

Reprogramming of immune system cures child with often-fatal fungal infection

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Dr. Manish Butte with Abraham Gonzalez-Martinez, who at age 4 was treated for a case of disseminated coccidioidomycosis. Credit: Nick Carranza / UCLA Health

In the June 11 issue of the *New England Journal of Medicine*, a team of

UCLA physicians and scientists describes the first case of immune modulation being used to cure a severe and often fatal fungal infection. The team "retuned" a 4-year-old's immune system so that it could fight off disseminated coccidioidomycosis.

The case, originally reported by UCLA in 2019, could pave the way for a new treatment for the infection, which affects hundreds of Americans each year, primarily in the Southwest, and kills approximately 40% of the people who contract it.

The technique described in the study could also suggest a new paradigm for treating other severe fungal infections, bacterial infections such as tuberculosis, and severe viral infections such as influenza and COVID-19.

"Immune modulation isn't currently part of the strategy with any of these severe infections," said Dr. Manish Butte, the report's senior author, who holds the E. Richard Stiehm Endowed Chair in Pediatric Allergy, Immunology and Rheumatology at the David Geffen School of Medicine at UCLA. "Our case suggests that rather than hoping to get the upper hand with more and more antibiotics or antifungals, we can have some success by combining these established approaches with the new idea of programming the patient's immune response to better fight the infection."

Each year, more than 100,000 people are infected with *Coccidioides* fungi, which reside in the soils of California, Arizona and West Texas. Most people who are infected are asymptomatic, and about 20,000 experience the minor respiratory illness commonly known as Valley fever. The vast majority of people with Valley fever respond well to antifungal medications, but approximately 1% of the infections progress to disseminated coccidioidomycosis, in which the infection spreads rapidly throughout the body, leading to bone and [tissue damage](#), and in

many cases death.

"Historically, severe infections have been seen as 'bad luck,'" Butte said. "Doctors haven't looked at how we can harness the immune systems of these patients to fight the infection."

According to a 2019 study in the *International Journal of Environmental Research and Public Health*, California spends between \$700 million and \$900 million a year in direct and indirect costs related to the care of people infected by the cocci fungus, including more than \$300 million to care for the approximately 200 people with disseminated coccidioidomycosis.

The boy who was treated by Butte and his team had previously been treated with high doses of multiple antifungal medicines, but by the time he arrived at UCLA, he could barely walk or talk and required a feeding tube to eat. When UCLA physicians homed in on the patient's [immune system](#), they concluded that his T cells—the [white blood cells](#) that play a key role in the body's [immune response](#)—were failing to properly recognize the invading fungus. The T cells were responding as though the infection was a parasitic infection rather than a fungal one.

That prompted the team to supplement the boy's antifungal medications with an immune stimulator called interferon-gamma. And Dr. Maria Garcia-Lloret, a pediatric allergist and immunologist, suggested adding yet another medication, dupilumab, which was developed as a medication for allergic diseases and had never before been used to treat infections. Dupilumab is a prescription drug that has not been approved by the FDA as a treatment for disseminated coccidioidomycosis.

The combination of immune modulators restored the proper programming to the patient's T cells—and the boy's [infection](#) went away in a month.

More information: Monica Tsai et al, Disseminated Coccidioidomycosis Treated with Interferon- γ and Dupilumab, *New England Journal of Medicine* (2020). [DOI: 10.1056/NEJMoa2000024](https://doi.org/10.1056/NEJMoa2000024)

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