

## THE BYRD LAB

Dr. Byrd's laboratory focuses on host defense against intracellular bacterial pathogens. Dr. Byrd was the first to demonstrate that activation of human macrophages with the cytokine IFN $\gamma$  restricts the availability of iron to intracellular *Legionella pneumophila*, thereby restricting its growth. This host defense mechanism has subsequently been found to be active against a number of other intracellular pathogens by various investigators. Other landmark studies include the first publication to describe the use of chloroquine as an active agent against intracellular pathogens through its effects on host cell iron metabolism, and the first description of a growth promoting effect of the cytokine TNF $\alpha$  on intracellular *Mycobacterium tuberculosis*.

In addition to having his own laboratory, Dr. Byrd is also Director of the *M. tuberculosis* BSL-3 at the University of New Mexico.

**Current studies are focused in two areas**, one involving the nontuberculous mycobacteria (NTM) *M. abscessus*, and *M. avium*, and the other involving *M. tuberculosis*:

**1) *Mycobacterium abscessus* / *Mycobacterium avium*** - These NTM causes a variety of clinical infections with *M. abscessus* being an emerging pathogen causing pulmonary infection in patients with bronchiectasis. Current work focuses on the role that *M. abscessus* / *M. avium* surface lipids play in modulating host-pathogen interactions. Specifically, the role that *M. abscessus* / *M. avium* glycopeptidolipids play in biofilm formation and host airway colonization, and the role that phosphatidylinositol mannosides play in stimulating host immune responses and facilitating macrophage invasion.

**2) *Mycobacterium tuberculosis*** - *M. tuberculosis* remains a worldwide problem, and the emergence of clinical strains characterized as extremely drug resistant (XDR-TB) is a particularly ominous development. Current work in this area focuses on manipulating the host immune response against *M. tuberculosis* to enhance the efficacy of standard antimicrobial TB drug therapy thereby preventing the emergence of drug resistance.

### Ongoing and completed grants:

*Mycobacterium abscessus* glycopeptidolipid and the pathogenesis of lung disease in cystic fibrosis.

Role: Principal Investigator  
Cystic Fibrosis Foundation  
July 1, 2008 – June 30, 2010

The role of *Mycobacterium abscessus* glycopeptidolipid in colonization and invasion.

Role: Principal Investigator  
American Lung Association DeSouza Award  
July 1, 2005 – June 30, 2008

Phenotypic characterization and genetic analysis of a *Mycobacterium abscessus* mutant.  
Role Principal Investigator  
VA Merit Review  
August 1999 - April 2003

Iron and TNF $\alpha$  in Cytokine Restriction of *M. tuberculosis*.  
Role: Principal Investigator  
National Institutes of Health First Award (R29).  
October 1993 - September 1999.

### **Selected Publications:**

Rhoades, E., Greendyke, R., Archambault, A., and **T.F. Byrd**. *Mycobacterium abscessus* glycopeptidolipid masks underlying cell wall phosphatidylinositol mannosides preventing their interaction with human monocyte toll receptor 2. Submitted for Publication.

Greendyke, R., and **T.F. Byrd**. 2008. Differential antibiotic susceptibility of *Mycobacterium abscessus* variants in biofilms and macrophages compared to that of planktonic bacteria. *Antimicrobial Agents and Chemotherapy*. In Press.

**Byrd, T.F.** and L.E. Davis. 2007. Multidrug-resistant tuberculous meningitis. *Current Neurology and Neuroscience Reports* 7:470-475.

Pang, X., Vu, P., **Byrd, T.F.**, Ghanny, S., Soteropoulos, P., Mukamolova, G.V., Wu, S., Samten, B., and S.T. Howard. 2007. Evidence for complex interactions of stress-associated regulons in an *mprAB* deletion mutant of *Mycobacterium tuberculosis*. *Microbiology* 153:1229-1242.

Howard, S.T., Rhoades, E., Recht, J., Alsup, A., Pang, X., Kolter, R., Lyons, C.R., and **T.F. Byrd**. 2006. Spontaneous reversion of *Mycobacterium abscessus* from a smooth to a rough morphotype results in reduced expression of glycopeptidolipid and reacquisition of an invasive phenotype. *Microbiology* 152: 1581-1590.

Howard, S.T., **Byrd, T.F.**, and C.R. Lyons. 2002. Characterization of a novel insertion sequence and a polymorphic region in *Mycobacterium abscessus*. *Microbiology* 148:2987-2996.

Howard, S.T. and **T.F. Byrd**, 2000. The rapidly-growing mycobacteria: Saprophytes and parasites. *Microbes and Infection* 2:1845-1853.

**Byrd, T.F.** and M.A. Horwitz. 2000. Aberrantly low transferrin receptor expression on human monocytes is associated with non-permissiveness for *Legionella pneumophila* growth. *The Journal of Infectious Diseases* 181:1394-1400.

**Byrd, T.F.** and C.R. Lyons. 1999. Preliminary characterization of a *Mycobacterium abscessus* mutant in human and murine models of infection. *Infection and Immunity* 67:4700-4707.

**Byrd, T.F.**, G.M. Green, S.E. Fowlston, C.R. Lyons. 1998. Differential growth characteristics and streptomycin susceptibility of virulent and avirulent *Mycobacterium tuberculosis* in a novel fibroblast-mycobacterium microcolony assay. *Infection and Immunity* 66:5132-5139.

**Byrd, T.F.** 1998. Multinucleated giant cell formation induced by IFN $\gamma$ /IL-3 is associated with restriction of virulent *Mycobacterium tuberculosis* cell to cell invasion in human monocyte monolayers. *Cellular Immunology*. 188:89-96.

**Byrd, T.F.** 1997. TNF $\alpha$  promotes growth of virulent *M. tuberculosis* in human monocytes: Iron-mediated growth suppression is correlated with decreased release of TNF $\alpha$  from iron-treated, infected monocytes. *The Journal of Clinical Investigation*. 99:2518-2529.

Green, G.M. and **T.F. Byrd**. The immune response to Legionella infection. In *Host Response to Intracellular Pathogens*. Stefan Kaufman, editor. 1997 R.G. Landes Co., Austin, Texas, USA, pp 97-114.

Lbraty, D.H. and **T.F. Byrd**. 1996. Cutaneous miliary tuberculosis in the AIDS era. Case report and review of the literature. *Clinical Infectious Diseases*. 23:706-710.

**Byrd, T.F.** 1994. Cytokines and legionellosis. *Biotherapy* 7:179-186.

**Byrd, T.F.** Cytokine treatment of *Legionella pneumophila* infection. In *Haematopoietic Growth Factors and Mononuclear Phagocytes*. Ralph van Furth, editor. 1993 Karger, Basel, Switzerland, pp.123-133.

**Byrd, T.F.** and M.A. Horwitz. 1993. Regulation of transferrin receptor expression and ferritin content in human mononuclear phagocytes: Coordinate upregulation by iron-transferrin and downregulation by interferon gamma. *The Journal of Clinical Investigation*. 91:969-976.

**Byrd, T.F.** and M.A. Horwitz. 1991. Lactoferrin inhibits or promotes *Legionella pneumophila* intracellular multiplication in nonactivated and interferon gamma-activated human

monocytes depending upon its degree of iron saturation. Iron lactoferrin and nonphysiologic iron chelates reverse monocyte activation against *Legionella pneumophila*. The Journal of Clinical Investigation. 88:1103-1112.

**Byrd, T.F.** and M.A. Horwitz. 1991. Chloroquine inhibits the intracellular multiplication of *Legionella pneumophila* by limiting the availability of iron. A potential new mechanism for the therapeutic effect of chloroquine against intracellular pathogens. The Journal of Clinical Investigation. 88:351-357.

**Byrd, T.F.** and M.A. Horwitz. 1989. Interferon gamma-activated human monocytes downregulate transferrin receptors and inhibit the intracellular multiplication of *Legionella pneumophila* by limiting the availability of iron. The Journal of Clinical Investigation. 83:1457-1465.

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