BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Beiting, Daniel P.	Research Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) BEITING	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Appalachian State University	B.S.	1995-1999	Exercise Science
Cornell University	Ph.D.	2001-2006	Immunology
University of Pennsylvania	Postdoc	2006-2012	Genomics/Immunity

A. Personal Statement

For the past 15 years I have studied the host-microbial interactions, with a primary focus on leveraging genomic and bioinformatics approaches to elucidate mechanisms that regulate inflammation and host defense. My early studies of chronic infection with the parasitic helminth, *Trichinella spiralis,* led to the elucidation of the cytokines IL10 and TGF-β, and eosinophils as critical regulators of inflammation and immunity to chronic helminth infection. As my work shifted from helminth to protozoan parasites, I began to employ genome-wide transcriptional profiling and genetic screens to identify novel players involved signaling pathways that regulate both immunity and pathogenic inflammation. The results of these studies have helped shed light on important immune effector mechanisms, ranging from IL27 signaling in Tregs, to reactive oxygen species production by infected monocytes, to TLR3-dependent type I interferon production. In my current position as Research Assistant Professor in Pathobiology and Technical Director of the Center for Host-Microbial interactions, I continue to utilize 'omics approaches to study host immunity and have shifted my focus from pathogenic organisms to commensal microbes, with the goal of trying to understand how gut-resident commensal bacteria can influence intestinal inflammation and disease.

B. Positions and Honors

Professional Experience

1999-2001	Research Technician, James A. Baker Institute for Animal Health, Cornell University, Ithaca, NY
2001-2006	Ph.D. candidate. James A. Baker Institute for Animal Health, Cornell University, Ithaca, NY
2006-2013	Post-doctoral Research Fellow, Department of Biology; Penn Genome Frontiers Institute, University of Pennsylvania, Philadelphia, PA
2007-2008	Project Leader and Lecturer - Penn Summer Science Academy (A competitive summer program for academically talented high school students); University of Pennsylvania
2007-2009	Course Lecturer - Biology of Infectious Disease (BIO 406); University of Pennsylvania
2009	Co-organizer and Instructor- First West African Regional Workshop on the Cell Biology of Protozoan Pathogens - July 13-24th, Accra, Ghana
2009-2013	Course Lecturer - Parasites and Parasitism- (CAMB 549) - University of Pennsylvania
2013-current	Research Assistant Professor. Department of Pathobiology, School of Veterinary Medicine. University of Pennsylvania, Philadelphia, PA

Awards/Service

2004	Trainee Award, The 11th International Conference on Trichinellosis
2006	American Society of Tropical Medicine and Hygiene (ASTMH) award for 'Scientific Excellence in Molecular, Cellular and Immunoparasitology'
2007	Selected as a participant in the Burroughs Wellcome Fund and Sigma Xi course in Grant Writing for Postdoctoral Fellows in Parasitology, held in Woods Hole, MA and Atlanta, GA.
2007	Guava Prize for best poster presentation, 9th International Congress on Toxoplasmosis
2012	Burroughs Wellcome Fund-ASTMH distinction award for outstanding scientific presentation

C. Contributions to Science

A full list of publications can be found at this link: http://www.ncbi.nlm.nih.gov/pubmed/?term=beiting+DP

Regulation of inflammation during chronic helminth infection - As a PhD student, I was struck the remarkable ability of parasitic worms to limit tissue inflammation during chronic infection, even in the face of substantial tissue damage and remodeling. Working with *Trichinella spiralis*, I developed an *in vivo* model for evaluating the immunoregulatory environment during chronic helminth infection. Using a combination of knockout mice, adoptive cell transfers and antibody neutralization, I showed that IL-10 produced by non-regulatory T cells (CD25 negative) was required to limit inflammation. These data, together with studies published by other groups later the same year, focused attention on effector T cells as a cell population with the capability to potently suppress inflammation. In addition, I showed that a combined deficiency in IL10 and TGFb during chronic *T. spiralis* infection, resulted in severe inflammation and worm destruction. This was the first study to identify host factors required for worm persistence outside of the intestine. These studies laid the foundation for additional work, on which I was a co-author, which showed that eosinophils recruited to *T. spiralis* infected tissue protect worms from destruction.

1. **Beiting DP**, Gagliardo LF, Hesse M, Bliss SK, Meskill D, and Appleton JA. Coordinated control of immunity to muscle stage Trichinella spiralis by IL-10, regulatory T cells and TGF-β. *J Immunol*. 2007 Jan 15;178(2):1039-47.
2. **Beiting DP**, Bliss SK, Schlafer DH, Roberts VL, and Appleton JA. Interleukin-10 limits local and body cavity inflammation during muscle infection with Trichinella spiralis. *Infect Immun*. 2004 Jun;72(6):3129-37
3. Fabre V, **Beiting DP**, Bliss SK, Gebreselassie NG, Gagliardo LF, Lee NA, Lee JJ, and Appleton JA. Eosinophil deficiency compromises parasite survival in chronic nematode infection. *J Immunol*. 2009 Feb 1; 182(3):1577-83. (Recommended by "Faculty of 1000")
4. Douglas DB, **Beiting DP**, Appleton JA, Bliss SK. Combinatorial effects of IL-10 and IL-4 determine the progression of hepatic inflammation following enteric parasite infection. *Hepatology*. Jun, 2010
5. Favre V*, **Beiting DP***, Bliss SH, and Appleton JA. Immunity to Trichinella spiralis muscle infection (Review). Vet Parasitol. 2009 Feb 23; 159(3-4):245-8. Epub 2008 Oct 22. (*co-first authors)

Regulation of interferon signaling and STAT1 mediated transcription – As a postdoctoral fellow in David Roos' laboratory, my research interests shifted from studying cellular and molecular mechanisms of immunity to helmith infection, to leveraging genomic approaches to study the host response to intracellular parasites. *Toxoplasma gondii*. Binding of IFN-g to its cell surface receptor triggers activation and nuclear translocation of the transcription factor STAT1. Activation of STAT1 targets is an essential part of the immune response to breadth of intracellular pathogens, yet there was a gap in our knowledge as to how STAT1 transcriptional activity is regulated in the nucleus. To address this issue, I carried out a genome wide screen in *Toxoplasma* infected cells that identified novel enhancers of STAT1-mediated transcription. These studies were the first to show that the orphan nuclear hormone receptor TLX, was one such enhancer and was required for proper induction of inflammatory gene expression in response to IFNg.

6. **Beiting DP**, Peixoto L, Akopyants NS, Beverley SM, Wherry EJ, Christian DA, Hunter CA, Brodsky IE, Roos DS. Differential Induction of TLR3-dependent Innate Immune Signaling by Closely Related Parasite Species. *PLoS One 9(2): Feb 5, 2014*
7. **Beiting DP.** Protozoan Parasites and Type I Interferons: a cold case reopened. *Trends in Parasitology*. 2014. Oct; 30(10)
8. Hall AO, **Beiting DP**, Tato C, John B, Oldenhove G, Lombana CG, Pritchard GH, Silver JS, Bouladoux N, Stumhofer JS, Harris TH, Grainger J, Wojno EDT, Wagage S, Roos DS, Scott P, Turka LA, Cherry S, Reiner SL, Cua D, Belkaid Y, Elloso MM, and Hunter CA. 2012. The cytokines interleukin 27 and interferon-γ promote distinct Treg cell populations required to limit infection-induced pathology. *Immunity* 37: 511–523.
9. **Beiting DP**, Hidano S, Baggs JE, Geskes JM, Wherry EJ, Fang Q, Hunter CA, Roos DS, Cherry S. 2015. The Orphan Nuclear Receptor TLX is an Enhancer of STAT1-mediated Transcription and Immunity to *Toxoplasma gondii*. Manuscript in press at PLOS Biology

Regulation of immunity and inflammation during *Leishmania* infection - Human skin infection with the intracellular parasite, *Leishmania braziliensis*, instigates a profound inflammatory response leading to severe skin lesions that continues unabated even after parasite replication is controlled, yet the mechanisms leading to this response had remained elusive. As part of an international collaborative team, I carried out genome-wide expression profiling of early and late stage human *L. braziliensis* lesions and control skin to define the transcriptional networks that underlie this disease. We found that early in lesion development when skin has not ulcerated and only a papule is evident, the transcriptional response in the skin is indistinguishable from that of late stage ulcerated lesions, suggesting transcriptional pathways evident early may be driving pathology. This was the first study to identify pathways driving pathology early after infection, and it helped set the stage for a number of subsequent studies carried out in mouse and in humans, on which I am a co-author, that continue to dissect the molecular and cellular basis for skin pathology following infection.

10. Novais FO, Carvalho LP, Passos S, Roos DS, Carvalho EM, Scott P, **Beiting DP**. Genomic Profiling of human Leishmania braziliensis lesions identifies transcriptional modules associated with cutaneous immunopathology. *Journal of Investigative Dermatology. Jul 18, 2014.*
11. Campos TM, Passos ST, **Beiting DP**, Costa RS, Queiroz A, Mosser D, Scott P, Carvalho EM, Carvalho LP. Matrix metalloproteinase 9 production by monocytes is enhanced by TNF and participates in the pathology of human cutaneous Leishmaniasisa. *PLoS Negl Trop Dis. 2014 Nov 13*
12. Novais FO, Carvalho LP, Graff JW, **Beiting DP**, Ruthel G, Roos DS, Betts MR, Goldschmidt MH, Wilson ME, de Oliveira CI, Scott P. 2013. Cytotoxic T cells mediate pathology and metastasis in cutaneous leishmaniasis. *PLoS Pathogens*, Jul;9(7)
13. Glennie ND, Yeramilli VA, **Beiting DP**, Volk SW, Weaver CT, Scott P. 2015. Skin Resident Memory CD4+ T Cells Enhance Protection Against Leishmania major Infection. Manuscript in press at Journal of Experimental Medicine
14. Novais FO, Nguyen BT, **Beiting DP**, Carvalho LP, Glennie ND, Passos S, Carvalho EM, Scott P. Human Classical Monocytes Control the Intracellular Stage of *Leishmania braziliensis* by Reactive Oxygen Species. *Journal of Infectious Diseases; Jan 7, 2014*

D. Research Support

Completed

F32AI075846 Beiting (PI) 2007-2010
NIH/NIAID/Ruth L. Kirschstein National Research Service Award (NRSA)
"CD8 T cell memory and mucosal immunity to *Toxoplasma gondii*"

T32-AI007643 E. Denkers, Cornell U. (PI) 2001-2003
NIH/NIAID **"Immunobiology of Parasitic Diseases"**

Current: N/A