

Team tracks the origins and spread of potentially deadly Valley Fever

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Using the latest in genomic analysis technologies, scientists at the Translational Genomics Research Institute (TGen) have tracked the likely origins and dispersal of the fungus that causes Valley Fever, according to a study published today in the journal *mBio*, the premiere journal for reporting high impact microbiological research.

In a story that spans 2 million years and includes the effects of glaciation and the pre-historic movements of animal hosts, the study sets the stage for tracking future outbreaks of this potentially deadly dust-bound disease as it spreads across arid regions of North and South America.

Valley Fever is an infection caused by the microscopic fungus *Coccidioides*, which lives in desert soils and typically enters the body through the lungs. An estimated 150,000 Americans are infected annually by Valley Fever, and as many as 500 die each year.

"The combination of whole genome sequencing and advanced statistical analysis provides for an understanding of the possible ancestry and dispersal pathways of this fungus," said Dr. David Engelthaler, Director of Programs and Operations for TGen's Pathogen Genomics Division or TGen North, and the study's lead author. "This application of paleo-epidemiology allows us to not only understand when the Valley Fever fungus was distributed throughout the western hemisphere, but also how."

"These data and analysis enhance our ability to conduct genomic

epidemiology today, and give us a better understanding of the changing distribution of this disease moving forward," said Dr. Paul Keim, Director of TGen North, Director of Northern Arizona University's Center for Microbial Genetics & Genomics, and one of the study's senior authors.

Nearly 60 percent of infected people—and other mammals, especially dogs—develop no significant symptoms from exposure to Valley Fever.

However some infected patients develop highly debilitating symptoms, such as cough, fever and fatigue. These symptoms are similar to other respiratory diseases caused by bacteria or virus, and often lead to delayed diagnoses and inappropriate treatment. Very severe Valley Fever can require lifelong treatment with antifungal drugs, and even death.

Valley Fever evolved in the Sonoran Desert

There are two distinct species of the fungus *Coccidioides* that cause Valley Fever: *C. posadasii*, the oldest species, which originated in the Sonoran Desert of southern Arizona and northern Mexico; and *C. immitis*, which is the species found in California's Central Valley, as well as parts of southern California and Baja Mexico.

Using the genetic data derived from 86 *Coccidioides* genomes, the study's analysis estimates that *C. posadasii* diverged, forming Arizona and non-Arizona subpopulations, between 820,000 and 2 million years ago.

The Arizona subtype today is found throughout central and southern Arizona. Within Arizona, TGen researchers identified multiple distinct genetic groups originating in the Tucson region, one of which also includes all the Phoenix isolates, where the largest concentrations of Valley Fever occur.

The study's authors also estimate that the fungus spread to Mexico and Texas as many as 675,000 years ago, to South America about 527,000 years ago, and to Guatemala in Central America less than 190,000 years ago.

C. immitis appears to have diverged from the Arizona-based *C. posadasii* species between 365,000 and 920,000 years ago in central California's San Joaquin Valley. This was an inland sea during periods of the Pleistocene epoch, up to 2.6 million years ago. It was submerged by glacial runoff as long as 700,000 years ago, and the emergence of *C. immitis* likely followed its drainage. The barrier formed by the Sierra Nevada mountain range also may have played a role in the formation of *C. immitis* as a separate species.

Valley Fever is spreading to new areas

The geographic range of the fungus is expanding. New clusters of *C. immitis* have been identified in eastern Washington state, which likely emerged from California. Valley Fever also is also known to occur in Argentina, Paraguay, Brazil and Honduras. The previous dispersal of this pathogen is attributed in large part to major animal migrations during the last several hundred thousand years. Highly susceptible mammals, besides humans, includes dogs and other canids, rodents, and in South America llamas, armadillos and bats. The cause of the more recent expansion to Washington remains uncertain.

"The genetic mechanisms and epidemiological consequences of this expansion are unknowns and require better understanding of the population structure and evolutionary history of these pathogens," said Dr. Bridget Barker, TGen Assistant Professor and head of TGen's Northern Arizona Center for Valley Fever Research, and another author of the study. Dr. Barker also heads TGen's research into dogs infected with the fungus, called Valley Fever PAWS.

The study concludes that the findings argue for additional large-scale population level sequencing of *Coccidioides*, particularly from under-represented areas, and especially from Sonora and other regions of northern Mexico, with an emphasis on isolates obtained from the environment.

More information: *mBio*, [DOI: 10.1128/mBio.00550-16](https://doi.org/10.1128/mBio.00550-16)

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