

BIOGRAPHICAL SKETCH

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NAME Heinzel, Frederick P, M.D.		POSITION TITLE Staff Researcher/Physician, James A Haley VAMC	
eRA COMMONS USER NAME FHEINZEL			
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California, Davis	B.S.	1972	Biochemistry
University of California, Irvine	M.D.	1981	Medicine
University of Washington, Seattle	Residency	1984	Medical Residency
University of Washington, Seattle	Fellowship	1987	Infectious Diseases

A. Positions and Honors**Positions and Employment**

1986-1988 Instructor, Dept. of Medicine, UC San Francisco
 1988-1991 Assistant Professor, Dept of Medicine, UC San Francisco
 1991-1996 Assistant Professor, Dept. of Medicine, Case Western Reserve University
 1991- present Staff Physician and Researcher, Cleveland Veterans Affairs Medical Center
 1996- 2003 Associate Professor, Dept. of Medicine & Pathology, Case Western Reserve University
 2003-2006 Associate Professor, Center for Global Health and Diseases, Case Western Reserve University
 2006-present Staff Physician and Researcher, James A Haley Veterans Affairs Medical Center

Awards and Other Professional Activities

1972 University of California Regent's Scholar, 1980 Alpha Omega Alpha
 1981 Senior Achievement Award, UCI Alumni Service Award (UCI School of Medicine)
 1987 AFRC Western Regional Post-Doctoral Trainee Award
 1989 National Foundation of Infectious Diseases Young Investigator Matching Grant Award
 1994 NIH KO4 Career Development Award
 1999 Temporary Member, NIAID Tropical Medicine and Parasitology Study Section
 2000 Section Editor, Journal of Immunology

B. Selected Peer-reviewed publications (in chronological order)

- Meyer, R., Stone, T. and **F. Heinzel**. 1978. Direct Sulfhydrolysis of cyclic AMP: A one-step synthesis of the cyclic ribonucleotide of 6-mercaptopurine. *J. Heterocyclic Chemistry*. 15:1511-1512.
- Sadick, M.D., **Heinzel, F.P.**, Shigekane, V.M., Fisher, W. L., and R.M. Locksley. 1987. Cellular and humoral immunity to *Leishmania major* in genetically susceptible mice following in vivo depletion of L3T4⁺ T cells. *J. Immunol.* 139:1303-1309.
- Heinzel, F.P.**, Sadick, M.D., and R. M. Locksley. 1988. *Leishmania major*: Analysis of lymphocyte and macrophage phenotypes during infection of susceptible and resistant mice. *Exp. Parasit.* 65:258-268.
- Locksley, R.M., **Heinzel, F.P.**, Shepard, H.M., Agosti, J., Eessalu, T.E., Aggarwal, B.B., Harlan, J.M. 1987. Tumor necrosis factors alpha and beta differ in their capacities to generate IL-1 release from endothelial cells. *J. Immunol.* 139:1891-1895.
- Locksley, R.M., **F. P. Heinzel**, J.E. Frankhauser, C.S. Nelson and M.D., Sadick. 1988. Cutaneous host defense in leishmaniasis. Interaction of isolated, dermal macrophages and epidermal Langerhans cells with the insect-stage promastigotes. *Infect. Immun.* 56:336-342.
- Locksley, R.M., Crowe, S., **Heinzel, F.P.**, McGrath, M.S. and J. Mills. 1988. Release of interleukin-1 inhibitory activity (contra-IL-1) by human monocyte-derived macrophages infected with human immunodeficiency virus in vitro and in vivo. *J. Clin. Invest.* 82:2097-2105.
- Heinzel, F.P.**, M.D, Sadick, B.J. Holaday and R.M. Locksley. 1989. Reciprocal expression of interferon gamma or interleukin-4 during resolution or progression of murine leishmaniasis. Evidence for expansion of distinct helper T-cell subsets. *J. Exp. Med.* 169:59-72.
- Sadick, M.D., **Heinzel, F.P.**, Holaday, B.J., Pu, R.T., Dawkins, R.S., and R.M. Locksley. 1989. Cure of murine leishmaniasis with anti-IL-4 monoclonal antibody. Evidence for a T cell-dependent, IFN- γ -independent mechanism. *J. Exp. Med.* 171:115-127.

9. Gibbons, RA, Martinez, OA, Matli, MR, **Heinzel, FP**, Bernstein, MS and RS Warren. 1990. The regulation of interleukin-6 production by recombinant interleukin-4 in vitro. *Lymphokine Research*. 9:283-293.
10. **Heinzel, F. P.** 1990. The role of interferon- γ in the pathology of experimental endotoxemia. *J. Immunol.* 145:2920-2924.
11. Jendroska, K., **F.P. Heinzel**, M. Torchia, L. Stowring, H.A. Kretzschmar, A. Kon, A. Stern, S.B. Prusiner and S.J. DeArmond. 1991. Proteinase-resistant prion protein accumulation in Syrian hamster brain correlates with regional pathology and scrapie infectivity. *Neurology*. 41:1482-90.
12. **Heinzel, F.P.**, M.D. Sadick, S. Mutha and R.M. Locksley. 1991. Production of interferon- γ , IL-2, IL-4 and IL-10 by CD4+ lymphocytes in vivo during healing and progressive murine leishmaniasis. *Proc. Natl. Acad. Sci. USA.* 88:7011-7015.
13. Holaday, B.J., M.D., Sadick, Z.E. Wang, **F.P., Heinzel**, T.G. Parslow and R.M. Locksley. 1991. Reconstitution of Leishmania immunity in scid mice using Th1 and Th2-like cell lines. *J. Immunol.* 147:1653-1658.
14. **Heinzel, F.P.**, R.M. Rerko, F. Hatam and R.M. Locksley. 1993. Interleukin-2 is necessary for the progression of leishmaniasis in susceptible murine hosts. *J. Immunol.* 150:3924—3931.
15. **Heinzel, F.P.**, D. Schoenhaut, R. Rerko, L. Roesser and M. Gately. 1993. Recombinant murine IL-12 cures infection with *Leishmania major* in susceptible mice. *J. Exp. Med.* 177: 1505-1510.
16. Wang, Z., S.L. Reiner, F. Hatam, **F.P. Heinzel**, J. Bouvier, C.W. Turck and R.M. Locksley. 1993. Targeted activation of CD8+ Cells and infection of $\alpha 2$ -Microglobulin-deficient mice fail to confirm a primary protective role for CD8+ cells in experimental leishmaniasis. *J. Immunol.* 151:2077-86.
17. **Heinzel, F.P.**, R.M. Rerko, P. Ling, J. Hakimi, D. S. Schoenhaut. 1994. Interleukin-12 is produced in vivo during endotoxemia and stimulates synthesis of interferon- γ . *Infect. Immun.* 62:4244-9.
18. Pearlman, E., **F. P. Heinzel**, F.E. Hazlett and J.W. Kazura. 1995. Interleukin-12 modulation of T helper responses to the filarial helminth, *Brugia malayi*. *J. Immunol.* 154: 4658-4664.
19. **Heinzel, F.P.**, R.M. Rerko, F. Ahmed and E. Pearlman. 1995. Endogenous interleukin-12 (IL-12) is required for control of Th2 cytokine responses capable of exacerbating leishmaniasis in normally resistant C57BL/6 mice. *J. Immunol.* 155: 730-39.
20. **Heinzel, F.P.**, F. Ahmed, A.M. Hujer and R.M. Rerko. 1995. Immunoregulation of murine leishmaniasis by interleukin-12. *Research in Immunology*. 146:153-60.
21. **Heinzel, F.P.**, R M. Rerko, F. Ahmed and A.M. Hujer. 1996. Interferon-gamma independent production of interleukin-12 during murine endotoxemia. *J. Immunol.* 157:5421-8.
22. **Heinzel, F.P.**, A.M. Hujer and F. Ahmed and R.M. Rerko 1997. In vivo production and function of IL-12 p40 homodimers. *J. Immunol.* 158:4381-88.
23. **Heinzel, F.P.** 1997. From Oriental Sore to Kala-azar: Clinical and therapeutic aspects of the Leishmaniasis. *Clin. Microbiol. Newsletter*. 19:121-6.
24. **Heinzel, F.P.**, R.M. Rerko, A.M. Hujer. 1998. Underproduction of interleukin-12 during progressive murine leishmaniasis is due to decreased CD40 activity. *Cell. Immunol.* 184: 129-142.
25. **Heinzel, F.P.**, R.M. Rerko, A.M. Hujer and R.A. Maier, Jr. 1998. Increased interleukin-2 synthetic capacity parallels disease progression in mice infected with *Leishmania major*. *Infect. Immun.* 66:4537-40.
26. Sang, D.K., Ouma, J.H., C. John, Whalen, C.C., King, C., Mahmoud, A.A.F. and **F.P. Heinzel**. 1999. Increased levels of soluble interleukin-4 receptor in serum of patients with visceral leishmaniasis. *J. Infect. Dis.* 179: 743-6.
27. Yip, H.C., A.Y. Karulin, M. Tary-Lehmann, P. Heeger, R.P. Trezza, **F.P. Heinzel**, T. Forsthuber and P.V. Lehmann. 1999. Adjuvant guided type 1 and type 2 immunity. *J. Immunol.* 162: 3942 - 3949.
28. Balkhy, H.H. and **F.P. Heinzel**. 1999. Endotoxin fails to induce interferon- γ in endotoxin tolerant mice: Deficiencies in both IL-12 heterodimer production and IL-12 responsiveness. *J. Immunol.* 162: 3633 – 3638.
29. **Heinzel, F.P.** and R.M. Rerko. 1999. Cure of progressive murine leishmaniasis: IL-4 dominance is abolished by transient CD4+ T cell depletion and Th1-selective cytokine therapy. *J. Exp. Med.* 189:1895-1905.
30. **Heinzel, F.P.** and R.A. Maier, Jr. 1999. IL-4 independent acceleration of cutaneous leishmaniasis in susceptible BALB/c mice following treatment with anti-CTLA4 antibody. *Infect Immun.* 67:6454-6460.
31. Diana Martin, E. Pearlman, C.L. King and **F.P. Heinzel**. 2000. Interferon- γ is necessary, but not sufficient for anti-CD40 antibody-mediated inhibition of the Th2 response to *Schistosoma mansoni* eggs. *J. Immunol.* 164:779-85.
32. Kremer, I.B., Cooper, K.D. and **F.P. Heinzel**. 2001. Pretreatment with recombinant Flt3 ligand partially protects against progressive cutaneous leishmaniasis in susceptible BALB/c mice. *Infect. Immun.* 69: 673-680.
33. Yadavalli, G.K., Auletta, J.J., Gould, M.P. Salata, R.A. Lee, J.H. and **F.P. Heinzel**. 2001. Deactivation of the innate cellular immune response following endotoxic and surgical injury. *Exp Mol Pathol.* 2001 71:209-221.
34. Kharti, S., J.H. Lass, **F.P. Heinzel**, W. M. Petroll, E. Diaconu, C.M. Kalsow and E. Pearlman. 2002. Regulation of endotoxin-induced keratitis by PECAM-1, MIP-2, and Toll-like receptor 4. *Invest. Ophth Vis Sci.* 43:2278-84.
35. Pantenburg, B., **F. Heinzel**, L. Das, P. Heeger and A. Valujskikh. 2002. T cells primed by *Leishmania major* infection cross-react with alloantigens and alter the course of allograft rejection. *J. Immunology* 169(7):3686-93.
36. Garhart, C.A., **F.P. Heinzel**, S.J. Czinn, and J.G. Nedrud. 2002. Vaccine-induced reduction of *Helicobacter pylori* colonization in mice is IL-12-dependent, but IFN- γ and iNOS-independent. *Infection and Immunity* 71:910-21.

37. Murray, H.W., Moreira, A.L., Lu, C.M., DeVecchio J.L., Matsushashi, M. Ma, X. and **F.P. Heinzel**. 2002. Determinants of response to interleukin-10 blockade immunotherapy in experimental visceral leishmaniasis. *J Infect Dis*. 188:458-64.
38. Garhart, C.A., J.G. Nedrud, **F.P. Heinzel**, S.J. Czinn. 2003. Vaccine-induced protection against *Helicobacter pylori* in mice lacking both antibodies and interleukin-4. *Infect Immun*. 71:3628-33.
39. Murray, H.W., E.B. Brooks, J. L. DeVecchio, **F. P. Heinzel**. 2003. Immunoenhancement combined with amphotericin B as treatment in experimental visceral leishmaniasis. *Antimicrob Agents Chemother*. 47:2513-7.
40. Murray, H.W., C.S. Lu, E.B. Brooks, R.E. Fichtl, J.L. DeVecchio and **F.P. Heinzel**. 2003. Modulation of T cell costimulation as immuno- or immunochemotherapy in experimental visceral leishmaniasis. *Infection and Immunity*. 71: 6453-6462.
41. Gould, M.P., J. Greene, V. Bhoj, J. DeVecchio and **F.P. Heinzel**. 2004. Distinct modulatory effects of lipopolysaccharide and CpG on IL-18-dependent IFN production. *J. Immunol*. 172:1754-62.
42. Anthony, D.D., N.L. Yonkers, A.B. Post, R. Asaad, **F.P. Heinzel**, M.M. Lederman, P.V. Lehmann and H. Valdez. 2004. Selective impairments in dendritic cell-associated function distinguish HCV and HIV infection. *J. Immunol*. 172:4907-16.
43. Auletta, J.J., J.L. DeVecchio, J.L.M. Ferrara and **F.P. Heinzel**. 2004. Distinct phases in recovery of reconstituted innate cellular mediated immunity following murine syngeneic bone marrow transplantation. *Biology of Blood and Marrow Transplantation*. 10:834-7.
44. Johnson, A.C., **F.P. Heinzel**, E. Diaconu, Y. Sun, A.G. Hise, D. Golenbock, J.H. Lass and E. Pearlman. 2004. Activation of toll-like receptor (TLR) 2, TLR4 and TLR9 in the mammalian cornea induces MyD88-dependent corneal inflammation. *IOVS*. 46: 589-95.
45. Yadavalli, G.K., J. W. Chien, K.M. Wener, J.L. DeVecchio, S. Gupta, R.A. Salata, J.H. Lee,, C. Caldeira, J.J. Auletta and **F.P. Heinzel**. 2005. IL-12 and interferon-gamma synthetic deficiency is associated with dendritic cell cytopenia after cardiac surgery. *Shock*. 24:26-33.
46. Das, L , J.L DeVecchio and **F.P. Heinzel**. 2005. Flt3L-based immunoprophylaxis against infection is improved by adjuvant treatment with anti-IL-10 antibody. *J of Infect Dis*. 192:693-702.
47. Greene, J.A., J.L. DeVecchio, M.P. Gould, J. A. Auletta and **F. P. Heinzel**. 2006. In vivo and in vitro regulation of type I IFN synthesis by synergistic effects of CD40 and Type II IFN. *J. Immunol*. 176:5995-6003.
48. Gupta, S., M.P. Gould, J. Devecchio, D. H. Canaday, J.J. Auletta and **F.P. Heinzel**. 2007. CpG-Induced IFN expands TLR4-specific IL-18 responses in vivo. *Cell. Immunol*. 243:75-82.
49. Daehnel, K., I. Gillette-Ferguson, A.G. Hise, E. Diaconu, M.J. Harling, **F.P. Heinzel** and E. Pearlman. 2007. Filaria/Wolbachia activation of dendritic cells and development of Th1-associated responses is dependent on Toll-like receptor 2 in a mouse model of ocular onchocerciasis (river blindness). *Parasite Immunol*. 29:455-65.
50. Yonkers, N.L. K.A. Milkovich, B. Rodriguez, A.B. Post, R. Asaad, **F.P. Heinzel**, M. Tary-Lehmann and D.D. Anthony. 2009. Accessory cell dependent NK cell mediated PBMC IFN-gamma production is defective in HIV infection. *Clin. Immunol*. 131:288-297

C. Funding

Pending

2009 DOD PR093237

"A mouse model of heterotopic ossification for experimental therapeutics development"
\$436,000 total direct costs (10/1/2010 – 09/31/2013)

Current or active in last three years

2008 DOD PT073012 Traumatic Brain Injury Concepts Grant

"Pathogenesis of Heterotopic Ossification in Traumatic Brain Injury"
\$140,358 total direct costs (03/17/08- 12/31/09)