BIOGRAPHICAL SKETCH

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NAME David A. Stevens	POSITION TITLE Professor, Department of Medicine, Stanford Univ. Medical School
eRA COMMONS USER NAME (credential, e.g., agency login) David_A_Stevens	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Cornell University, Ithaca, NY	B.A.	1960	Amer. Studies, Pre-Med
University of Rochester, Rochester, NY	M.D.	1965	Medicine
University of Wisconsin, Madison, WI	(Intern, Asst. Resident)	1965-1967	Medicine
University of California, Los Angeles, CA	(Assoc. Resident)	1969-1970	Medicine
Stanford University, Stanford, CA	(Fellow)	1970-1972	Infectious Diseases

Positions and Honors

Professional Experience

1962-1963	U.S. Public Health Service Research Fellow, Experimental Pathology, Chester Beatty Institute, Royal Cancer Hospital, University of London, London
1967-1969	Research Associate, National Institutes of Health, Bethesda, MD
1972-1978	Assistant Professor, Department of Medicine, Stanford University
1972-2014	Chief, Division of Infectious Diseases, Santa Clara Valley Medical Center (affiliated hospital, Stanford University), San Jose, CA
1972-2014	Co-Director, Microbiology Laboratory, Santa Clara Valley Medical Center, San Jose, CA
1972-2014	Hospital Epidemiologist, Santa Clara Valley Medical Center, San Jose, CA
1973-	Principal Investigator, Infectious Disease Research Lab., California Institute for Medical Research, San Jose, CA
1978-1985	Associate Professor, Department of Medicine, Stanford University
1979	Mycology Reference Laboratory, Public Health Laboratory Service and Department of Microbiology, London School of Hygiene and Tropical Medicine, University of London, (sabbatical, Wellcome Fund Grant)
1980-	Director, Clinical Laboratories, California Institute for Medical Research, San Jose
1985-	Professor, Department of Medicine, Stanford University (Emeritus, 2012)
1992-98	President, California Institute for Medical Research, San Jose, CA
1992-2003	Associate Chief, Division of Infectious Diseases and Geographic Medicine, Stanford University
2001- current	President, California Institute for Medical Research, San Jose, CA

Select Honors

Amer. Soc. for Clinical Investigation, 1981
Fellow, American Academy of Microbiology, 1994
Rhoda Benham Medal, Medical Mycology Society of the Americas, 1999
Lucille Georg Medal, International Society for Human and Animal Mycology, Paris, 2006
Charles E. Smith Memorial Award, Coccidioidomycosis Study Group, 2006

Fellowships: American College of Physicians, the Infectious Diseases Society of America, American Academy of Microbiology.

A. Personal Statement

I feel my experiences qualify me to contribute. These include a tenured professorial appointment at Stanford since 1978. I was previously Director of the NIH Fogarty International Training Grant at Stanford. Our laboratory has been engaged in laboratory and clinical research in mycology for 45 years, including host defenses, therapy, epidemiology, and pathogenesis. I have had Fellows, students, graduate students in my research unit continuously for 46 years. Twelve of my former trainees are full professors in the faculty of professional graduate schools. I was Chair, Mycology Division, Amer. Soc. Microbiol., and 3 of my former Fellows have been elected Chair. I was Chief of a teaching hospital Infectious Diseases service for 42 years. I have been elected President of a research institute for 24 of the past 26 years. I have authored or co-authored >700 published full articles, chapters and editorials. I was a Project Leader in the NIAID Mycoses Study Group 1990-2000 (Chair of Opportunistic Infections). Modern genomics has enabled me to participate in the discovery of 6 new microbes (3 bacteria, 3 fungi), one of which was named after me, by Korean scientists, owing to my efforts in study of the genus. My overall scientific abilities are thus suited to the position.

Stevens, D.A., Hamilton, J.R., Johnson, N., Kim, K., Lee, J-S. Halomonas, a newly recognized human pathogen, causing infections and contamination in a dialysis center; 3 new species. Medicine 88:244-249, 2009.

Contributions to science

1. My first training and studies were in virology, where I first developed an interest in cell-mediated immunity and in chemotherapy. I was engaged in the study of herpesviruses, including their role in tumorigensis. During this period I described a new disease, leukemia with Burkitt lymphoma cells; was the senior author of the first controlled trial of the systemic use of an antiviral; and showed the importance of interferon in arresting progression of disease. As a result of continuation of this interest, I have published papers on interferon in 5 different decades. The text of a seminal review article I co-authored on viral infections in non-congenital forms of immunodeficiency was later used when others were searching for a name for a new disease, namely acquired immune deficiency disease (AIDS) (Harold Varmus/Tom Merigan, personal communication).

a. Stevens, D.A., O'Conor, G.T., Levine, P.H., Rosen, R.B. Acute leukemia with "Burkitt lymphoma cells" (a new entity) and Burkitt's lymphoma. Annals Intern. Med. 76:967-973, 1972.
b. Stevens, D.A., Jordan, G.W., Waddell, T.F., Merigan, T.C. Adverse effect of cytosine arabinoside on disseminated zoster in a controlled trial. New Eng. J. Med. 289:873-878,1973.
c. Stevens, D.A., Merigan, T.C. Interferon, antibody, and other host factors in the dissemination of herpes zoster. J. Clin. Invest. 51:1170-1178, 1972.
d. Stevens, D.A., Brummer, E., Clemons, K.V. Interferon-gamma as an antifungal. J. Infect. Dis. 194:S33-S37, 2006.

2. While transitioning to study of cellular immunity in mycoses, the opportunity presented itself to study and introduce the first systemically useful azole antifungal, miconazole, at a time when therapy for this emerging area of infections was extremely limited. This has led to the development of a dominant class of the antifungals. Continuing work with industry, I published the first paper on the first oral agent of this class, ketoconazole, and then on the first triazole. Our studies established a scientific base for inoculum-independent susceptibility testing of antifungals in vitro; ours was the first demonstration of utility of fluconazole in prophylaxis of the immunocompromised; the utility of cyclodextrin for delivery of water-insoluble azoles; demonstration that lifelong azole therapy was required for coccidioidal meningitis; and

our team reported the first case of itraconazole-resistant *Aspergillus* (now swollen to an international concern), and the only randomized therapeutic trial in coccidioidomycosis. I had many of the first reports of side effects of azoles, and of cytochrome P450 interactions of azoles with other drugs. Perhaps the most important of these was our demonstration of blockade of host steroidal hormone synthesis (related chronologically in a reference below), since this has led to the use of azoles as endocrinologic tools. Other studies first revealed anti-*Aspergillus* activity of the echinocandins in vitro and in vivo, first showed the power of combined inhibition of cell wall glucan and chitin synthesis, and showed the "paradoxical effect" of echinocandins (losing inhibition at higher concentrations). Our study was the first randomized trial of therapy in allergic bronchopulmonary aspergillosis- the first demonstration that an antimicrobial could ameliorate an allergic disease. Finally, we introduced categorization of mycoses for entry into clinical trials, and an outcome scoring system; the former became known as "the NIAID Mycoses Study Group criteria', eventually evolving into the now canonical EORTC/MSG criteria.

a. Stevens, D.A., Levine, H.B., Deresinski, S.C. Miconazole in coccidioidomycosis. II. Therapeutic and pharmacologic studies in man. Amer. J. Med. 60:191-202, 1976.
b. Stevens, D.A. Ketoconazole metamorphosis: an antimicrobial becomes an endocrine drug. Arch. Intern. Med. 145:813-815, 1985.
c. Stevens, D.A., Lee, J.Y. Analysis of compassionate use itraconazole therapy by the NIAID Mycoses Study Group criteria. Arch. Intern. Med. 157:1857-1862, 1997.
d. Stevens, D.A., Schwartz, H.J., Lee, J.Y., Moskovitz, B.L., Jerome, D., Catanzaro, A., Bamberger, D., Weinmann, A., Tuazon, C.U., Judson, M.A., Platts-Mills, T.A.E., DeGraff, A.C. Randomized double blind study of itraconazole in allergic bronchopulmonary aspergillosis (NIAID Mycoses Study Group, Study 22). New Eng. J. Med. 342:756-762, 2000.

3. In the area of host-pathogen interactions, my laboratory has performed extensive preclinical studies to understand the role of cytokines in defense against mycoses, with the goal of using recombinant cytokines in clinical immunotherapy. These studies have mostly focused on gamma interferon, colony stimulating factors and IL-12 (example below). To that end, and for utility in therapy studies, my laboratory has developed many models of mycoses in mice, rabbits, and avian species, some in use globally. Most recently, we have been developing, in preclinical studies, a possible panfungal vaccine, relying on shared glycan and protein components in pathogenic fungi.
We have also been the leaders in studies of how host hormones directly modulate fungal pathogen activity in vivo.

a. Choi, J-H., Brummer, E., Kang, Y.J., Jones, P.P., Stevens, D.A. IkB and NFkB in GM-CSF antagonism of dexamethasone suppression of macrophage response to Aspergillus fumigatus conidia. J. Infect. Dis. 193:1023-1028, 2006.
b. Capilla, J., Clemons, K.V., Stevens, D.A. Animal models: an important tool in mycology. Med. Mycol. 45:657-684, 2007.
c. Clemons, K.V., Danielson, M., Michel, K. S., Liu, M., Martinez, M., Chen, V., Ottosen, N.C., Leonardo, S.M., Antonysamy, M.A., Stevens, D.A. Whole glucan particles as a vaccine against murine aspergillosis. J. Med. Microbiol. 63:1750-1759, 2014.
d. Shankar, J., Restrepo, A., Clemons, K.V., Stevens, D.A. Hormones and the resistance of women to paracoccidioidomycosis. Clin. Micro. Rev. 24:296-313, 2011.

4. Application of molecular biologic and genomic tools to mycology enabled us to explore molecular epidemiology, molecular diagnostic methods, and gene expression in fungal biologic processes. A robust typing system of ours for *Candida* was in use for 15 years in various laboratories.

a. Scherer, S. Stevens, D.A. A Candida albicans dispersed, repeated gene family and its epidemiologic applications. Proc. Nat. Acad. Sci. 85:1452-1456, 1988.
b. van Asbeck, E.C., Clemons, K.V., Markham, A.N., Stevens, D.A. Molecular epidemiology of the global and temporal diversity of Candida parapsilosis. Scand. J. Infect. Dis. 40:827-834, 2008.

c. Gago, S., Buitrago, M.J., Clemons, K.V., Cuenca-Estrella, M., Mirels, L.F., Stevens, D.A. Development and validation of a quantitative Real-Time PCR assay for the early diagnosis of coccidioidomycosis. Diag. Micro. Infect. Dis. 79:214-221, 2014.

d. Monteiro, J.P., Clemons, K.V., Mirels, L.F., Coller, J.A., Wu, T.D., Shankar, J., Lopes, C.R., Stevens, D.A. Genomic DNA microarray comparison of gene expression patterns in Paracoccidioides brasiliensis mycelia and yeasts in vitro. Microbiology 155:2795-2808, 2009.

5. A current focus in my laboratory is the nature of the interactions between the prominent microbes affecting the course of airway disease in cystic fibrosis, *Aspergillus fumigatus* and *Pseudomonas aeruginosa*. The concerns are their respective biofilms, inter-microbial inhibition and the correlation of source and phenotype of the isolates, effects on epithelium, influence of *Pseudomonas* phage, possibilities of modulating the interaction by affecting iron metabolism, the composition of the extracellular matrix, and molecular epidemiologic approaches.

a. Sabino, R., Ferreira, J.A.G., Moss, R., Valente, J., Verissimo, C., Carolino, E., Clemons, K.V., Everson, C., Banaei, N., Penner, J., Stevens, D.A. Molecular epidemiology of Aspergillus from cystic fibrosis patients. J. Cystic Fibrosis 14:474-481, 2015.

b. Nazik, H., Penner, J.C., Ferreira, J.A.G., Haagensen, J.A.J., Cohen, K., Spormann, A.M., Martinez, M., Chen, V., Hsu, J.L., Clemons, K.V., Stevens, D.A. Effect of iron chelators on the formation and development of Aspergillus fumigatus biofilm. Antimicrob. Agents Chemother. 59:6514-6520, 2015.

c. Reichhardt, C., Ferreira, J.A.G., Joubert, L., Clemons, K.V., Stevens, D.A., Cegelski, L. Analysis of the Aspergillus fumigatus biofilm extracellular matrix by solid-state nuclear magnetic resonance. Eukaryotic Cell 14:1064-1072, 2015.

d. Sass, G., Nazik, H., Penner, J., Shah, H., Ansari, S.R., Clemons, K.V., Groleau, M-C., Dietl, A-M., Visca, P., Haas, H., Déziel, E., Stevens, D.A. Studies of *Pseudomonas aeruginosa* mutants indicate pyoverdine as the central factor in inhibition of *Aspergillus fumigatus* biofilm. J. Bacteriol.200(1): e00345-17, 2018.