

Principal Investigator/Prom Director (Last, First, Middle): \_\_\_\_\_

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
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NAME Joshua Fierer, M.D.	POSITION TITLE Professor of Medicine and Pathology in Residence		
eRA COMMONS USER NAME J_FIERER			
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
Columbia College, New York City	A.B.	1959	History
New York University S.O.M., N.Y. City	M.D.	1963	Medicine
Yale New Haven Hospital		1963-64, 1966-68	Internal Medicine

### **A. Positions and Honors:**

#### Professional Experience:

1971-1979 Assistant Professor of Medicine in Residence, University of California, San Diego  
1979-1986 Associate Professor of Medicine in Residence, University of California, San Diego  
1980-1981 Sabbatical Leave in Immunology Division, National Institute for Medical Research, Mill Hill, London, UK (B.A. Askonas, Ph.D.)  
1998-2002 Consultant, Center for Biologics Evaluation and Research, Food and Drug Administration, Dept. of Health and Human Services  
1991-2005 Head, Division of Infectious Diseases, University of California, San Diego  
1980-present Chief, Microbiology Section, Laboratory Service, Veterans Affairs Medical Center, San Diego  
1986-present Professor of Medicine and Pathology in Residence, University of California, San Diego  
1997-present Research Scientist, Veterans Medical Research Foundation

#### Awards and Other Professional Activities:

1997 Fellow, American Association for the Advancement of Science  
1998 Fellow, American Academy of Microbiology

### **B. Selected Peer-reviewed Publications (selected from over 100 publications)**

- 1) Fang, F.C., Krause, M., Roudier, C., Fierer, J., and Guiney, D.G.: Growth regulation of a *Salmonella* plasmid gene essential for virulence. *J Bacteriol* 173:6783-6789, 1991.
- 2) Fierer, J., Krause, M., Tauxe, R., and Guiney, D.: *Salmonella typhimurium* bacteremia: association with the virulence plasmid. *J Infect Dis* 166:639-42, 1992.
- 3) Heffernan, E.J., Reed, S., Hackett, J., Fierer, J., Roudier, C., and Guiney, D.: Mechanism of resistance to complement-mediated killing of bacteria encoded by the *Salmonella typhimurium* virulence plasmid gene *rck*. *J Clin Invest* 90:953-964, 1992.
- 4) Eckmann, L., Kagnoff, M.F., and Fierer, J.: Epithelial cells secrete the chemokine interleukin-8 in response to bacterial entry. *Infect Immun* 61:4569-74, 1993.
- 5) Fierer, J., Eckmann, L., Fang, F., Pfeifer, C., Finlay, B.B., and Guiney, D.: Expression of the *Salmonella* virulence plasmid gene *spvB* in cultured macrophages and nonphagocytic cells. *Infect Immun* 61:5231-36, 1993.
- 6) Heffernan, E.J., Wu, L., Louie, J., Okamoto, S., Fierer, J., and Guiney, D.G.: Specificity of the complement resistance and cell association phenotypes encoded by the outer membrane protein genes *rck* from *Salmonella typhimurium* and *ail* from *Yersinia enterocolitica*. *Infect Immun* 62:5183-6, 1994.
- 7) Jung, H.C., Eckmann, L., Yang, S.-K., Panja, A., Fierer, J., Morzycka-Wroblewska, E., and Kagnoff, M.F.: A distinct array of proinflammatory cytokines is expressed in human colon epithelial cells in response to bacterial invasion. *J Clin Invest* 95:55-65, 1995.

- 8) Eckmann, L., Fierer, J., and Kagnoff, M.F.: Genetically resistant (*Ity*<sup>r</sup>) and susceptible (*Ity*<sup>s</sup>) congenic mouse strains show similar cytokine responses following infection with *Salmonella dublin*. *J Immunol* 156:2894-2900, 1996.
- 9) Cirillo, D.M., Heffernan, E.J., Wu, L., Harwood, J., Fierer, J., and Guiney, D.G.: Identification of a domain in Rck, a product of the *Salmonella typhimurium* virulence plasmid, required for both serum resistance and cell invasion. *Infect Immun* 64:2019-23, 1996.
- 10) Chen, C.-Y., Eckmann, L., Libby, S.J., Fang, F.C., Okamoto, S., Kagnoff, M., Fierer, J., and Guiney, D.G.: Expression of *Salmonella typhimurium rpoS* and *rpoS*-dependent genes in the intracellular environment of eukaryotic cells. *Infect Immun* 64:4739-43, 1996.
- 11) Rasmussen, S.J., Eckmann, L., Quayle, A.J., Shen, L., Zhang, Y.-X., Anderson, D.J., Fierer, J., Stephens, R.S., and Kagnoff, M.F.: Secretion of proinflammatory cytokines by epithelial cells in response to *Chlamydia* infection suggests a central role for epithelial cells in chlamydial pathogenesis. *J Clin Invest* 99:77-87, 1997.
- 12) Weintraub, B.C., Eckmann, L., Okamoto, S., Hense, M., Hedrick, S.M., and Fierer, J.: Role of  $\alpha\beta$  and  $\gamma\delta$  T cells in the host response to *Salmonella* infection as demonstrated in T-cell-receptor-deficient mice of defined *Ity* genotypes. (Erratum in: *Infect Immun* 1998 Feb;66(2)882.) *Infect Immun* 65:2306-12, 1997.
- 13) Eckmann, L., Stenson, W.F., Savidge, T.C., Lowe, D.C., Barrett, K.E., Fierer, J., Smith, J.R., and Kagnoff, M.F.: Role of intestinal epithelial cells in the host secretory response to infection by invasive bacteria. Bacterial entry induces epithelial prostaglandin H synthase-2 expression and prostaglandin E<sub>2</sub> and F<sub>2 $\alpha$</sub>  production. *J Clin Invest* 100:296-309, 1997.
- 14) Eckmann, L., Rudolf, M.T., Ptasznik, A., Schultz, C., Jiang, T., Wolfson, N., Tsien, R., Fierer, J., Shears, S.B., Kagnoff, M.F., and Traynor-Kaplan, A.E.: D-myo-Inositol 1,4,5,6-tetrakisphosphate produced in human intestinal epithelial cells in response to *Salmonella* invasion inhibits phosphoinositide 3-kinase signaling pathways. *Proc.Natl.Acad.Sci.USA* 94:14456-14460, 1997.
- 15) Vassiloyanakopoulos, A.P., Okamoto, S., and Fierer, J.: The crucial role of polymorphonuclear leukocytes in resistance to *Salmonella dublin* infections in genetically susceptible and resistant mice. *PNAS* 95:7676-7681, 1998.
- 16) Fierer, J., Walls, L., Eckmann, L., Yamamoto, T., and Kirkland, T.N.: Importance of interleukin-10 in genetic susceptibility of mice to *Coccidioides immitis*. *Infect Immun*, 66:4397-4402, 1998.
- 17) Fierer, J., Walls, L., Wright, F., and Kirkland, T.N.: Genes influencing resistance to *Coccidioides immitis* and the Interleukin-10 response map to chromosomes 4 and 6 in mice. *Infect. Immun.* 67:2916-2919, 1999.
- 18) Fierer, J., Walls, L., Kirkland, T.N.: Genetic evidence for the role of the *Lv* locus in early susceptibility but not IL-10 synthesis in experimental coccidioidomycosis in C57BL mice. *J.Infect.Dis.* 2000;181:681-685.
- 19) Lesnick, M.L., Reiner, N.E., Fierer, J., and Guiney, D.G.: The *Salmonella spvB* virulence gene encodes an enzyme that ADP-ribosylates actin and destabilizes the cytoskeleton of eukaryotic cells. *Mol. Microbiol.* 39:1464-1470, 2001.
- 20) Fierer, J., Swancutt, M.A., Heumann, D., and Golenbock, D.: The role of lipopolysaccharide binding protein in resistance to *Salmonella* infections in mice. *J. Immunol.* 168:6396-6403, 2002.
- 21) Asensi, V., Alvarez, V., Valle, E., Meana, A., Fierer, J., Coto, E., Carton, J.A., Maradona, J.A., Paz, J., Dieguez, M.A., de la Fuente, B., Moreno, A., Rubio, S., Tuya, M.J., Sarasúa, J., Llamas, S., Arribas, J.M.: IL-1 $\alpha$  (-889) promoter polymorphism is a risk factor for osteomyelitis. *American Journal of Medical Genetics.* 119A:132-136, 2003.
- 22) Obonyo, M., Guiney, D.G., Fierer, J., Cole, S.P.: Interactions between inducible nitric oxide and other inflammatory mediators during *Helicobacter pylori* infection. *Helicobacter.* 8:495-502, 2003.
- 23) Asensi, V., Valle, E., Meana, A., Fierer, J., Celada, A., Alvarez, V., Paz, J., Coto, E., Carton, J.A., Maradona, J.A., Dieguez, A., Sarasua, J., Ocana, M.G., Arribas, J.M.: In vivo interleukin-6 protects neutrophils from apoptosis in osteomyelitis. *Infect.Immun.* 72:3823-3828, 2004.
- 24) Viriyakosol, S., Fierer, J., Brown, G.D., and Kirkland, T.N.: Innate immunity to the pathogenic fungus *Coccidioides posadasii* is dependent on toll-like receptor 2 and dectin 1. *Infect. Immun.* 73:1553-1560, 2005.
- 25) Liu, G.Y., Essex, A., Buchanan, J.T., Datta, V., Hoffman, H.M., Basian, J.F., Fierer, J., Nizet, V.: Staphylococcus aureus golden pigment impairs neutrophil killing and promotes virulence through its antioxidant activity. *J.Exp.Med.* 202:209-215, 2005.
- 26) Braff, M.H., Zaiou, M., Fierer, J., Nizet, V., Gallo, R.L.: Keratinocyte production of cathelicidin provides direct activity against bacterial skin pathogens. *Infect.Immun.* 73:6771-6781, 2005.

- 27) Montes, A.H., Asensi, V., Alvarez, V., Valle, E., Ocana, M.G., Meana, A., Carton, J.A., Paz, J., Fierer, J., Celada, A.: The Toll-like receptor 4 (Asp299Gly) polymorphism is a risk factor for Gram-negative and haematogenous osteomyelitis. *Clin. Exp. Immunology*. 143:404-413, 2006.
- 28) Kim, Y.K., Brinsmadem, S.R., Yang, Z., Escalante-Semerena, J., Fierer, J.: Mutation of phosphotrans-Acetylase but not isocitrate lyase reduces the virulence of *Salmonella enterica* serova Typhimurium in mice. *Infect. Immunity*. 74:2498-2502, 2006.
- 29) Fierer, J., Waters, C., and Walls, L.: Both CD4+ and CD8+ T cells can mediate vaccine-induced protection against *Coccidioides immitis* infections in mice. *J. Infectious Diseases*, 193:1323-1331, 2006.
- 30) del Pilar Jimenez, M., Walls, L., Fierer, J.: High levels of interleukin-10 impair resistance to pulmonary coccidioidomycosis in mice in part through control of nitric oxide synthase 2 expression. *Infect. Immun.* 74:3387-3395, 2006.
- 31) Datta, S.K., Okamoto, S., Hayashi, T., Shin, S.S., Mihajlov, I., Fermin, A., Guiney, D.G., Fierer, J., and Raz, E.: Vaccination with irradiated *Listeria* induces protective T cell immunity. *Immunity* 25:1-10, 2006.
- 32) Fierer, J.: IL-10 and susceptibility to *Coccidioides immitis* infection. *Trends Microbiol.* 14:426-427, 2006.
- 33) Fierer, J.: Editorial MDR-TB and HIV: the perfect storm? *Am. J. Trop. Med. Hyg.* 75:1025-1026, 2006.
- 34) Asensi, V., Montes, A.H., Valle, E., Ocana, M.G., Astudillo, A., Alvarez, V., Lopez-Anglada, E., Solis, A., Coto, E., Meana, A., Gonzalez, P., Carton, J.A., Paz, J., Fierer, J., Celada, A.: The NOS3 (27-bp repeat, intron 4) polymorphism is associated with susceptibility to osteomyelitis. *Nitric Oxide* 16:44-53, 2007.
- 35) Cachay, E., Mathews, W.C., Reed, S.L., Swancutt, M.A., Fierer, J.: Gonococcal meningitis diagnosed by DNA amplification: case report and review of the literature. *Aids Pt Care & STDs* 21: 2007.
- 36) Fierer, J.: The role of IL-10 in genetic susceptibility to *coccidioidomycosis* on mice. *Ann. N.Y. Acad. Sci.* 2007.
- 37) Ocana, M., Valle-Garay, E., Montes, A.H., Meana, A., Carton, J.A., Fierer, J., Celada, A., Asensi, V.: Bax gene G(-248)A promoter polymorphism is associated with increased lifespan of the neutrophils of patients with osteomyelitis. *Genet. Med.* 9: 2007.
- 38) Weisman, M.H., Paulus, H.E., Burch, F.X., Kivitz, A.J., Fierer, J., Dunn, M., Kerr, D.R., Tsuji, W., Baumgartner, S.W.: A placebo-controlled, randomized, blind-study evaluating the genetic and pharmacological inhibition of IKKbeta. *Rheumatology* 46(7): 2007.
- 39) Greten, F.R., Arkan, M.C., Bollrath, J., Hsu, L.-C., Goode, J., Miething, C., Goktuna, S.L., Neuenhahn, M., Fierer, J., Paxian, S., Van Rooijen, N., Xu, Y., O'Cain, T., Jaffee, B.B., Busch, D.H., Duyster, J., Schmid, R.M., Eckmann, L., Karin, M.: NF-KB is a negative regulator of IL-1B secretion as revealed by genetic and pharmacological inhibition of IKKB. *Cell* 130: 2007.
- 40) Makri, S., Purdy, A.E., Bartlett, D., Fierer, J.: Pathogenicity of environmental isolates of *V. cholerae* in mice. *Microbes Infect.* 2007.
- 41) Kolla, R.V., Chintalapati, S., Sabet, M., Santelli, E., Liddington, R.C., David, M., Fierer, J., Guiney, D., Rickert, R.C.: Complement CRd conjugation to anthrax protective antigen promotes a rapid, sustained, and protective antibody response. *PLOS One* 10:2007.
- 42) Woo, H., Okamoto, S., Guiney, D., Gunn, J.S., Fierer, J.: A model of *Salmonella colitis* with features of diarrhea in *SLC11A1* wild-type mice. *PLOS One* 2:2008.
- 43) Browne, S.H., Hasegawa, P., Okamoto, S., Fierer, J., Guiney, D.G.: Identification of *Salmonella* SPI-2 secretion system components required for SpvB-mediated cytotoxicity in macrophages and virulence in mice. *FEMS Immunol Med Microbiol* 52:2008.
- 44) del Pilar Jimenez, M., Viriyakosol, S., Walls, L., Datta, S.K., Heinsbroek, S.E.M., Brown, G., Fierer, J.: Susceptibility to *Coccidioides* species in C57BL/6 mice is associated with expression of a truncated splice variant of Dectin-1 (Clec7a). *Genes & Imm*, 9: 2008.
- 45) Maves, R.C., Cachay, E.R., Young, M.A., Fierer, J.: Secondary syphilis with ocular manifestations in older adults. *Clin Infect Dis* 46: 2008.
- 46) Wu, C.C., Sabet, M., Hayashi, T., Tawatao, R., Fierer, J., Carson, D.A., Guiney, D.G., Corr, M.: In vivo efficacy of a phosphodiester TLR-9 aptamer and its beneficial effect in a pulmonary anthrax infection model. *Cell Immunol Epub ahead of print*, 2008.

**C. Research Support: Research Projects Ongoing or Completed During the Last 3 Years:**

Ongoing Research Support:

Innate Immunity to Salmonella Infections

Principal Investigator: Joshua Fierer, M.D. Agency: NIH/NIAID  
Type: 5 R01 AI47884-05 Period: 3/1/01-2/28/06 (no-cost extension)  
Purpose: To investigate the role of PMNs in natural resistance to Salmonella.

Plasmid-mediated Virulence in Salmonella

Principal Investigator: Donald Guiney, M.D. Agency: NIH/ NIAID  
Type: Period: 5/1/08 – 4/30/13  
Purpose: To study the pathogenesis of diarrhea in Salmonella.  
Role: Co-investigator

Innate Immunity to Salmonella Infections

Principal Investigator: Joshua Fierer, M.D. Agency: UCSD Bridge Grant.  
Type: 5RH038H Period: 7/1/07 – 6/30/08  
Purpose: To investigate the role of PMNs in natural resistance to Salmonella.

Natural and Acquired Immunity to *Coccidioides immitis*

Principal Investigator: Joshua Fierer, M.D.  
Type: Department of Veteran Affairs Period: 10/1/08 – 9/30/12  
Purpose: To study the pathogenesis of Coccidioidomycosis.

Completed Research Projects (within the past 3 years)

2003 – 2007	Optimized Synthetic TLR Ligands for Biodefense	N.I.H.
1995-2005	Natural Resistance to <i>Coccidioides immitis</i>	V.A.
1993 – 2008	Plasmid-mediated Virulence in Salmonella	N.I.H.