Vaccines to prevent coccidioidomycosis

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Coccidioidomycosis (San Joaquin Valley Fever) is a systemic fungal infection of the southwestern US and other parts of the western hemisphere. A third of infections results in many weeks to many months of disability and a small percentage are progressive and even life-threatening. Infection, even in those who develop complications, induces protective cellular immunity and suggests that a preventative vaccine strategy is biologically possible. Whole cell killed vaccines were not sufficiently immunogenic and recombinant protein-based vaccines were economically not feasible for this orphan disease. A gene (CPS1) of the corn pathogen, Cochliobolus, is involved in virulence. Deleting its homolog in Coccidioides posadasii produced Δ-cps1 which did not cause disease in three susceptible inbred mouse strains, including one that lacked T, B and NK cells. Using an inoculum one million times above the LD95 or infecting neutropenic mice also did not result in disease. Nearly all infecting spores failed to complete a full tissue-cycle of replication. Vaccination with 105 cfu of Δ-cps1, either subcutaneously or intranasally, protected mice from a lethal intranasal C. posadasii or C. immitis infection. Compared to unvaccinated mice, lung fungal burden was reduced approximately 5 logs and often no fungal growth was evident. Protection persists at least four months (longest delay thus far evaluated). Δ-cps1 grows nearly as quickly and produces nearly as many spores as wild type. As a result, manufacturing and formulation methodology should be feasible. We conclude that Δ-cps1 is an attractive candidate as a preventative vaccine for both dogs and humans.

Biography

John N Galgiani has received his BS from Stanford University, MD from Northwestern University and Infectious Diseases Fellowship from Stanford University. Since 1978, he has been a Faculty Member of the University of Arizona College of Medicine and Founder of the UA Valley Fever Center for Excellence. His research interests include the development of vaccines, therapeutics and diagnostics for coccidioidomycosis.

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