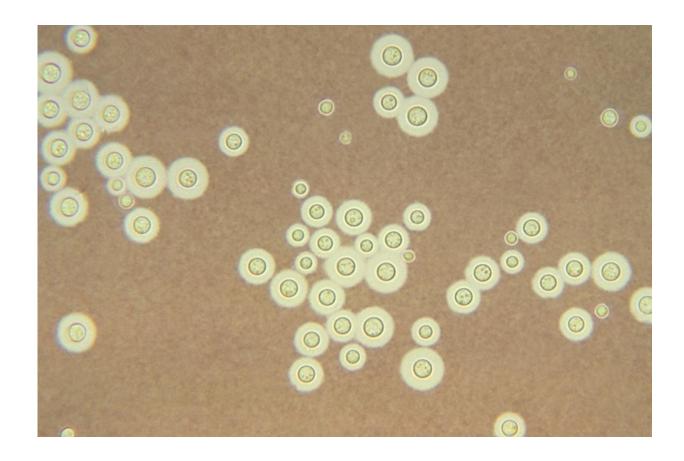


Global fungus tied to continental drift

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This photomicrograph depicts Cryptococcus neoformans using a light India ink staining preparation. Credit: CDC

Cryptococcus, a type of fungi found worldwide that is responsible annually for upwards of 625,000 deaths, was likely originally spread across the globe in conjunction with continental drift, according to a report by the Translational Genomics Research Institute (TGen).



Cryptococcus—Greek for "hidden sphere"—is a fungus usually found in decaying trees and soils. It grows in cultures as yeast. Two primary species of Cryptococcus—Cryptococcus neoformans (C. neoformans) and Cryptococcus gattii (C. gattii)—can cause severe illness, including meningitis, and death.

In a letter published today in the journal mSphere, TGen researchers advance a growing hypothesis that currently separated populations of Cryptococcus fungi were once connected as part of the super-continent known as Pangea. The separation of the populations likely occurred millions of years ago through continental drift, rather than through other methods of dispersal, like wind, or from human causes.

For example, the subtype of C. gattii called "VGI" is commonly found in southwestern Europe's Iberian Peninsula (Spain and Portugal) and in sub-Saharan Africa. Now separated by the Mediterranean Sea, Spain was the only European connection to Africa in Pangea.

Likewise, a subtype in India matches those in southern Africa. India and southern Africa were once joined in Pangea. Also in Africa, the subtype of C. gattii called "VGII" is only found in Senegal. This subtype was recently shown by TGen researchers and others to originate from Brazil. Now separated by the Atlantic Ocean, Senegal and Brazil were once joined in Pangea.

"What we see with the dispersal of various species and subspecies of Cryptococcus across the globe are distinct genomic ties between areas once connected as part of the supercontinent of Pangea, but which now are separated in some cases by thousands of miles of ocean," said Dr. David Engelthaler, Co-Director of TGen's Pathogen Genomics Division in Flagstaff, Ariz. "Much of the focus on global pathogen dispersal has been on possible human causes. What seems clear is that Cryptococcus largely dispersed millions of years ago, quite likely through continental



drift."

In 2014, an international team led by Engelthaler determined that a new emergence of Cryptococcus in the Pacific Northwest likely originated from Brazil. In that case, it was probably human-caused, sometime during the previous century.

Dr. Engelthaler led another international collaboration last year that determined that a different pathogenic fungus, Coccidioides, the cause of Valley Fever in the American Southwest, likely originated out of southern Arizona and possibly northern Mexico. It then spread to South America with mass migration of mammals that began nearly a million years ago, following the final uplift of the Panamanian isthmus, or land bridge, between North and South America.

"We are starting to understand that, while humans can and do move pathogens around the globe fairly efficiently, many microbes owe their current geographic locations to movements of land masses or animals long before humans trekked around the planet," Dr. Engelthaler said.

The TGen Valley Fever study, and the earlier Cryptococcus study, were both published in the journal mBio, which like mSphere is published by the American Society for Microbiology.

Today's article in mSphere builds on initial work led by Dr. Arturo Casadevall of John Hopkins University and colleagues at the University of California Berkeley, who commended Dr. Engelthaler and Dr. Wieland Meyer of the University of Sydney for providing "new information extending our hypothesis."

"These concepts now need to be ground-truthed with advanced statistical analyses to better understand linkages between ancient populations," Engelthaler added, an approach that both groups are working on.



C. neoformans and C. gattii can affect different human populations. C. neoformans typically produces no symptoms in healthy individuals, but it infects up to 1 million people each year, and kills a many as 625,000, mostly those in underdeveloped nations who have immune systems weakened by HIV/AIDS or cancer, according to the U.S. Centers for Disease Control. On the other hand, the C. gattii subtypes more frequently infect healthy immune-competent adults.

Cryptococcus is not contagious. It does not spread from person-toperson. It usually is contracted from inhaling contaminated dust, often associated with bird droppings (C. neoformans) or rotten wood (C. gattii).

Meningitis is an inflammation of the meninges, which are the membranes that cover the brain and spinal cord. It can be caused by an array of germs, including bacteria, fungi, and viruses. Symptoms include headaches, nausea, vomiting, lethargy, sensitivity to light and mental problems, including confusion, hallucinations and personality changes.

More information: David M. Engelthaler et al. Furthering the Continental Drift Speciation Hypothesis in the PathogenicSpecies Complexes, *mSphere* (2017). DOI: 10.1128/mSphere.00241-17

Provided by Translational Genomics Research Institute

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