised packages in R[xxix,xxxiv] or Python[xxxv,xxxvi], functional analysis in databases[xxxvii–xxxix] can be performed to extract the important biological information.

Data integration remains a critical challenge, as traditional supervised methods, while powerful, can introduce biases and inadvertently overlook cross-modality interactions. Unsupervised methods, such as clustering similar data points[xl], identifying relationships through regression-association analysis[xli,xlii], and mapping interaction networks[xliii,xliv], offer a more robust approach for capturing complex biological relationships [11]. Deep learning approaches, including non-generative frameworks (feedforward neural networks,

graph convolutional neural networks, and autoencoders) and generative frameworks (variational methods, generative adversarial models, and generative pretrained models), are powerful tools for multiomics data integration [12]. Generative models can also predict missing molecular features, enhancing single-cell multiomics studies. Foundation models[xlv] can effectively distil biological insights concerning the relationships between genes and cells and benefit tasks such as cell type annotation, multi-batch integration, multiomic integration, perturbation response prediction, and gene network inference. While deep learning models show promise for pattern recognition and prediction tasks, they require large, well-annotated datasets and remain limited in interpretability. For many parasitology datasets, traditional statistical models or hybrid approaches may be more appropriate for now.

While the potential of multiomics cannot be undersold, there remain challenges that hinder broad adoption, such as high costs, limited accessibility, and specialised equipment. However, ongoing innovations in automation[xlvi], scalable analytics[xii], and user-friendly integration tools[xix] are poised to make multiomics increasingly accessible and central to parasitology research. This integration offers a more comprehensive view of biological systems and enables cross-validation of findings, which is crucial for uncovering mechanisms of pathogenicity, drug resistance, and host phenotypic responses.

Tomorrow's tools for today's questions

Parasitic infections often comprise a complex mixture of divergent lineages, causing pronounced variations in disease progression and treatment response. Although bulk single- and multiomics research have revolutionised parasitology, it lacks the resolution to measure heterogeneity on the individual cell level. For example, single-cell transcriptomics data, such as Malaria Cell Atlas[xlvii], have revealed key gene expression patterns and developmental transitions in individual parasites.

Beyond transcriptomics, single-cell multiomic integration will enrich our understanding of parasite biology. Integrating different molecular layers from the same cell will expose post-transcriptional regulatory mechanisms, metabolic adaptations, and drug resistance mechanisms that individual -omics might miss. Current advanced technologies[xlvi] enable parallel multiomics analysis within the same cell through different combinations of the transcriptome, proteome, and metabolome, delivering unprecedented cross-modality depth [13]. These approaches will enable researchers to tackle previously inaccessible questions, such as: How do parasites coordinate development across tissues? Which molecular pathways drive transitions between life stages? How does parasite metabolism adapt within different host environments? Such high-resolution multiomics could provide us with a unique opportunity to answer these questions by connecting transcriptional programs to downstream protein function and metabolite output.

While single-cell multiomics dives deep into the molecular analysis of individual parasites or cell groups, spatial -omics at cellular or subcellular resolution provides insight into another critical dimension: histology. By achieving three-dimensional spatial mapping across thick tissue sections or whole organs using matrix-assisted laser desorption/ionisation (MALDI), expansion microscopy (ExM), or light sheet fluorescence microscopy (LSFM) [14], we could visualise parasite development within host tissues. Artificial intelligence (AI)-driven image analysis[xlviii] provides deep learning for pattern recognition and spatially informed network models. Spatial -omics combined with advanced microscopy and AI tools enable researchers to better understand the integration, visualisation, and interpretation of large spatial datasets and further map immune-related protein distributions within tissues [15]. By integrating advanced multiomics with spatial resolution, we can generate comprehensive atlases of host–parasite interactions and tissue-specific pathways activated during infections for novel therapeutic targets.

An integrative molecular future

While our focus here is on multiomics, functional validation remains critical. Technologies such as CRISPR-Cas9 and its equivalents are enabling precise manipulation of parasite genomes to validate gene function and dissect pathways. Moreover, epigenetic regulation through histone modifications and DNA methylation (epigenome) plays a key role in parasite life stage transitions and should be considered as an important layer within the multiomics landscape. Genomics and transcriptomics have laid a critical foundation for modern parasitology. As proteomics, metabolomics, and lipidomics become more accessible, and as single-cell and spatial technologies mature, the field has an opportunity to expand that foundation. However, applying multiomics to host–parasite systems, particularly non-model organisms, remains technically challenging. It requires coordinated workflows, robust data processing, and often complex sample handling. These hurdles are best addressed through close collaboration across molecular biology, parasitology, and bioinformatics. Successful integration hinges not only on technology but also on interdisciplinary teams equipped to bridge diverse expertise.

Embracing multiomics is not about abandoning existing methods but about integrating complementary layers of information to achieve a more complete view of parasite biology. Doing so will require new tools, training, and collaborative efforts. But the rewards are clear: richer

biological resolution, better diagnostics and therapeutics, and deeper insights into host–parasite dynamics. With the right tools and integrative mindset, multiomics can transform parasitology into a more predictive and mechanistic discipline.

Author contributions

J.-F.D. conceived the idea for the paper in consultation with all other authors; J-F.D. led the writing with significant contributions to core sections and figures from all other authors. All authors gave final approval for publication.

Acknowledgments

This forum article was prepared during a working retreat. We thank the two anonymous reviewers for their helpful comments. We also thank Granville Island Brewing for their generous liquid sponsorship. J-F.D. was supported by a Natural Sciences and Engineering Research Council of Canada (NSERC) Postdoctoral Fellowship (PDF-578318-2023).

Declaration of interests

The authors declare no competing interests.

Resources

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[iii]https://fragpipe.nesvilab.org/

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[v]https://github.com/vdemichev/DiaNN

[vi]https://biognosys.com/software/spectronaut/

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[xxiv]https://massbank.us/

[xxv]http://planmaxdb.riken.jp/menta.cgi/planmax/download/plant/core/contents

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[xxxvi]https://github.com/scverse/scanpy

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[xl]https://github.com/evelinag/clusternomics

[xli]https://biofam.github.io/MOFA2/

[xlii]https://github.com/ehsanhajiramezanali/BayReL

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[xliv]https://github.com/richrr/TransNetDemo

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Supplemental information

Supplemental information associated with this article can be found online https://doi.org/10.1016/j.pt.2025.07.006.

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https://doi.org/10.1016/j.pt.2025.07.006

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