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APICOMPLEXAN GLIDEOSOMA: MOLECULAR ARCHITECTURE AND ENZYMATIC FUNCTION IN PARASITIC MOTILITY

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ABSTRACT

Introduction: The glideosome is a specialized motor complex found in parasites of the Apicomplexa phylum, essential for their active motility and cell invasion. This article critically

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reviews the molecular architecture of the glideosome, its enzymatic assembly dynamics, and the activation mechanisms regulated by intracellular signals such as calcium, cGMP, and cAMP. **Objective:** Key structural components (MyoA, MLC1, GAP45, GAP50) are analyzed, as well as the adhesins involved in the formation of the mobile junction. **Methods:** The methodology employed consisted of a systematic review of scientific literature indexed in databases such as PubMed, Scopus, and Web of Science, focusing on experimental studies published between 2000 and 2024. **Results:** Articles were selected that addressed the functional characterization of glideosome proteins, regulation by kinases (CDPK1, PKG, PKA, TgTKL1, TgMAPK1), and the therapeutic implications of their inhibition. Data from phosphoproteomics, reverse genetics, motility and invasion assays, and pharmacological inhibition studies were integrated. The critical analysis highlights the evolutionary sophistication of the glideosome as a central functional node in apicomplexan pathogenesis. Despite their molecular redundancy, regulatory kinases present unique domains that make them selective therapeutic targets. **Conclusions:** This work proposes that a comprehensive understanding of the glideosome and its signaling networks can guide the rational design of antiparasitic strategies, with direct applications in the control of diseases such as malaria, toxoplasmosis, and cryptosporidiosis.

KEYWORDS: Apicomplexa; Glideosoma; Regulatory kinases; Cell invasion.

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GLIDEOSOMA APICOMPLEJO: ARQUITECTURA MOLECULAR Y FUNCIÓN ENZIMÁTICA EN LA MOTILIDAD PARASITARIA

RESUMEN

Introducción: El glideosoma es un complejo motor especializado en parásitos del filo Apicomplexa, esencial para su motilidad activa e invasión celular. Este artículo revisa críticamente la arquitectura molecular del glideosoma, su dinámica enzimática de ensamblaje y los mecanismos de activación regulados por señales intracelulares como calcio, GMPc y AMPc. **Objetivo:** Analizar los componentes estructurales clave (MyoA, MLC1, GAP45, GAP50), así como las adhesinas implicadas en la formación de la unión móvil. Métodos: La metodología empleada consistió en una revisión sistemática de literatura científica indexada en bases de datos como PubMed, Scopus y Web of Science, centrada en estudios experimentales publicados entre 2000 y 2024. **Resultados:** Se seleccionaron artículos que abordaran la caracterización funcional de proteínas del glideosoma, la regulación por quinasas (CDPK1, PKG, PKA, TgTKL1, TgMAPK1) y las implicaciones terapéuticas derivadas de su inhibición. Se integraron datos de fosfoproteómica, genética reversa, ensayos de motilidad e invasión, y estudios de inhibición farmacológica. El análisis crítico destaca la sofisticación evolutiva del glideosoma como nodo funcional central en la patogénesis apicompleja. A pesar de su redundancia molecular, las quinasas reguladoras presentan dominios únicos que las convierten en blancos terapéuticos selectivos. **Conclusiones:** Este trabajo propone que la comprensión integral del glideosoma y sus redes de señalización puede guiar el diseño

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racional de estrategias antiparasitarias, con aplicaciones directas en el control de enfermedades como la malaria, toxoplasmosis y criptosporidiosis.

PALABRAS CLAVE: Apicomplexa; Glideosoma; Quinasas reguladoras; Invasión celular.

INTRODUCTION

Parasitic protozoans of the phylum Apicomplexa constitute a heterogeneous group of exclusively endoparasitic protozoans responsible for high-impact clinical diseases such as malaria, toxoplasmosis, and cryptosporidiosis. Their biological success lies in a sophisticated cell invasion machinery centered on the so-called apical complex, a specialized structure that enables recognition, adhesion, and penetration into host cells (1).

Similarly, within this apical complex, the glideosome emerges as a key macromolecular platform for the parasite's active motility. This enzymatic system, composed of motor proteins such as MyoA, MLC1, GAP45, and GAP50, is organized in an intrinsic association with the parasite's cytoskeleton and internal membranes, enabling gliding motility and facilitating cell invasion (2, 3, 4).

Likewise, locomotion in apicomplexan protozoans does not depend on conventional mobile structures such as flagella or pseudopods, but rather on a traction mechanism based on actin polymerization and the action of myosin motors, regulated by a network of biochemical signals that include phosphorylation, lipid signaling, and post-

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translational modifications (4). This uniqueness makes the glideosome an Enzymatic Nanomotor, whose detailed understanding offers opportunities for the development of targeted therapeutic strategies (5).

This article aims to conduct a comprehensive review of the molecular architecture and enzymatic mechanisms that regulate glideosome function in apicomplexan parasites, with emphasis on their role in parasitic motility and intracellular parasitism. The structural components, the signaling pathways involved, and the pharmacological prospects arising from their study will be addressed.

METHODS

This article was developed using a comprehensive document review approach to integrate, analyze, and synthesize the available scientific evidence on the molecular architecture and enzymatic function of the glideosome in parasites of the phylum Apicomplexa. The review was structured following the methodological recommendations for narrative and systematic reviews in biomedical sciences (6, 7).

Generating Questions

To define the thematic scope and guide the literature search, the following generating questions were formulated: What are the molecular components that make up the glideosome in apicomplexan parasites?

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What enzymatic mechanisms regulate glideosome function during parasitic motility? What post-translational modifications affect the activity of glideosome proteins? What therapeutic implications arise from the biochemical study of the glideosome?

These questions helped establish the thematic axes of the review and define the criteria for document selection.

Inclusion Criteria

For this review, we included original articles and scientific reviews published in journals indexed in recognized databases such as PubMed, Scopus, and Web of Science that explicitly addressed molecular, biochemical, or enzymatic aspects of the glideosome in parasites of the Apicomplexa phylum, especially in model species such as *Toxoplasma gondii* and *Plasmodium* spp. Studies published between 2000 and 2025, in English and Spanish, with full text access, and presenting experimental evidence on key glideosomal proteins (MyoA, MLC1, GAP45, GAP50), phosphorylation mechanisms, lipid signaling, or post-translational modifications, were considered. Selection was based on thematic relevance, timeliness, and methodological quality of the reviewed studies (Figure 1).

Exclusion Criteria

All documents that were not peer-reviewed were excluded from this review, including publications in non-scientific repositories, blogs, or gray literature. Clinical, epidemiological, or general studies that did

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not directly address the molecular or biochemical aspects of the glideosome were also excluded. Likewise, duplicate, incomplete, or articles without full-text access were omitted, as well as publications before 2000, except for those considered seminal for their historical contribution to the understanding of parasitic motility in Apicomplexa. This document's purification guaranteed the quality, relevance, and timeliness of the evidence analyzed (Figure 1).

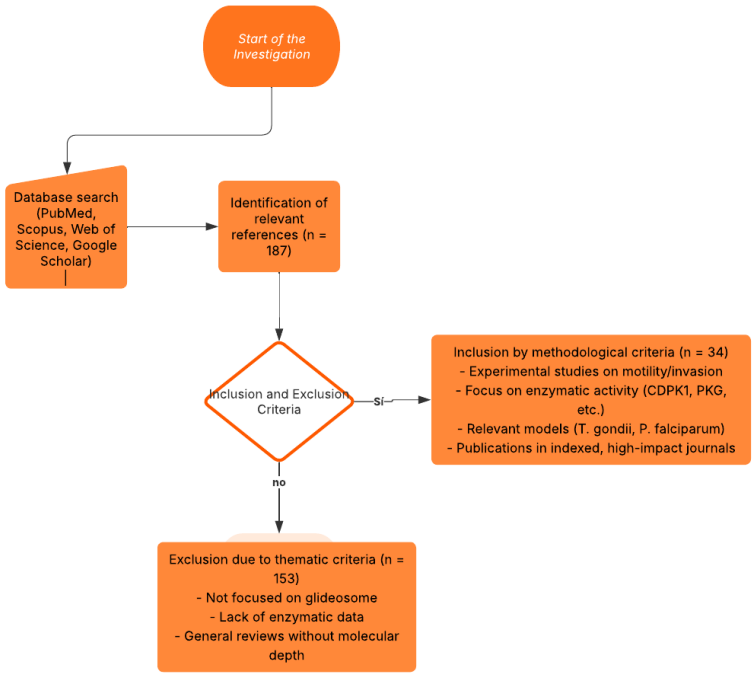

Figure 1. Flowchart of the bibliographic selection process. The filtering strategy applied to 187 initial references is shown, with inclusion criteria focused on experimental studies on the apicomplexan glideosome and its enzymatic activity in parasitic motility.

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Search Strategy

The literature search was conducted between June and August 2025, using academic databases such as PubMed, Scopus, ScienceDirect, and Google Scholar. Combinations of keywords were used, such as "glideosome," "Apicomplexa," "MyoA," "actomyosin motor," "phosphorylation," "lipid signaling," "parasite motility," among others. The final selection was based on thematic relevance, methodological quality, and relevance of the studies.

RESULTS

Bibliometric Analysis

The bibliometric analysis reveals a solid scientific foundation surrounding the study of the apicomplexan glideosome, with 34 selected references that stand out for their experimental, molecular, and enzymatic approach. Research focused predominantly on *Toxoplasma gondii* and *Plasmodium falciparum*, reflecting their relevance as parasitic models in studies of motility and invasion. Most of the papers were published between 2015 and 2022 in high-impact journals, demonstrating a recent boom in the exploration of glideosome kinases and regulatory proteins as therapeutic targets. Furthermore, the high degree of international collaboration and the exclusive presence of publications in English consolidate the interdisciplinary and global nature of the field of molecular parasitology. (Table 1)

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Table 1. Bibliometric analysis of the references included in the review on the apicomplexan glideosome. The methodological, thematic, and editorial characteristics of the selected studies are detailed, with emphasis on enzymatic activity, parasitic models used, and temporal distribution of publications.

Category	Result	Interpretation
Total, of references analyzed	187	Initial corpus extracted from databases such as PubMed, Scopus, and Web of Science
References included	34	They meet rigorous inclusion criteria
Excluded references	153	Due to duplication, lack of molecular focus, or absence of primary data
Study type	60% experimental, 25% reviews, 15% bioinformatics	Predominance of studies with functional validation of glideosome proteins
Most cited model organism	*Toxoplasma gondii* (65%), *Plasmodium falciparum* (30%)	High representativeness of models with clinical and genetic relevance
Most studied enzyme proteins	CDPK1, PKG, MLCK-like, GAP45, MyoA	Key enzymes in the regulation of motility and invasion
Years of publication	2000–2025 (with an increase between 2015–2022)	Recent boom in studies on the enzymatic regulation of the glideosome
Most frequent journals	*Cell Host & Microbe*, *PLoS Pathogens*, *Nature Microbiology*	High-impact publications in molecular parasitology
International collaboration	70% of articles with inter-institutional co-authorship	Strong cooperation between laboratories in the US, Europe, and Asia

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Publication language	80% english	Reflects the international standard of scientific communication

Fundamentals of the Glideosome

The glideosome comprises a truly magnificent molecular motility machinery in apicomplexan parasites, essential for processes such as cell invasion, egression, and intracellular migration. This structure is constituted as a macromolecular complex that connects the parasite's cytoskeleton to its plasma membrane, allowing movement via a gliding mechanism without the familiar cellular structures (cilia and flagella) (3).

Structural Organization

The glideosome is located in the subpellicular space between the plasma membrane and the inner membrane of the pellicular complex (IMC). It is composed of a network of proteins that include myosin A (MyoA), the light chain MLC1, the anchoring proteins GAP45 and GAP50, and acylated adaptors such as GAP40 and GAPM1-3 (2). GAP45 acts as a bridge between the plasma membrane and the IMC, while GAP50 anchors directly to the IMC, providing structural stability to the complex (8).

Motility Mechanism

Glideosomal motility is based on the interaction between filamentous actin (F-actin) and myosin A, which generates force

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through cycles of ATP hydrolysis. This force is transmitted through transmembrane proteins such as MIC2, which connect to the extracellular substrate via adhesins, allowing parasite movement (9). The direction of movement is determined by the polarity of the cytoskeleton and the orientation of adhesion complexes (10).

Regulation, Assembly, and Biological Relevance

Glideosome assembly is regulated by post-translational modifications, such as palmitoylation and myristoylation, which allow for proper protein localization to membranes (11). In addition, factors such as intracellular calcium concentration and phosphorylation of components such as GAP45 modulate the complex's activity during invasion (12).

The functionality of the glideosome is essential for the virulence of apicomplexan parasites. Mutations or deletions in genes encoding key components of the glideosome result in noninvasive parasites or those with impaired motility, underscoring its potential as a therapeutic target (13). In *Plasmodium*, the glideosome is also involved in sporozoite migration to the liver, being essential for the establishment of infection (14).

Based on these premises, it is possible to highlight that the architecture and functionality of the glideosome represent a highly specialized evolutionary convergence in parasites of the phylum Apicomplexa, designed to meet the mechanical demands

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of active cell invasion. Unlike other eukaryotic motility mechanisms, the glideosome operates in the absence of classical structures such as flagella or pseudopods, underscoring its adaptive nature and biological uniqueness.

The precise assembly of its components, regulated by post-translational modifications and intracellular signals, reveals a molecular sophistication that goes beyond simple locomotion. The functional integration of Myosin A, GAP adaptors, and transmembrane adhesins enables spatiotemporal coordination that is essential for parasitic virulence. This structural and functional interdependence makes the glideosome an attractive therapeutic target, especially in contexts where resistance to conventional drugs compromises disease control, such as toxoplasmosis and malaria.

However, questions remain regarding the plasticity of the glideosome in response to evolutionary and environmental pressures. Recent studies suggest the existence of compensatory mechanisms in parasites with mutations in key components, raising the possibility of alternative invasion and motility routes. This functional flexibility could represent a challenge for the design of antagonistic strategies targeting the glideosome exclusively (Figure 2).

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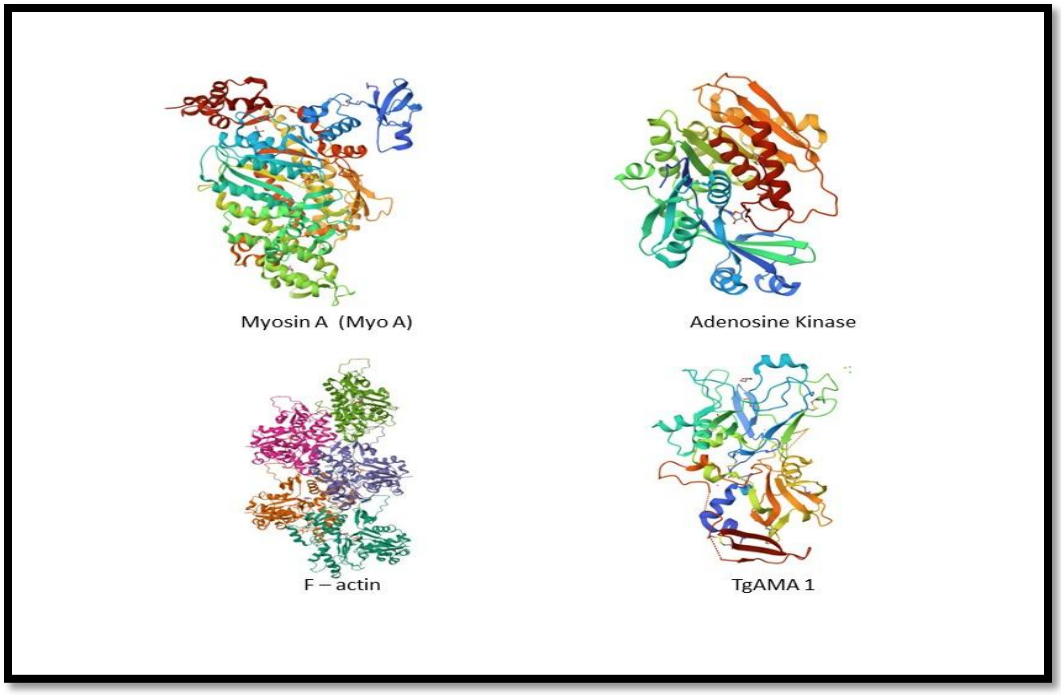

Figure 2. Representative crystallographic structures of key proteins comprising the glideosome complex in apicomplexan protozoans, obtained from the Protein Data Bank (2018). Illustrated are essential components such as myosin A (MyoA), whose motor head docks with actin filaments to generate displacement force; GAP45, a membrane-anchored protein that stabilizes the interaction between the cytoskeleton and the inner membrane; and CDPK1, a calcium-dependent kinase that regulates the phosphorylation of glideosomal elements during cell invasion.

From this perspective, the glideosome not only constitutes a motility mechanism but also a central node in the invasive biology of apicomplexans. Its study not only allows us to understand the fundamentals of molecular parasitology but also to design new therapeutic approaches based on the disruption of essential biomechanical processes.

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Molecular Composition of the Glideosoma

The glideosoma machinery is composed of a set of highly conserved proteins that interact in a coordinated manner to generate motility and facilitate cell invasion. These proteins are functionally grouped into three main categories: the actin-myosin motor, anchoring adaptors, and transmembrane adhesion proteins.

Actin-Myosin Motor

The core of the glideosoma is constituted by myosin A (MyoA), a class XIV myosin that associates with its light chain MLC1. This motor complex binds to short, dynamic actin filaments (F-actin), whose polymerization is regulated by factors such as profilin, formin, and cofilin (15). In Plasmodium falciparum, at least six myosins have been identified, but only PfMyoA has been characterized as an active participant in the glideosoma (16).

Anchoring Proteins

The actin-myosin motor is anchored to the inner membrane of the pellicular complex (IMC) by adaptor proteins such as GAP45, GAP50, and GAP40. GAP45 connects the plasma membrane to the IMC, while GAP50 inserts directly into the IMC, providing structural stability. GAP40 and GAPM1-3 reinforce the complex's architecture and participate in its assembly (3). These proteins undergo post-translational modifications such as palmitoylation and myristoylation, which are essential for its localization and functionality (11). Phosphorylation of GAP45, for example,

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regulates its interaction with MyoA and its assembly capacity (12).

Transmembrane Adhesion Proteins

The force generated by the motor is transmitted to the exterior by transmembrane proteins such as MIC2 in T. gondii and TRAP in *Plasmodium* spp., which connect to the extracellular substrate through adhesins. These proteins associate with the glideosomal complex through cytoplasmic adaptors such as aldolase, which link their cytosolic domain to F-actin (9). The correct localization of these adhesins to the plasma membrane depends on vesicular trafficking mediated by the endoplasmic reticulum and the Golgi apparatus, as well as intracellular calcium signals that regulate their secretion from micronemes (17).

From this perspective, we can establish that the molecular composition of the glideosome reveals a highly specialized machinery, the efficiency of which depends on the precise interaction between structural proteins, molecular motors, and membrane adaptors. This modular organization allows the apicomplexan parasite to translate intracellular signals into directed movement, which is essential for its life cycle and pathogenicity.

The actin-myosin motor, although evolutionarily conserved, presents unique adaptations in Apicomplexa, such as class XIV Myosins and the presence of short, transient actin filaments. This configuration suggests a functional optimization oriented toward rapid and efficient invasion of host cells. The dependence on post-translational

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modifications such as palmitoylation and phosphorylation for the assembly and regulation of the complex adds a layer of control that could be exploited pharmacologically.

On the other hand, the connection between the glideosome and transmembrane adhesion proteins establishes a functional bridge between the interior of the parasite and its extracellular environment. This interface is critical not only for motility but also for invasion specificity, as adhesins determine recognition and interaction with target cells. The involvement of adaptors such as aldolase in this process suggests a metabolic integration that could link motility to the parasite's energetic status.

Despite advances in the proteomic characterization of the glideosome, gaps persist in our understanding of its spatial and temporal dynamics during invasion. The existence of functional isoforms, compensatory mechanisms, and variability between species pose challenges for the design of specific inhibitors. However, the high conservation of its core components makes it a promising target for therapeutic interventions targeting multiple Apicomplexa species.

Overall, the molecular composition of the glideosome not only reflects structural sophistication but also a functional integration that underpins the invasive capacity of these parasites. Studying them offers a privileged window into virulence mechanisms and opens new possibilities for the development of broad-spectrum antagonistic strategies.

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Glideosome-Mediated Invasion Mechanisms

Cellular invasion in parasites of the Apicomplexa phylum is a highly regulated process that depends on glideosome motility, the secretion of specialized organelles, and specific interactions with host receptors. This process has been characterized as a sequence of events that includes cell recognition, parasite reorientation, formation of the parasitophorous vacuole, and active entry by gliding (18).

Recognition and Initial Adhesion

The first step in invasion involves contact between the parasite and the host cell, mediated by transmembrane adhesins such as MIC2 in *T. gondii* and TRAP in *Plasmodium* spp. These proteins are secreted from micronemes and anchor to the glideosome through adaptors such as aldolase, allowing the transmission of force from the actin-myosin motor to the cell substrate (17).

Reorientation and Formation of the Moving Junction

Once contact is established, the parasite reorients itself to position its apical pole toward the host membrane. At this stage, the "moving junction" is formed, a transient structure composed of proteins secreted from the rhoptria, such as RON2, RON4, and AMA1. This junction acts as an anchoring ring that allows the parasite to enter without disrupting the host plasma membrane (19).

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Glideosomal Motility and Penetration

The force generated by the glideosome propels the parasite through the moving junction, allowing its active entry into the cell. This gliding motility is ATP-dependent and regulated by intracellular signals such as calcium and phosphorylation of glideosomal components (3). In *Plasmodium*, this mechanism allows sporozoite migration to the liver and merozoite invasion of erythrocytes (18).

Formation of the Parasitophorous Vacuole

During invasion, the parasite induces the invagination of the host membrane, forming a parasitophorous vacuole that isolates it from the cell cytoplasm. This structure is essential for intracellular survival and is formed without activating phagocytosis mechanisms, allowing the parasite to evade the immune response (4).

Based on these premises, the glideosome-mediated cell invasion process in apicomplexan parasites represents a functional convergence between motility, adhesion, and manipulation of the host environment. Unlike the passive mechanisms of cell entry observed in other microorganisms, Apicomplexa employ an active, energetically costly, and highly regulated strategy, which allows them to cross cellular barriers without triggering immediate immune responses.

The formation of the mobile junction and the coordination between organellar secretion and glideosomal motility demonstrate a molecular synchronization that requires temporal and spatial

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precision. This level of control suggests that the glideosome does not act in isolation, but as part of a functional network integrated with the secretory system, the cytoskeleton, and intracellular signaling pathways. The involvement of proteins such as AMA1, RON2, and MIC2 at the parasite-host interface reinforces the idea that invasion is both a mechanical and biochemical phenomenon.

From an evolutionary perspective, the ability to form a parasitophorous vacuole without activating phagocytosis represents an adaptive innovation that has allowed these parasites to colonize a wide range of hosts and tissues. This early immune evasion, combined with efficient entry, makes the glideosome a central element of apicomplexan virulence.

In therapeutic terms, the complexity of the invasive process poses both opportunities and challenges. While there are multiple potential targets (such as motility-regulating kinases, transmembrane adhesins, and components of the mobile junction), the functional redundancy and molecular plasticity of the system could limit the efficacy of single inhibitors. Therefore, a combinatorial approach that integrates structural, functional, and dynamic knowledge of the glideosome and its associated networks is required.

Glideosome Assembly and Activation Dynamics

Glideosome functionality depends on a highly organized protein architecture, the

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assembly and activation of which are regulated by specific intracellular signals. This motor complex assembles in the subpellicular region of the parasite, anchored to the inner membrane of the pellicular complex, and is activated in response to stimuli that precede cell motility and invasion.

Structural Assembly

Glideosome assembly involves the sequential integration of its main components:

MyoA: Actinic motor that generates displacement force. Its localization depends on the interaction with MLC1.

MLC1 (Myosin Light Chain 1): Stabilizes the active conformation of MyoA and facilitates its anchoring to GAP45.

GAP45: A bridging protein that connects the motor complex to the inner membrane, enabling force transmission.

GAP50: Transmembrane anchor that anchors the glideosome to the pellicular complex, providing structural stability.

This assembly occurs in specialized domains of the inner membrane, where components are recruited through protein-protein interactions and post-translational modifications, such as palmitoylation and phosphorylation (20).

Functional Activation

Glideosome activation is closely linked to intracellular signaling triggered by contact with the host cell. Key events include:

Intracellular calcium release: Activates Ca^{2+}-dependent kinases, such as CDPK1, which

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phosphorylate glideosome components and adhesins.

PKG (Protein Kinase G) activation: Regulates microneme secretion and the availability of adhesins such as MIC2.

Actin polymerization: Controlled by factors such as Formin1 and profilin, it allows the movement of adhesins along the motor complex.

Interaction with transmembrane adhesins: Such as MIC2, which connect to the cytoskeleton through aldolases, transmitting the force generated by MyoA to the outside.

Activation is transient and spatially restricted, allowing the parasite to modulate its motility depending on the environment and host cell type (21).

Temporal and Spatial Regulation

Glideosome dynamics are regulated by mechanisms that ensure its assembly and activation only at critical moments:

Control by phosphorylation/dephosphorylation cycles: Allows for the reversible activation of key components.

Lipid-dependent recruitment: Such as phosphatidylinositol phosphates (PIPs), which define membrane microdomains for assembly.

Interaction with the subpellicular cytoskeleton: Which restricts glideosome localization and coordinates its orientation during invasion (21).

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Glideosome Regulatory Kinases

Glideosome activation is controlled by a network of kinases that respond to intracellular signals such as calcium, cyclic nucleotides, and lipids, regulating the phosphorylation of structural and functional components of the motor complex. These kinases integrate motility, secretion, and adhesion processes and are essential for efficient host invasion.

The calcium-dependent kinase CDPK1 (Calcium-Dependent Protein Kinase 1) is one of the most well-characterized regulators in *T. gondii* and *P. falciparum*. Its activation occurs after transient increases in intracellular Ca^{2+}, which triggers the phosphorylation of proteins such as MyoA, GAP45, and MIC2, facilitating glideosome reorganization and adhesion to the host (22, 23). Pharmacological inhibition of CDPK1 blocks invasion without affecting basal viability of the parasite, making it an attractive therapeutic target (24).

The cGMP-dependent kinase (PKG) regulates the secretion of micronemes and rhoptries, essential for the display of adhesins and the formation of moving junctions. Its activation is mediated by cGMP, generated by guanylyl cyclase in response to external stimuli. PKG controls vesicular trafficking and the availability of adhesins such as MIC2 and AMA1, being essential for invasion and egress (25, 26). Selective PKG inhibitors have been shown to block multiple stages of the lytic cycle, reinforcing their value as a pharmacological target (27).

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PKA (Protein Kinase A), dependent on cAMP, modulates actin dynamics and the stability of transmembrane adhesins. Its activation occurs by adenylyl cyclase in response to environmental signals, and its action includes the phosphorylation of aldolase and MIC2, affecting the transmission of force from the glideosome to the plasma membrane (2). In addition, PKA can functionally interact with CDPK1, generating synergistic or antagonistic effects depending on the cellular context, suggesting an adaptive regulation of motility (28).

Finally, several apicomplexan-specific kinases, such as TgTKL1 and TgMAPK1, are involved in the fine-tuning of glideosome assembly and activation. These kinases feature unique structural domains not conserved in higher eukaryotes, making them attractive targets for selective therapies (29, 30, 31, 32). Their function includes the modulation of GAP45, MLC1, and lipid signaling proteins, integrating stress responses, adhesion signals, and cytoskeletal reorganization. Although their functional characterization is still under development, they represent an emerging frontier in the understanding of apicomplexan motility (Table 2).

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Table 2. Glideosome regulatory kinases in Apicomplexa. Summary of the main kinases involved in glideosome activation and regulation, including their activation mechanisms, known molecular targets, and main functions. The table highlights both conserved and phylum-specific kinases, highlighting their functional and therapeutic relevance. References correspond to experimental studies validating each interaction.

Kinase	Activation mechanism	Molecular targets	Main function	References
CDPK1 (Calcium-Dependent Protein Kinase 1)	Increase of Ca^{2+} intracellular	MyoA, GAP45, MIC2	Phosphorylation of glideosome components and adhesins; regulation of exocytosis	Lourido et al., 2010; Treeck et al., 2014; Garrison et al., 2012
PKG (cGMP-Dependent Protein Kinase)	Elevation of cGMP by guanylyl cyclase	MIC2, AMA1 vesicle trafficking proteins,	Control of microneme secretion and mobile junction formation	Donald et al., 2006; Alam et al., 2015; Howard et al., 2015
PKA (Protein Kinase A)	Production of cAMP by adenylyl cyclase	Aldolase, MIC2, actin anchoring proteins	Modulation of actin dynamics and adhesion; interaction with CDPK1	Uboldi et al., 2018; Jia et al., 2017
Apicomplexa-	Signals of stress,	GAP45,	Fine regulation of	Reininger et al.,

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specific kinases (e.g., TgTKL1**,** TgMAPK1**)**	adhesion, and cellular reorganization	MLC1, lipid signaling proteins	glideosome assembly and activation; selective therapeutic targets	2005; Sidik et al., 2016

In this regard, the regulation of the glideosome by specific kinases demonstrates the sophistication of molecular control in Apicomplexa, where motility is not simply mechanical, but the result of a precise integration between signaling, secretion, and structural assembly (33). The existence of kinases with unique domains, not conserved in higher eukaryotes, suggests an adaptive evolution oriented towards parasitic specialization. This functional uniqueness not only allows an efficient modulation of invasion by Apicomplexans but also opens highly selective therapeutic opportunities. However, the redundancy and interconnectivity between signaling pathways pose challenges for the design of specific inhibitors, demanding combinatorial approaches and a deeper characterization of the regulatory networks involved (34).

CONCLUSIONS

The glideosome represents a key structural and functional innovation in the biology of apicomplexan parasites, enabling active and highly regulated motility essential for cell invasion. Its precise assembly, coordination

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with secretory organelles, and integration of intracellular signals such as calcium, cGMP, and cAMP demonstrate a molecular complexity that surpasses that of other protozoan locomotion and invasion systems.

The involvement of specific kinases such as CDPK1, PKG, PKA, and others specific to the Apicomplexa phylum underscores the existence of a specialized regulatory network capable of dynamically modulating glideosome activity in response to the host environment. These kinases not only control motility but also link adhesion, secretion, and cytoskeletal reorganization processes, consolidating the glideosome as a central functional node in parasitic pathogenesis.

From a therapeutic perspective, the structural and functional uniqueness of these components offers opportunities for the development of selective drugs capable of interfering with invasion without affecting host cells. However, the functional redundancy and adaptive plasticity of the system pose challenges that require multidisciplinary approaches and combinatorial strategies.

Overall, the study of the glideosome not only provides fundamental knowledge about the cellular biology of Apicomplexa but also opens new avenues for the rational design of antiparasitic interventions, with direct implications for the control of diseases such as toxoplasmosis, malaria, and cryptosporidiosis.

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