

Michal Olszewski, D.M.V., Ph.D.

Faculty Appointment: Assistant Professor (UM)
Research Biologist (VA)

Research Interests: Pulmonary Immunology, Pulmonary Infections

Degree: D.V.M. 1988, Warsaw University of Life Sciences
Ph.D. 1997, Michigan State University

Fellowships: Postdoctoral Research Fellow, University of Michigan Health System 1998-2003
Post-DVM Fellow and Ph.D. Candidate, Michigan State University 1995-1998

Faculty Appointment Date: 2003

Academic Office Address: Ann Arbor VA Healthcare System
Research Service (11R)
2215 Fuller Road
Ann Arbor, MI 48105

Academic Office Telephone: (734) 845-5238 (office), (734) 845-3980 (lab)

Academic Office Fax: (734) 845-3241

Research Interests:

Scientific interest of our group focuses on the host-pathogen interaction at the interface of the adaptive and innate immunity. The effects of these interactions on the development of protective responses against fungal and bacterial pathogens are a common theme of these studies. Following areas of investigation have been established

- Mechanisms involved in pathogenesis of *Cryptococcus neoformans* infection and persistence of this microbe are main focus of our work. The interplay between the host and microbial factors especially, the role of microbial factors, urease, Hsp70 homologue Ssa1, and other factors on different aspects of host response to this pathogenic yeast are extensively studied. This includes effects on innate immune response, the development of the adaptive immunity and on dissemination of this pathogen into the CNS.
- Alternative activation of macrophages promotes persistence of *C. neoformans* we look into the mechanisms that promote and or prevent the alternative activation. These mechanisms include cytokines, direct effects of cryptococcal virulence factors, and pattern recognition receptors such as TLR9. We study how these factors affect macrophage biology in context of cryptococcal infection.



- Differential outcomes of infections are observed in various strains of mice infected with *C. neoformans*. We are interested in inheritance of these factors and the evaluation how genetic differences affect phenotype of the immune response to *C. neoformans*.
- Mechanisms modulating the development of the adaptive immune responses to *C. neoformans*, particularly the role of cytokines, chemokines and growth factors including TNF- α and IL-12, MIP-1 α /CCL3 and GM-CSF. Effects of these factors during the early responses (dendritic cells and macrophages) and their subsequent effects on T cell response polarization are studied.

Recent Articles:

- Chen GH, Olszewski MA, McDonald RA, Wells JC, Huffnagle GB, Toews GB. Role of Granulocyte Macrophage Colony Stimulating Factor in Host Defense Against Pulmonary *Cryptococcus neoformans* Infection During Murine Allergic Bronchopulmonary Mycosis Am J Pathol. Mar;170(3):1028-40, 2007
- Olszewski MA, Falkowski NR, Surana R, Sonstein J, Hartman A, Huffnagle GB, Toews GB I Effect of Laparotomy on Clearance and Cytokine Induction in *Staphylococcus aureus*-infected Lungs. Am J Respir Crit Care Med.;176: 921-929, 2007
- Chen GH, McNamara DA, Hernandez Y, Huffnagle GB, Toews GB and Olszewski MA. Inheritance of Immune Polarization Patterns is linked to Resistance versus Susceptibility to *Cryptococcus neoformans* in a Mouse Model. Infection and Immunity; 76: 2379–2391, 2008
- Osterholzer JJ, Surana R, Milam JE, Montano GT, Sonstein J, Curtis JL, Huffnagle GB, Toews GB, and Olszewski MA. Cryptococcal Urease Acts as a Pulmonary Virulence Factor by Shifting the Balance of the Adaptive Immune Response from a Protective T1 Response towards a Non-Protective T2 Response. American Journal of Pathology; 174 (3):932-943, 2009
- Osterholzer JJ, Milam JE, Chen GH, McDonald R, Huffnagle GB, Toews GB, and Olszewski MA. “Dendritic Cells and/or Alveolar Macrophages are Critical for Early Protection against Pulmonary Infection with *Cryptococcus neoformans*”. Infection and Immunity; 77: 3749–3758, 2009
- Wozniak KL, Ravi S, Macias S, Young ML, Olszewski MA, Steele C, Wormley FL: Insights into the mechanisms of protective immunity against *Cryptococcus neoformans* infection using a mouse model of pulmonary cryptococcosis, PLoS One; 4: e6854, 2009
- Jain A, Zhang Y, Fields BW, McNamara DA, Choe MY, Chen GH, Erb-Downward JR, Osterholzer JJ, Toews GB, Huffnagle GB, and Olszewski MA. Th2 but not Th1 Immune Bias Results in Altered Lung Functions in Murine Model of Pulmonary *C. neoformans* Infection. Infection and Immunity; 77: 5389-99 (12) 2009
- Zhang Y, Wang F, Tompkins KC, McNamara A, Jain AV, Moore BB, Toews GB, Huffnagle GB, Olszewski MA: Robust Th1 and Th17 immunity supports pulmonary clearance but cannot prevent systemic dissemination of highly virulent *Cryptococcus neoformans* H99. Am J Pathol; 175: 2489-2500 2009
- Osterholzer JJ, Chen G, Olszewski MA, Curtis JL, Huffnagle GB, Toews GB. Accumulation of CD11b+ Lung Dendritic Cells in Response to Fungal Infection Results from the CCR2-Mediated Recruitment and Differentiation of Ly-6Chigh Monocytes, J. Immunol. 183(12): 8044-53, 2009
- Milam JE, Erb-Downward JR, Chen GH, Osuchowski MF, McDonald R, Chensue SW, Toews GB, Huffnagle GB, Olszewski MA: CD11c+ Cells Are Required to Prevent Progression from Local Acute Lung Injury to Multiple Organ Failure and Death, Am J Pathol; 176(1):218-26, 2010
- Hardison SE, Ravi S, Wozniak KL, Young M, Olszewski MA, Wormley FL. Pulmonary Infection with an Interferon-gamma Producing *Cryptococcus neoformans* Strain Results in Classical Macrophage Activation and Protection. Am J Pathol; 176: 774–785, 2010
- Zhang Y, Wang F, Huffnagle GB, Toews GB, Bhan U, Standiford TJ, Olszewski MA. The Role of Toll Like Receptor 9 (TLR9) in Anticryptococcal Host Defenses. Am J Pathol; 177:754-65, 2010
- Olszewski MA, Zhang Y, Huffnagle GB. Mechanisms of Cryptococcal Virulence and Persistence. (Invited Review) Future Microbiology; 5:1269-88, 2010

- Olszewski MA, Zhang Y, Zeltzer S. Th1, Th2 and beyond; what we know about the adaptive immunity for fungal infections. (Invited Review) *J Invasive Fungal Infect*; 4(3):96–103, 2010.
- Osterholzer JJ, Chen G, Olszewski MA, Curtis JL, Huffnagle GB, Toews GB. Fungal Lung Infection Induces Accumulation of Classically Activated. CD11c+ CD11b+ Exudate Macrophages Derived from Recruited Ly-6C^{high} Monocytes. *Am J Pathol*; 178(1):198-211, 2011
- Arora S, Olszewski MA, Tsang TM, McDonald R, Toews GB, Huffnagle GB. Effect of Cytokine Interplay on Macrophage Polarization during Chronic Pulmonary Infection with *Cryptococcus neoformans*. *Infect Immun*. 2011;79:1915-26