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Biomedical Sciences

Original article

Genomics of thermally pathogenic dimorphic human fungi: From the mitochondrion to the pangenome

Genómica de hongos dimórficos térmicos patógenos en humanos: de la mitocondria al pangenoma

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Abstract

The genomics of human pathogenic thermally dimorphic fungi has advanced significantly thanks to international initiatives such as the 1000 Fungal Genomes Project, which has reported a wide range of complete genomes in public repositories. This has driven the genomic characterization of genera such as *Histoplasma*, *Paracoccidioides*, and *Sporothrix*, including clinically relevant Colombian isolates. Genomic studies have revealed key aspects of their diversity, evolution, and host adaptation, while enabling comparative analyses based on orthologous genes that highlight both conservation and divergence among lineages. Beyond their description, the availability of complete genomes has had direct applications in diagnostics through systematic comparison algorithms that identify unique genomic regions serving as highly specific molecular targets. This has facilitated the design and validation of innovative PCR assays for the above-mentioned genera, overcoming the limitations of traditional candidate-gene approaches. In Colombia, significant challenges remain, including the limited availability of clinical isolates, biosafety requirements, and difficulties in timely diagnosis. In this context, we aimed to analyze the current state of assembled genomes of these dimorphic fungi available in public databases for Colombia and their use in the development of highly specific molecular diagnostic tools.

Keywords: Dimorphic fungi; Genomics; Mitochondria; Pangenome.

Resumen

La genómica de hongos dimórficos térmicos patógenos en humanos ha avanzado significativamente gracias a iniciativas internacionales como el proyecto 1000 Fungal Genomes, lo que ha permitido disponer de una amplia variedad de genomas completos en repositorios públicos. Este recurso ha impulsado la caracterización genómica de géneros como *Histoplasma, Paracoccidioides* y el complejo *Sporothrix schenckii*, incluidos aislamientos colombianos de importancia clínica. Los estudios genómicos han revelado aspectos claves de su diversidad, evolución y adaptación al hospedero, permitiendo análisis comparativos mediante genes ortólogos que muestran tanto la conservación como la divergencia entre linajes. Más allá de la descripción, la disponibilidad de genomas completos ha tenido aplicaciones directas en el diagnóstico mediante algoritmos de comparación sistemática con los cuales se han identificado regiones genómicas únicas que sirven como blancos moleculares muy específicos. Ello ha permitido diseñar y validar ensayos de PCR innovadores para los géneros ya mencionados, evitando las limitaciones de los enfoques tradicionales basados en genes candidatos. En Colombia persisten retos significativos como la escasa disponibilidad de aislamientos clínicos, las exigencias de bioseguridad y la dificultad del diagnóstico oportuno. En este contexto, nos propusimos analizar el estado actual de los genomas ensamblados de estos hongos dimórficos disponibles en bases de datos públicas y su uso en el desarrollo de herramientas diagnósticas moleculares de alta especificidad.

Palabras claves: Hongos dimórficos; Genómica; Mitocondria; Pangenoma.

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Introduction

Fungi are diverse eukaryotic organisms that play essential roles in ecosystems, including the decomposition of organic matter and nutrient recycling. Although most are beneficial, some species can infect and cause diseases in humans, animals, and plants (**Bonifaz-Trujillo**, 2020). For a fungus to be considered pathogenic to humans, it should grow at a temperature of at least 37°C, reach the tissues it will parasitize, digest and absorb components of human tissues, and, finally, resist the host's immune system. Taxonomically, pathogenic fungi have been described in the phyla *Ascomycota, Mucoromycota*, and *Basidiomycota,* with *Ascomycota* comprising most pathogenic species, including various filamentous, yeast-like, and dimorphic fungi (**Köhler *et al.***, 2015).

Dimorphism in fungi refers to the reversible ability to alternate between mycelial and yeast-like forms depending on factors such as temperature. In thermally dimorphic fungi, the filamentous phase occurs in nature (18–28°C), while the yeast-like phase develops in the host (37°C) (**Hibbett *et al.***, 2007). Most thermally dimorphic fungi are taxonomically related, with the order *Onygenales* containing the largest number of species, including *Histoplasma* spp., *Blastomyces spp.*, *Coccidioides* spp., *Paracoccidioides* spp., and *Emergomyces* spp. Other orders that include dimorphic fungi are *Ophiostomatales* and *Eurotiales,* where *Sporothrix* spp. and *Talaromyces marneffei* are found, respectively (**Sil & Andrianopoulos**, 2015). In Colombia, histoplasmosis, paracoccidioidomycosis, sporotrichosis, and coccidioidomycosis cases have been reported, although native isolates of *Coccidioides* spp. are scarce, which limits their genomic study.

Genomics, an interdisciplinary branch of molecular biology focused on the study of DNA, has been key to elucidating the structure, function, and evolution of fungi (**Gregory**, 2011). The information generated in this field is stored in specialized repositories that provide access to DNA sequences, among which GenBank, maintained by the National Center for Biotechnology Information (NCBI), as well as fungal-focused databases such as MycoCosm and FungiDB, stands out. In this context, the concept of the pangenome emerges, integrating the conserved genes of all strains within a species (the core genome) and variable or accessory genes associated with adaptive processes such as pathogenesis and antimicrobial resistance. This perspective provides a useful framework for understanding the genomic diversity of thermally dimorphic fungi and their potential application in comparative studies **(McCarthy & Fitzpatrick**, 2019).

Despite the growing use of sequencing technologies that have expanded the genomic knowledge of thermally dimorphic fungi, the number of assembled genomes available in public databases remains limited. This scarcity restricts the use of these resources in comparative genomic studies, functional research, and biotechnological applications. Given this situation, here we aimed to analyze the status of assembled genomes of thermally dimorphic human-pathogenic fungi isolated in Colombia and available in public databases, and to highlight their potential for the development of highly specific molecular diagnostic tools.

The genomics of thermally dimorphic fungi

Currently, complete and annotated genomes are available for a wide range of representative species of thermally dimorphic fungi thanks to initiatives such as the Fungal Genome Initiative of the Broad Institute (**Broad Institute**, 2025) and the 1000 Fungal Genomes Project, led by the Joint Genome Institute (JGI), whose goal since 2012 has been to sequence at least two representative species from each described family (**Joint Genome Institute**, 2023). As a result of these efforts, there has been an exponential increase in the availability of fungal genomes in repositories such as NCBI Genome Assembly, which currently hosts around 220 assembled genomes of thermally dimorphic fungi relevant to human health (**NCBI**, 2025b).

Additionally, MycoCosm and FungiDB also provide genomic data for thermally dimorphic fungi, although the number of available assemblies is considerably lower and

largely corresponds to genomes already represented in NCBI (**FungiDB**, s. f.; **Grigoriev *et al.***, 2025). It is important to clarify that the genome assemblies described were selected as the most representative for each genus and do not encompass all assemblies currently available in NCBI. **Figure 1** shows several genomic and morphological characteristics of the main thermally dimorphic fungi of medical importance in humans.

Histoplasma spp.

Histoplasma spp. is the agent responsible for histoplasmosis, the leading cause of fungal respiratory disease worldwide. Until 2003, this mycosis was thought to be caused exclusively by *H. capsulatum*, a species classified into three varieties: *H. capsulatum* var. *capsulatum*, corresponding to human pathogens from the New World; *H. capsulatum* var. *duboisii*, associated with African human pathogens, and *H. capsulatum* var. *farciminosum*, related to infections in horses and donkeys from the Old World (**Guého *et al.***, 1997). However, subsequent phylogenetic studies demonstrated that this traditional classification does not reflect the true diversity of the species. Instead, eight phylogenetic clades were recognized, corresponding to North American classes 1 and 2 (NAm1 and NAm2), Latin

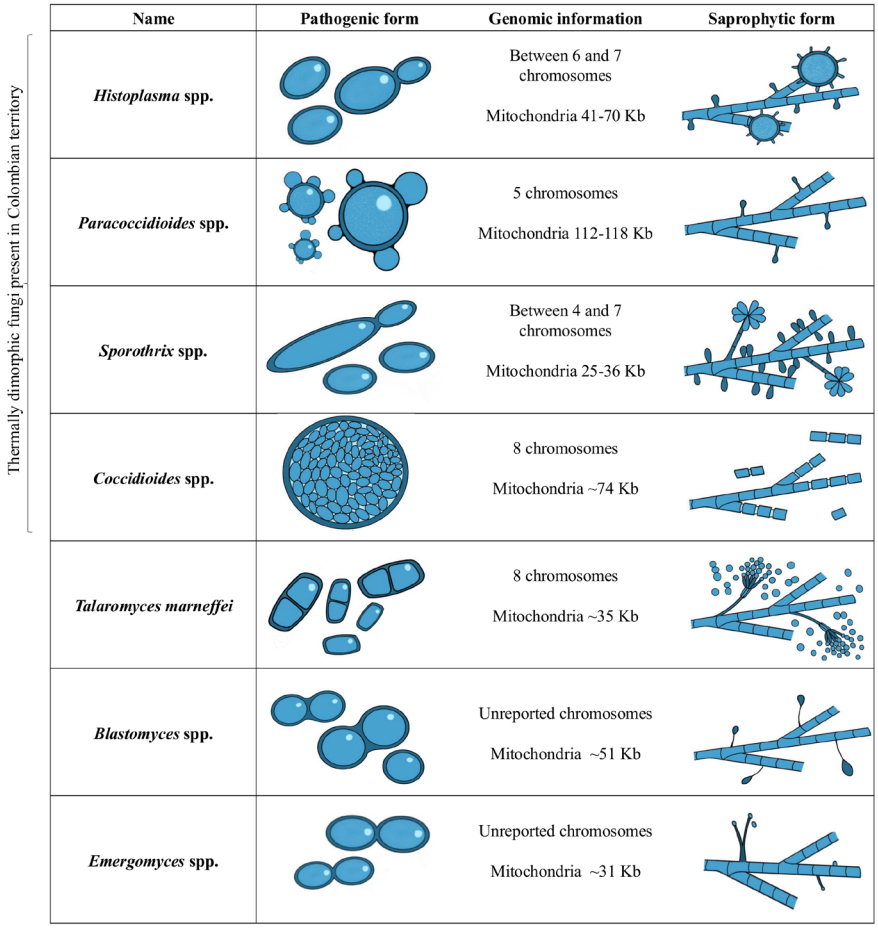

Figure 1. Genomic and Morphological Features of Dimorphic Fungi of Human Health Relevance. The figure presents the reported number of chromosomes and the average mitochondrial genome size for each mentioned genus. It also includes graphical representations of the morphology of each fungus in its pathogenic phase at 37°C, corresponding to the yeast-like form (except for the genus *Coccidioides*, which develops spherules), and in its saprophytic phase at 25°C. The genomic characteristics of representative strains from these genera are summarized in **Table 1S,** https://raccefyn.co/index.php/raccefyn/article/view/3320/5302

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American groups A and B (LAm A and LAm B), and the Eurasian, Netherlands, Australian, and African groups, along with a distinct lineage formed by Panamanian isolates (H81) (**Kasuga *et al.***, 2003).

Recently, phylogenomic analyses have redefined the genus *Histoplasma* into five genetically distinct species. Four of them were renamed as four different cryptic species: *H. capsulatum* (H81 lineage), *H. mississippiense* (NAm1), *H. ohiense* (NAm2), and *H. suramericanum* (LAm A) (**Sepúlveda *et al.,*** 2017). Although the distribution of these species is linked to specific geographic locations, genomic characterization has revealed a high degree of synteny among *Histoplasma* isolates from geographically distant regions **(Voorhies *et al.***, 2022).

As of 2025, 14 assembled genomes from 10 *Histoplasma* spp. strains have been documented. The first, published in July 2007, pertains to the *H. mississippiense* (Nam1 strain), whose scaffold-level assembly functions as the reference genome for this species. Subsequently, between December 2007 and July 2020, six more scaffold-level assemblies were published for *H. capsulatum*, *H. ohiense*, and *H. capsulatum* var. *duboisii*, originating from strains G217B, G186AR, H143, H88, TMU, and G186A. Among these, the assembly of strain G186AR, published in March 2009 using ABI 3730 sequencing technology, was established as the reference genome for *H. capsulatum* (**NCBI**, 2024).

In March 2021, the University of California published two new genomes corresponding to *H. mississippiense* and *H. capsulatum*, from strains WU24 and G184AR, respectively, and updated the genomes of strains G217B, H88, and G186AR using third-generation Oxford Nanopore sequencing technology. This enabled chromosome-level assemblies for strains WU24, H88, and G186AR, and contig-level assemblies for G217B and G184AR (**Voorhies *et al.***, 2022). More recently, in July 2025, the genomes of strains G217B-UCSF2 and G217B-UCSF3 were published, both with chromosome-level assemblies obtained using the same technology (**Voorhies *et al.***, 2025).

Additionally, (**Voorhies *et al.*,** 2022) described the chromosome-level assembly of several of these strains and characterized their mitochondrial genomes. These genomes, ranging from 41 to 70 kb, retain the typical fungal mitochondrial genes involved in ATP synthesis, cytochrome c oxidase, NADH dehydrogenase, and rRNA, as well as a complete set of tRNAs. Despite this high conservation in gene content, variations were identified in genome organization and intron size, providing valuable insights into the intraspecific diversity within the genus *Histoplasma* (**Voorhies *et al.***, 2022).

Paracoccidioides spp.

Paracoccidioides is a dimorphic fungus recognized as the etiologic agent of paracoccidioidomycosis (PCM), a non-contagious granulomatous mycosis that may present in chronic, subacute, or, less frequently, acute forms (**Restrepo-Moreno *et al.***, 2020). Until 2006, *P. brasiliensis* was considered the sole etiological agent of this disease; however, molecular taxonomy studies revealed the existence of five distinct phylogenetic species, designated S1a, S1b, PS2, PS3, and PS4 (**Matute *et al.***, 2006; **Theodoro *et al.***, 2012). Subsequently, the *P. brasiliensis* complex was reclassified into four species: *P. brasiliensis* (S1), *P. americana* (PS2), *P. restrepiensis* (PS3), and *P. venezuelensis* (PS4) (**Turissini *et al.***, 2017). In addition to these, a divergent monophyletic species, *P. lutzii*, has been described, differing from the others both by its distinctive genome and by morphological traits, particularly the larger size of its yeast-form daughter cells (**Teixeira *et al.***, 2009).

In Colombia, the highest prevalence of PCM cases is attributed to *P. restrepiensis*, the species that predominantly circulates within the country and was named in honor of Dr. Ángela Restrepo Moreno, a pioneer in the study of this fungus (**Turissini *et al.***, 2017). Species within the *Paracoccidioides* genus exhibit marked genetic differentiation, are haploid, and show strong divergence, suggesting that the genus is undergoing an advanced stage of speciation. However, population studies have revealed a reduction in the effective population size, indicating a genetic impoverishment among the currently circulating species (**Mavengere *et al.***, 2020; **McEwen *et al.***, 2022).

To date, six genome assemblies of the genus *Paracoccidioides* are available. The first of these corresponded to the Pb03 strain of *P. americana*, published in November 2007 by the Broad Institute using Illumina sequencing and assembled at the scaffold level. Subsequently, in March 2008, the same institute released the genomes of the Pb18 strain of *P. brasiliensis* and the Pb01 strain of *P. lutzii*, also obtained using Illumina and assembled to the scaffold level. In 2011, **Desjardins *et al.*** successfully mapped the supercontigs of the Pb18 genome and organized them into five chromosomes using optical mapping, thereby improving its structural resolution. Later, in 2014, the Broad Institute updated the Pb03, Pb18, and Pb01 genomes to include gene annotation; since then, Pb18 and Pb01 have been established as the genomic references for their respective species and were officially designated as reference strains in the NCBI RefSeq database in November of the same year. (**Desjardins *et al.***, 2011).

In August 2016, the Broad Institute completed the sequencing of the remaining *Paracoccidioides* species, publishing the assembled genomes of strains Pb300 and PbCNH, corresponding to *P. venezuelensis* and *P. restrepiensis*, respectively. Both were obtained using the Illumina HiSeq platform, assembled at the scaffold level, and included their respective gene annotations. Subsequently, in October 2024, the Regional Institute of Medicine at the National University of the Northeast (Argentina) published the genome of the *P. brasiliensis* strain IMR-M-Pb369, which to date represents the only assembly of this species obtained using long-read sequencing with the Oxford Nanopore MinION platform. This genome was assembled at the contig level; however, the corresponding gene prediction has not yet been reported (**Lorenzini-Campos *et al.***, 2024).

The first mitochondrial genome of the genus *Paracoccidioides* was reported by **Cardoso *et al*.** in 2007 from the *P. brasiliensis* strain Pb18, with a length of 71,334 bp organized as a circular molecule containing two gaps in the *nad5* gene. Later, in 2020, **Misas *et al.*** used long-read sequencing with Oxford Nanopore to complete these genomes and additionally reported that of the *P. americana* strain Pb03, with sizes ranging from 112 to 118 kb and a detailed annotation of mitochondrial genes encoding respiratory complexes, rRNAs, and tRNAs. Owing to their extensive intronic regions, the mitochondrial genomes of *Paracoccidioides* are considerably larger than those described in other Onygenales.

Sporothrix spp.

Species of the genus *Sporothrix* are the causative agents of sporotrichosis, a subacute or chronic fungal infection that occurs worldwide (**Barros *et al*.**, 2011). Phylogenetic analyses based on genes such as β-tubulin and calmodulin have allowed the identification of multiple species, including *S. brasiliensis*, *S. schenckii*, *S. globosa*, *S. mexicana*, *S. pallida*, and *S. luriei*. In Colombia, the circulation of *S. schenckii* and *S. globosa* has been documented (**Hernández-Castro *et al*.**, 2022; **Marimon *et al*.**, 2006; **Zhou *et al*.**, 2014).

The first assembled genome of *Sporothrix* spp. was published in 2013 by the Broad Institute and corresponded to the *S. schenckii* strain ATCC 58251, sequenced using Illumina technology (**Cuomo *et al*.**, 2014). Since then, the number of assembled genomes has increased to 43. The species with the greatest representation is *S. globosa* with nine genomes, followed by *S. schenckii* with four, *S. pallida* with two, and *S. brasiliensis*, *S. mexicana*, and *S. luriei* with one genome each (**Huang *et al.***, 2020; **Teixeira *et al*.**, 2014). These genomes were published between October 2013 and January 2022 and were sequenced using second-generation sequencing technologies, mainly 454 and Illumina. However, despite the large number of assembled genomes, only the *S. schenckii* strain 1099-18 and the *S. brasiliensis* strain 5110 have been deposited in the NCBI RefSeq database since 2022, although both had already been available in GenBank since 2015 (**Teixeira *et al*.**, 2014). Most genomes within the *Sporothrix* genus are assembled at the scaffold level, except for three genomes—strains 1099-18 of *S. schenckii sensu stricto*, SPA8 of *S. pallida*, and 5110 of *S. brasiliensis*—which were assembled at the contig level.

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Among the 43 assembled genomes, those corresponding to *S. schenckii* strains SsMS1 and SsEM7 stand out, published by **Gómez *et al.*** between December 2017 and February 2018. Both isolates, of Colombian origin, were sequenced using the Illumina HiSeq 2000 platform (**Gómez *et al.***, 2018). The relevance of these genomes lies in their direct representation of the genetic diversity present in Colombia. Their genomic availability not only strengthens comparative studies at both regional and global levels but also enables the assessment of potential genetic adaptations associated with local ecological conditions and the epidemiology of sporotrichosis in the Colombian territory.

The mitochondrial genome of species within the *Sporothrix spp.* was reported by **Teixeira *et al.*** in 2014, with lengths ranging from 26 to 36 kb depending on the species. These genomes include the expected set of genes encoding respiratory complexes, rRNAs, and tRNAs, and they are characterized by a relatively compact structure compared to the Onygenales, with fewer and smaller introns. This reduced structure reflects a differential evolutionary pattern within the order, contrasting with the intronic expansions observed in other genera (**Teixeira *et al***., 2014).

Coccidioides spp.

Coccidioides spp. is the causal agent of coccidioidomycosis, a systemic mycosis endemic to certain arid and semi-arid regions of the United States, Central America, and South America. The genus comprises two species, *C. immitis*, which is endemic to California's San Joaquin Valley, and *C. posadasii*, which is distributed across Texas, Arizona, New Mexico, Mexico, and various regions of Central and South America (**Kirkland *et al.***, 2022). In the genomic context, 18 assembled genomes of *Coccidioides* spp. are currently available, of which five correspond to *C. immitis* and the remaining 13 to *C. posadasii* (**NCBI**, 2025a). The first genomes were published in 2006, when the Broad Institute released the assemblies of *C. immitis* strains H538.4 and RMSCC 2394. Subsequently, in 2007, the genomes of several *C. posadasii* strains— including CPA 0001, RMSCC 3700, RMSCC 2133, and RMSCC 3488— were published, all sequenced using Illumina Technology (**Neafsey *et al.***, 2010).

Among the 18 available genomes, two of the most widely used stand out. The first corresponds to the RS strain of *C. immitis*, published in 2009 by the Broad Institute and sequenced using the Sanger method, with an assembly totaling 28.9 Mb across six scaffolds. The second corresponds to the Silveira strain of *C. posadasii*, published in 2022 by Northern Arizona University using a hybrid strategy that combined the PacBio and Illumina platforms, with a total size of 28.2 Mb distributed across eight chromosomes. The Silveira strain represents the only assembly currently available at the chromosomal level within the genus (**Sharpton *et al.***, 2009; **Teixeira *et al.***, 2022). Both genomes constitute the reference sequences deposited in the NCBI RefSeq database.

Regarding the mitochondrial genome, **Teixeira *et al.*** assembled the mitochondrial genomes of the *C. immitis* strain WA221 and the *C. posadasii* strain Tucson-2, with lengths of 68,597 bp and 75,194 bp, respectively. In addition, the mitochondrial genome of the reference strain Silveira of *C. posadasii* is available, with a total length of 74,407 bp (**Teixeira *et al.***, 2021, 2022). These mitochondrial genomes share a gene repertoire like that of other dimorphic fungi in the order *Onygenales*, such as *Paracoccidioides* spp. and *Histoplasma* spp., and exhibit a highly conserved gene organization. In Colombia, although several cases of coccidioidomycosis have been documented, most correspond to isolated clinical reports and, in a few instances, to the molecular identification of *C. immitis* from formalin-fixed, paraffin-embedded tissue samples (**Canteros *et al.***, 2015). However, to date, no viable isolates or high-quality DNA suitable for whole-genome sequencing have been obtained, representing a significant gap in current knowledge. This limitation hinders the development of comparative and phylogenomic studies aimed at understanding the genetic diversity of *Coccidioides* in the country and its relationship to strains from other endemic regions across the Americas.

Comparative overview of orthologous genes in dimorphic fungi

The availability of assembled and annotated genomes from different thermally dimorphic fungi constitutes a fundamental resource for the comparative study of their biological, evolutionary, and genetic diversity characteristics. These data allow the identification of genes associated with dimorphism, host adaptation, and virulence, as well as the establishment of phylogenomic relationships that clarify speciation processes within this group. Moreover, comparative analyses between species and isolates from different geographic regions provide valuable insights into intraspecific variability and possible local adaptations, which in turn inform the understanding of their epidemiology, distribution, and potential impact on human health.

To characterize aspects such as the total number of genes, the proportions of genes assigned to and unassigned from orthogroups, and the relationships among different genera of dimorphic fungi, we conducted an orthology analysis using genomic data from public databases. Orthologous genes were identified with OrthoFinder (version 2.5.4) (**Emms & Kelly**, 2015), using as input the protein sequences retrieved from NCBI corresponding to dimorphic fungi of the family *Ajellomycetaceae*, other medically important dimorphic fungi, and *Aspergillus fumigatus*. Detailed information on the strains included in this analysis is presented in **Table 2S,** https://raccefyn.co/index.php/raccefyn/article/view/3320/5302. Additionally, a species tree was constructed from orthologous genes using the Species Tree Inference from All Genes (STAG) method and rooted with STRIDE to infer evolutionary relationships among the analyzed strains. The representation of the orthologous gene analysis performed with OrthoFinder is shown in **Figure 2**.

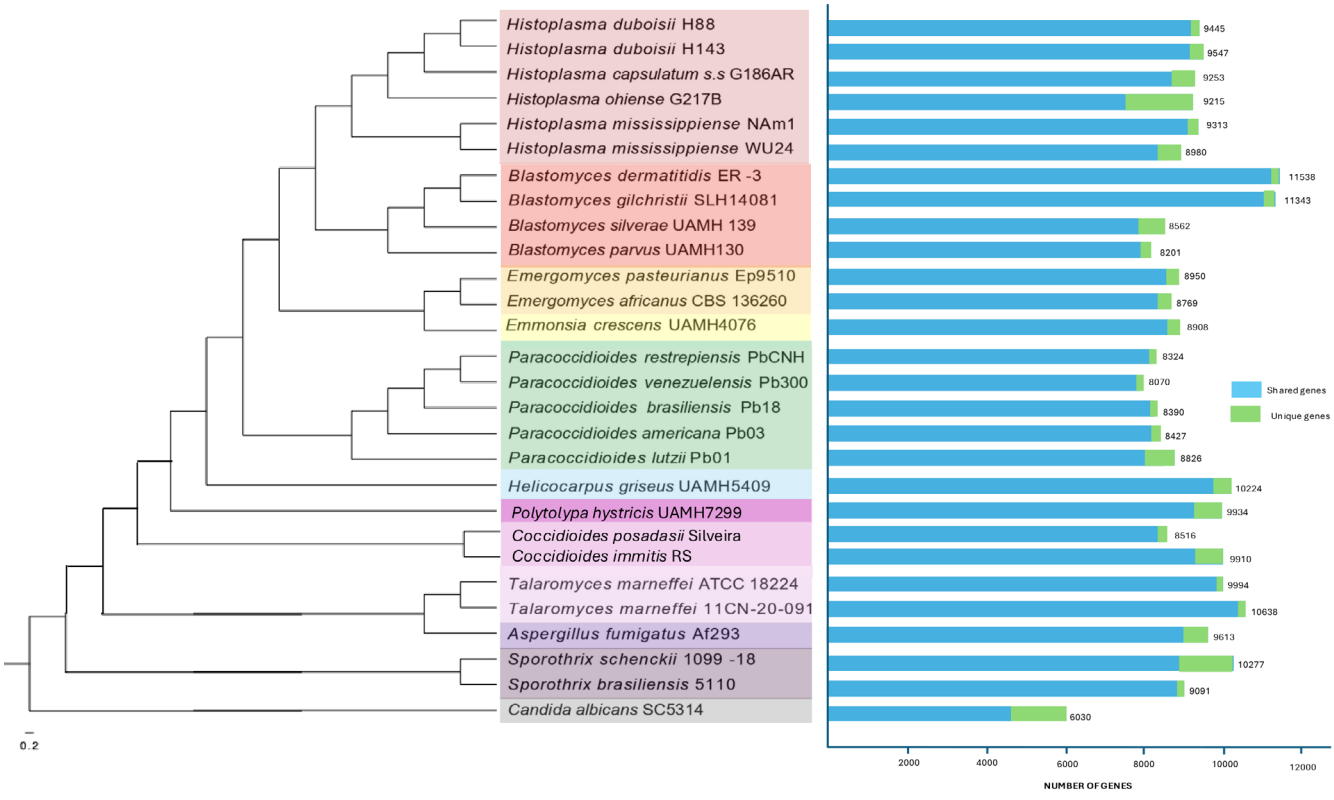

Figure 2. Orthologous gene analysis with OrthoFinder. A. Species tree inferred using STAG from 30 genomes, including *Ajellomycetaceae*, other medically important dimorphic fungi, and *Aspergillus fumigatus*. **B.** Total number of genes per species, showing genes in orthogroups (blue) and unassigned genes (green).

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The species tree shows a clear separation among the analyzed fungal genera. Species of the genera *Histoplasma* and *Blastomyces* form a well-supported monophyletic cluster. The *Emergomyces/Emmonsia* group appears as a sister clade to this *Histoplasma–Blastomyces* cluster. Species of the genus *Paracoccidioides* constitute a distinct and cohesive clade positioned basal to these groups within the family Ajellomycetaceae. In contrast, *Coccidioides* forms an independent and more distantly related lineage. Fungi outside Ajellomycetaceae, including *Talaromyces*, *Aspergillus fumigatus*, and *Sporothrix*, cluster in progressively more distant clades. *Candida albicans*, located at the root of the tree, serves as the outgroup.

Regarding gene assignment, most species exhibit a high proportion of genes assigned to orthogroups, reflecting strong genetic conservation among the analyzed genera. However, *B. gilchristii* and *B. dermatitidis* exhibit the highest total number of genes (11,343 and 11,538, respectively), suggesting greater genetic divergence compared to the other dimorphic fungi considered. In contrast, due to its phylogenetic distance and status as outgroup, *C. albicans* has the fewest genes (6,030) and a significantly lower proportion of genes assigned to orthogroups.

These findings provide a comparative overview of genetic conservation and variation in medically relevant dimorphic fungi. The clear separation of clades, together with the differences in the number and distribution of genes across orthogroups, highlights both the evolutionary stability within certain genera and the divergence processes that have shaped the observed diversity.

Application of genomes in diagnosis

The availability of complete genomes of thermally dimorphic pathogenic fungi has facilitated the development of innovative diagnostic tools. Through years of collaborative effort, an algorithm has been created to identify unique genomic regions that can serve as potential molecular targets for the accurate detection of these pathogens (**Figure 3**). The process starts with systematically comparing complete genomes against those of hosts, related microbiomes, and other pathogenic fungi, to find species-specific unique regions. These regions are then prioritized as molecular targets for designing highly specific PCR assays.

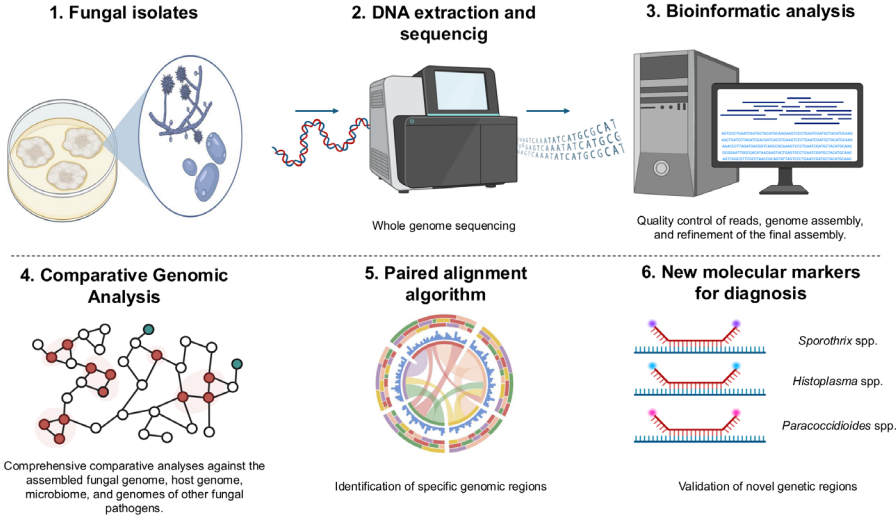

Figure 3. Algorithm for the rational design of PCR assays from complete genomes. The diagram shows the workflow used to identify unique genomic regions through systematic comparisons against host, microbiome, and other fungal pathogen genomes. These regions are prioritized as highly specific molecular targets for PCR assay development. This strategy, validated in the genera *Histoplasma*, *Paracoccidioides*, and *Sporothrix*, represents an innovative tool for the precise diagnosis of endemic mycoses. Made using https://app.biorender.com

Unlike traditional methods based on candidate genes such as rRNA or ITS, this approach utilizes the entire genomic repertoire, enhancing accuracy and lowering the risk of cross-reactivity. Based on this principle, a proof-of-concept study was carried out in *Histoplasma*, leading to the development of two new PCR assays targeting these unique regions (**Gallo *et al.***, 2021). The same approach was later applied to *Paracoccidioides* spp., aiding both experimental research and the clinical diagnosis of a paracoccidioidomycosis case through a PCR assay targeting 2DROP (**Gallo-Bonilla**, 2017; **Osorio-Cock *et al.***, 2023). Similarly, our team has created two PCR assays focused on exclusive *Sporothrix* regions, which are currently undergoing validation (**Gómez *et al.***, 2018). These advancements demonstrate how comparative genomics moves beyond a purely descriptive framework to become a practical tool capable of improving the timely diagnosis of endemic mycoses in our region.

Conclusion

Overall, the increasing availability of complete and annotated genomes of thermally dimorphic fungi has enabled significant advances in understanding their genetic diversity, evolution, and mechanisms of host adaptation. However, in endemic countries such as Colombia, major challenges remain in isolating, characterizing, and studying these pathogens. Factors such as the difficulty of timely diagnosis, limited availability of representative clinical cultures, and stringent biosafety requirements for handling these organisms restrict access to sufficient numbers of isolates. This limitation hinders the understanding of intraspecific diversity and local adaptation mechanisms, posing an additional obstacle to the design of more effective diagnostic and therapeutic strategies within the Colombian context.

Comparative analysis of orthologous genes shows both genetic conservation within certain genera and divergence among lineages. This provides a strong base for future research on dimorphism, pathogenicity, and the epidemiology of these mycoses. Notably, the availability of complete genomes has already led to real-world applications, such as new diagnostic tools. Our team used an algorithm to identify unique genomic regions, which allowed us to design PCR tests for *Histoplasma*, *Paracoccidioides*, and *Sporothrix*. These examples demonstrate that comparative genomics goes beyond simple description and becomes a practical tool with clinical benefits. This highlights the importance of sequencing local isolates, maintaining reference collections, and fostering collaborative networks. Such efforts can help develop more accurate diagnostic methods and surveillance strategies in endemic areas (**Gallo *et al.***, 2021).

Supplementary information

See the supplementary information in https://raccefyn.co/index.php/raccefyn/article/view/3320/5302

Author Contributions

All authors actively participated in the preparation of the manuscript. **SMC, MSG, MPJ, JMcE, OMG** conceived and designed the article; **SMC, MSG, OMG** collected and analyzed the data; **MPJ, JMcE, OMG** were responsible for the administrative and logistical management of the manuscript, as well as for style revision and verification of the document's coherence. All authors critically reviewed the intellectual content, made substantial contributions, and approved the final version for submission.

Conflicts of interest

The authors declare no conflict of interests that could have influenced the results or interpretation of this work.

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Ethical considerations

All authors are aware of and approve the submission of the manuscript, its content, authorship, and the established order. This study did not require ethical approval, as the data used correspond exclusively to genomic information available in public databases with access to biological sequences.

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