

Pulmonary Histoplasmosis, Taiwan, 1997–2024

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To the Editor: We read with interest about the cases of *Histoplasma capsulatum* infection in Taiwan, described by Kao et al. (1). However, molecular characterization of clinical isolates from Taiwan remains limited.

We report a case of disseminated histoplasmosis diagnosed in southern Taiwan in 2024. A 57-year-old man had persistent fever, weight loss, and progressive dyspnea. He had no history of diabetes, autoimmune disease, immunosuppressive therapy, or HIV infection. Imaging revealed diffuse pulmonary infiltrates and hepatosplenomegaly. Laboratory tests showed pancytopenia, hyperferritinemia, hypertriglyceridemia, and elevated liver enzymes, raising suspicion for hemophagocytic lymphohistiocytosis. Bone marrow examination demonstrated intracellular yeast forms within histiocytes, and metagenomic next-generation sequencing detected *H. capsulatum* fungi. The patient received liposomal amphotericin B (3 mg/kg/d) for 10 days, followed by oral itraconazole (200 mg 2×/d), with gradual clinical improvement. A bone marrow fungal culture yielded *H. capsulatum* fungi 28 days after sample collection. The patient never traveled to histoplasmosis-endemic regions, but he did engage in vegetable gardening on farmland in suburban Kaohsiung, where bat activity has been documented, although he reported no direct contact with bat guano, bird roosts, or imported animals.

Our phylogenetic analysis showed that the isolate clustered within the Latin American A1 lineage, together with reference strains from Mexico and Honduras (Figure). That finding was unexpected because most Asia isolates belong to the Eurasian clade (2). Possible explanations include imported infection, historical introduction, or unrecognized environmental reservoirs. Because *H. capsulatum* fungi commonly inhabit soil enriched with bat guano or bird droppings, suitable ecological niches might exist in subtropical Taiwan (2–4). Our findings suggest that lineage diversity of *H. capsulatum* fungi circulating in Asia might be underestimated.

Our findings provide molecular epidemiologic evidence of an unexpected *H. capsulatum* Latin American A1 lineage in Taiwan. Given the increase in histoplasmosis in Taiwan (1,5), expanded molecular surveillance and environmental sampling are needed to clarify the geographic distribution and transmission ecology of *H. capsulatum* fungi.

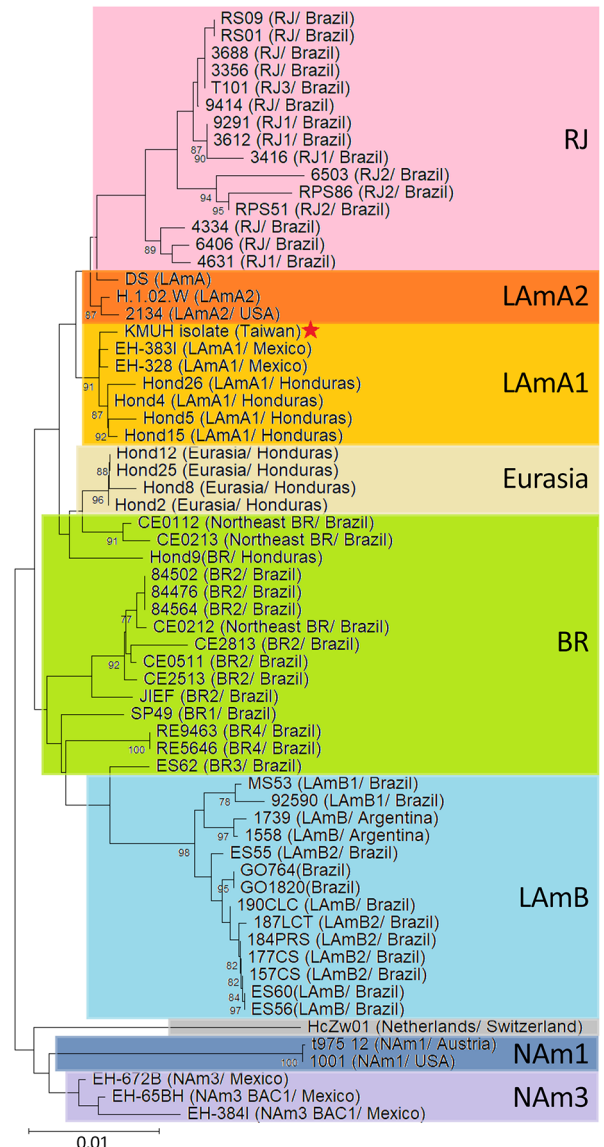


Figure. Phylogenetic analysis of *Histoplasma capsulatum* fungi sequences from a case of disseminated histoplasmosis, Taiwan, 2024. Phylogenetic tree was constructed by using the neighbor-joining method on the basis of concatenated multilocus sequence typing analysis of 4 genes (*arf*, *H-anti*, *ole*, and *tub*). Bootstrap support for the relevant internal node was 91% on the basis of 1,000 replicates. Red star indicates isolate sequenced from our study (GenBank accession nos. PX954369 [*arf*], PX954370 [*H-anti*], PX954371 [*ole*], and PX954372 [*tub*]). Scale bar indicates nucleotide substitutions per site. BR, Brazilian; LAmA1, Latin American A1; LAmA2, Latin American A2; LAmB, Latin American B; NAM1, North American 1; NAM3, North American 3; RJ, Rio de Janeiro.

We used ChatGPT (OpenAI, <https://openai.com>) to assist with English-language editing. All authors reviewed and approved the final manuscript and take full responsibility for its content.

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In Response: We sincerely thank Lin et al. for their insightful comments on our article (1) and for

providing valuable molecular epidemiologic evidence regarding *Histoplasma capsulatum* in Taiwan. The identification of a Latin American A1 lineage isolate in a patient without a travel history raises interesting questions regarding the local epidemiology of histoplasmosis. Their report highlights the increasing role of molecular approaches in understanding transmission dynamics and phylogeography of *Histoplasma* spp. fungi. Such molecular characterization might represent a necessary direction for future epidemiologic investigations. However, our retrospective study spanned nearly 3 decades, during which fungal isolates were not routinely preserved for molecular characterization. Consequently, comparable genomic data were unavailable for most patients.

The case report shared notable similarities with our findings. Both studies identified patients with histoplasmosis without a travel history, supporting the possibility of local acquisition or previously unrecognized environmental exposure. Also, both studies demonstrate that histoplasmosis is not restricted to immunocompromised persons and should not be regarded only as an imported infection in Taiwan. The report used molecular analysis to characterize a fungal isolate obtained from culture. In contrast, fungal cultures were infrequently positive in our cohort, highlighting one of the major diagnostic challenges encountered in routine clinical practice.

Whether these cases reflect local environmental reservoirs, historical introduction events, or previously unrecognized transmission pathways remains unclear. Expanded environmental sampling, preservation of fungal isolates, and molecular surveillance are needed to clarify the geographic distribution, lineage diversity, and transmission ecology of *Histoplasma* spp. fungi in Taiwan and other traditionally nonendemic regions. That limitation also could contribute to underrecognition of locally acquired histoplasmosis.

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