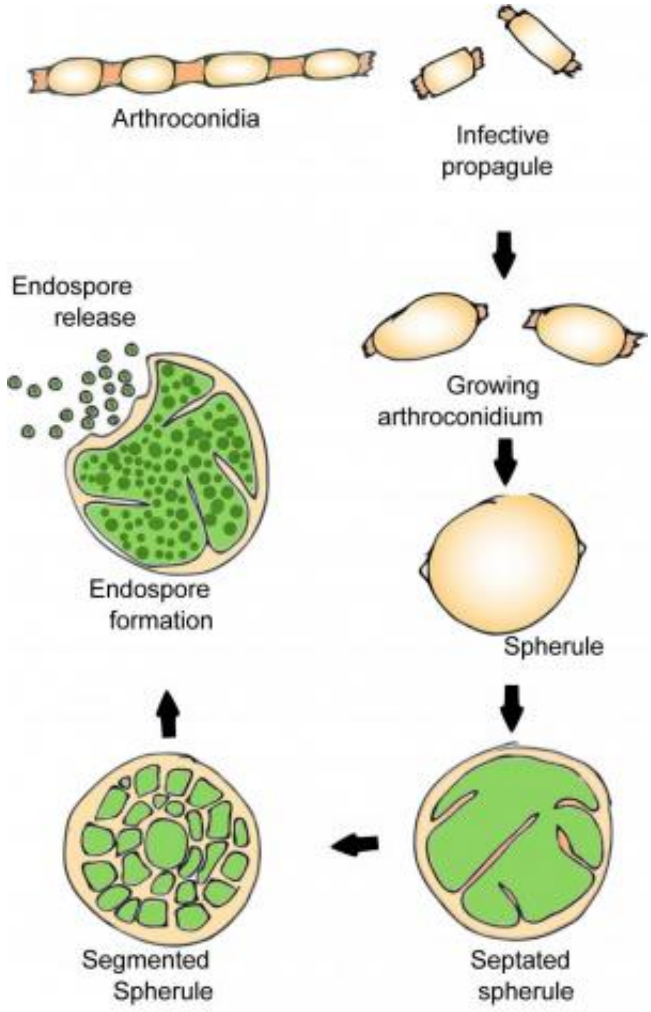
Dangers of desert dust: New diagnostic tool for valley fever

July 22 2014, by Richard Harth



This graphic outlines the life cycle of *Coccidioides*, a fungal pathogen responsible for Valley Fever. Credit: Public Domain

On July 5, 2011, a massive wall of dust, ("haboob," in Arabic), blanketed Phoenix, Arizona, creating an awesome spectacle, (or stubborn nuisance, depending on your perspective). Dust storms are a common occurrence in the arid desert environments of the American Southwest.

But windborne dust can be a serious health risk, lofting spores of a sometimes-lethal fungus known as *Coccidioides*. The resulting ailment, known as coccidioidomycosis or valley fever, has been perplexing researchers since it was first described in 1892. It is currently on an alarming ascent in the United States.

Dr. Stephen Albert Johnston, Krupa Navalkar and their colleagues at Arizona State University's Biodesign Institute have been investigating Valley Fever. Navalkar is the lead author of a new study describing a promising strategy known as immunosignaturing, which can provide clinicians with an accurate identification of valley fever, a potentially serious affliction that is often misdiagnosed.

"The incidence of this disease is seemingly low due to non-sensitive diagnostic assays," Navalkar says. As Johnston further notes, "immunosignatures could easily change those false assumptions if made available in the clinical setting."

Navalkar is a researcher in Biodesign's Center for Innovations in Medicine, under the direction of Stephen Albert Johnston, who is also a co-author of the new study.

The group's findings appear in the current issue of the journal ASM *Clinical and Vaccine Immunology*.

Valley fever is a fungal respiratory infection. It can be acquired when microscopic spores of the soil-dwelling fungus are inhaled. Two forms of the fungus exist, *Coccidioides* immitis and *Coccidioides* posadasii.

They are endemic to regions of Arizona, New Mexico, California, Nevada, Utah, Texas and northern Mexico.

During extended periods of dryness, the fungal spores remain dormant. With rainfall, the spores or arthroconidia develop elongated filaments, which break off and can be lofted into the air by soil disruption due to farming, construction, earthquakes or dust storms.

Most individuals inhaling *Coccidioides* particles are assumed to be able to naturally resolve the infection, developing immunity to future spore infections.Often such non-symptomatic individuals are unaware they have been exposed. Others are not so fortunate, however.

In around 40 percent of cases, valley fever causes flu-like symptoms including cough, headache, muscle and joint pain and rash. For reasons still unclear, those of Filipino, African American and Native American descent are more vulnerable to the severe disseminated form of the infection. The disease is also more severe in people with weakened immune systems as well as pregnant women.

Infection with *Coccidioides* can progress through three stages of increasing severity. Valley fever is the acute form of the disease, which, if left untreated, can develop into a second-stage chronic infection, lasting months or years. This form affects roughly 40 percent of those exposed. The third stage of the disease, known as disseminated *Coccidioides*, occurs when the infection spreads throughout the body, affecting skin, bones and nervous system and causing skin ulcers, swollen joints and severe pain, abscesses, bone lesions, heart inflammation, urinary tract infection and (potentially lethal) meningitis. Disseminated *Coccidioides* affects 5-10 percent of those with chronic infection.

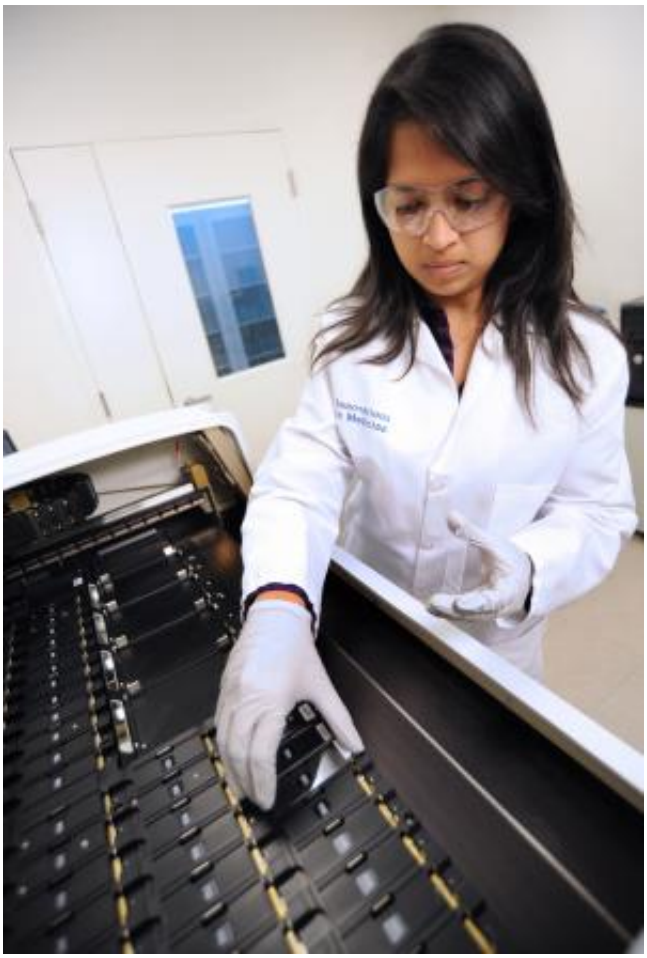
The rapid rise in valley fever cases in the arid southwest has become a

serious health concern, as human habitation has pushed further into desert areas where the soil spores are widespread. Currently, Valley Fever affects an estimated 150,000 people a year, with most cases occurring in Arizona, California, Nevada, New Mexico and Utah. The disease has no cure at present and is notoriously tricky to diagnose. One reason is that valley fever is readily confused with other community-acquired pneumonias.

Currently, diagnosis is carried out through a technique known as immunodiffusion, which tests the blood for antibodies against Coccidioidal antigens. As the authors note, such tests are less than satisfactory, with a false negative rate as high as 50-70 percent. Around 5 percent of symptomatic patients display no measurable antibody levels to Valley Fever by immunodiffusion.

The current study describes an alternate method used to address the poor accuracy of immunodiffusion, applying an innovative new technique known as 'Immunosignaturing'. The technique can produce a detailed profile of system-wide immune activity from a small droplet of blood—typically, less than a microliter.

To produce its detailed immune portrait or immunosignature, the technique uses a microarray platform. This consists of a glass slide imprinted with 10,000 peptides. Each peptide consists of a string of 20 amino acids, randomly arranged. The power of the technology resides in the fact that the randomly generated peptides are not based on natural antigens to *Coccidioides* or indeed, any disease. They are "unbiased" to the nature of particular disease antibodies and can therefore act as a sort of universal diagnostic.



Krupa Navalkar is a researcher at the Biodesign Institute at Arizona State University. Credit: The Biodesign Institute at Arizona State University

When a droplet of antibody-containing blood is smeared across the microarray, the random peptides behave like naturally occurring antigens, binding with blood antibodies in a specific pattern. Global analysis of the resulting immunosignature is used to establish disease-specific blueprints of immune activity.

The method potentially offers much higher resolution and sensitivity to disease, compared with diagnostic tests measuring a single antibody-antigen binding event or a small ensemble of molecules.

In the first round of experiments in the current study, the group used immunosignatures to determine if Valley Fever infected individuals could be accurately distinguished from three other patient groups afflicted with bacterial or fungal infections.

Once an immunosignature for Valley Fever was established using the 10K peptide microarray, a smaller diagnostic array was composed from relevant diagnostic peptides. This smaller 96-peptide array was then tested for accuracy against the current immunodiffusion diagnostic standard.

The 10K peptide array successfully distinguished Valley Fever from 3 other infections, with 98 percent accuracy. Impressively, the method also was able to classify false negative Valley Fever patients in a blinded test, with 100 percent accuracy, easily outpacing existing immunodiffusion methods, which could only identify 28 percent of false negatives.

The smaller, 96 peptide diagnostic array showed less specificity than the 10K peptide array in terms of identifying false negatives. The authors propose that the larger 10K peptide array be used in initial screenings, followed by subarrays with reduced complements of carefully selected peptides, used for clinical diagnosis.

Immunosignaturing holds of promise for rapid, cost-effective and highly accurate diagnosis of Valley Fever. The versatile platform has the potential to separate Valley Fever patients from those afflicted with other bacterial or fungal infections. Making use of the same microarray, researchers can also identify false negatives with 100 percent accuracy.

Provided by Arizona State University

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