

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Howe, Daniel Keith		POSITION TITLE Professor	
eRA COMMONS USER NAME (credential, e.g., agency login) DANIEL.HOWE			
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
Western Illinois University	B.S.	05/88	Biology
Western Illinois University	M.S.	05/90	Parasitology
Purdue University	Ph.D.	12/92	Molecular Parasitology
Washington University School of Medicine	Postdoc	01/93-06/99	Microbial Pathogenesis

**A. Personal Statement**

My research interests are on the genetics and molecular biology of apicomplexan parasites, with a particular emphasis on the two-host coccidia (i.e., *Sarcocystis neurona*, *Toxoplasma gondii*, and *Neospora* spp.). My research program over the past decade has been focused heavily on gaining genetic information for *S. neurona* and developing molecular tools to investigate this parasite. To that end, we have conducted a project to sequence and annotate the genome for *S. neurona*, to examine gene transcription during different developmental stages of the parasite, and to identify novel virulence factors that allow the organism to survive as an intracellular parasite.

**B. Positions and Honors**

**Professional Appointments:**

- 1993-1999 Postdoctoral Fellow, Department of Molecular Microbiology, Washington University School of Medicine, Laboratory of Dr. David Sibley
- 1999-2005 Assistant Professor, Department of Veterinary Science, M.H. Gluck Equine Research Center, University of Kentucky
- 2005-2012 Associate Professor, Department of Veterinary Science, M.H. Gluck Equine Research Center, University of Kentucky
- 2009-present Director of Graduate Studies, Department of Veterinary Science, M.H. Gluck Equine Research Center, University of Kentucky
- 2012-present Professor, Department of Veterinary Science, M.H. Gluck Equine Research Center, University of Kentucky
- 2014-present Associate Chair, Department of Veterinary Science, M.H. Gluck Equine Research Center, University of Kentucky

**Academic Achievements and Honors:**

- 2001-2003 Editorial Board, Journal of Eukaryotic Microbiology
- 2004-present Recipient of the Amerman Family Equine Research Endowment
- 2004 Faculty Futures Award, University of Kentucky
- 2006-2010 Editorial Board, Veterinary Parasitology
- 2009 Presiding Officer, Annual Midwestern Conference of Parasitologists, Delaware, OH
- 2010-2012 Wethington Award, University of Kentucky

2010-2017 Co-Editor-in-Chief, Veterinary Parasitology  
2012-present Editorial Board, Infection and Immunity

### C. Contributions to Science:

1. My early work on coccidian parasites emphasized parasite genetics and revealed the highly clonal population structure of *Toxoplasma gondii*. These publications helped to establish the genotyping system that remains in use today and provided foundation for a multitude of studies examining both the population biology and pathogenicity of this important human pathogen.
  - a. **Howe, D.K.**, and L.D. Sibley. 1995. *Toxoplasma gondii* comprises three clonal lineages: correlation of parasite genotype with human disease. *Journal of Infectious Diseases* 172:1561-6.
  - b. **Howe, D.K.**, B.C. Summers, and L.D. Sibley. 1996. Acute virulence in mice is associated with markers on chromosome VIII in *Toxoplasma gondii*. *Infection and Immunity* 64:5193-5198
  - c. **Howe, D.K.**, S. Honoré, F. Derouin, and L.D. Sibley. 1997. Determination of genotypes of *Toxoplasma gondii* strains isolated from patients with toxoplasmosis. *Journal of Clinical Microbiology* 35:1411-1414.
  - d. Su, C., **D.K. Howe**, J.P. Dubey, J. Ajioka, and L.D. Sibley. 2002. Identification of quantitative trait loci controlling acute virulence in *Toxoplasma gondii*. *Proceedings of the National Academy of Sciences* 99:10753-10758.
  
2. Since arriving at the University of Kentucky, my research has focused on the coccidian *Sarcocystis neurona*, which causes the debilitating neurologic disease equine protozoal myeloencephalitis (EPM). The initial work by my research program investigated a variety of factors that likely play important roles in *S. neurona*'s lifestyle as an intracellular pathogen. Subsequent studies translating our finding into clinical applications led to development of diagnostic tests that are used widely by veterinary practitioners for diagnosis of EPM.
  - a. Hoane, J.S., V.B. Carruthers, B. Striepen, R. Entzeroth, and **D.K. Howe**. 2003. Analysis of the *Sarcocystis neurona* microneme protein SnMIC10: protein characteristics and expression during intracellular development. *International Journal for Parasitology* 33:671-679.
  - b. **Howe, D.K.**, R. Gaji, M. Mroz-Barrett, M-J. Gubbels, B. Striepen, and S. Stamper. 2005. *Sarcocystis neurona* merozoites express a family of immunogenic surface antigens that are orthologues of the *Toxoplasma gondii* surface antigens (SAGs) and SAG-related sequences. *Infection and Immunity* 73(2):1023-1033.
  - c. Zhang, D., R.Y. Gaji, and **D.K. Howe**. 2006. Identification of a dithiol-dependent nucleoside triphosphate hydrolase in *Sarcocystis neurona*. *International Journal for Parasitology* 36:1197-1204.
  - d. Hoane, J.S. \*, J.K. Morrow, W.J. Saville, J.P. Dubey, D.E. Granstrom, and **D.K. Howe**. 2005. Enzyme-linked immunosorbent assays for the detection of equine antibodies specific to *Sarcocystis neurona* surface antigens. *Clinical and Diagnostic Laboratory Immunology* 12(9):1050-1056.
  - e. Reed, S.M., **D.K. Howe**, J.K. Morrow, A. Graves, M.R. Yeargan \*, A.L. Johnson, R.J. MacKay, W.J.A. Saville, and N.M. Williams. 2013. Accurate antemortem diagnosis of equine protozoal myeloencephalitis (EPM) based on detecting intrathecal antibodies against *Sarcocystis neurona* using the SnSAG2 and SnSAG4/3 ELISAs. *Journal of Veterinary Internal Medicine* 27:1193-1200. doi:10.1111/jvim.12158.
  
3. The advent of the “omics” disciplines has greatly enhanced capabilities for investigating organisms. To enable these studies of *S. neurona*, recent work has been directed toward large collaborative efforts to sequence and annotate the *S. neurona* genome and to conduct phylogenomic analyses with related parasites, primarily *T. gondii*. The resulting database represents a tremendous resource for ongoing and

future studies to dissect the molecular composition of *S. neurona*, which holds high potential for leading to clinical applications.

- a. Blazejewski, T., N. Nursimulu, V. Pszenny, S. Dangoudoubiyam\*, S. Namasivayam, M.A. Chiasson, K. Chessman, M. Tonkin, S. Seshadri, S.S. Hung, J. Bridgers, S.M. Ricklefs, M.J. Boulanger, S.F. Porcella, J.C. Kissinger, **D.K. Howe**, M.E. Grigg, and J. Parkinson. 2015. Systems-based analysis of the *Sarcocystis neurona* genome identifies pathways that contribute to a heteroxenous life cycle. *mBio* 6(1):e02445-14. doi:10.1128/mBio.02445-14.
- b. Lorenzi, H., A. Khan, M.S. Behnke, S. Namasivayam, L.S. Swapna, M. Hadjithomas, S. Karamycheva, D. Pinney, B. Brunk, J.W. Ajioka, D. Ajzenberg, J.C. Boothroyd, J.P. Boyle, M.L. Dardé, M.L. Diaz-Miranda, J.P. Dubey, H.M. Fritz, S.M. Gennari, B.D. Gregory, K. Kim, J. Saeij, C. Su, M.W. White, XQ Zhu, **D.K. Howe**, B.M. Rosenthal, M.E. Grigg, J. Parkinson, L. Liu, J.C. Kissinger, D.S. Roos, L.D. Sibley. 2016. Local admixture of amplified and diversified secreted pathogenesis determinants shapes mosaic *Toxoplasma gondii* genomes. *Nature Communications* 7:10147. doi:10.1038/ncomms10147.
- c. Ojo, K.K., S. Dangoudoubiyam\*, S.K. Verma, S. Scheele, A.E. DeRocher, M. Yeargan\*, R. Choi, T.R. Smith, K.L. Rivas, M.A. Hulverson, L.K. Barrett, E. Fan, D.J. Maly, M. Parsons, J.P. Dubey, **D.K. Howe**, W.C. Van Voorhis. 2016. Selective Inhibition of *Sarcocystis neurona* Calcium-Dependent Protein Kinase 1 for Equine Protozoal Myeloencephalitis Therapy. *International Journal for Parasitology* 46(13-14):871-880. doi: 10.1016/j.ijpara.2016.08.003.

#### D. Research Support

##### Ongoing Research Support:

USDA/NIFA Hatch project #KY014054      Howe (PI)      2017-2022

*Sarcocystis neurona*: investigation of host cell interactions that contribute to parasite survival

The primary objectives of this project are to examine host cell invasion and establishment of the intracellular niche by *S. neurona* merozoites, and to investigate protein secretion by the parasite during invasion and intracellular growth.

Role: PI

##### Completed Research Support (past 5 years):

USDA/CSREES #2009-65109-05918      Howe (PI)      2009-2013

Genome Sequence for the Apicomplexan *Sarcocystis neurona*

This project's aim was to sequence and annotate the genome from *Sarcocystis neurona*, an apicomplexan parasite and the primary cause of equine protozoal myeloencephalitis.

Role: PI

Bill and Melinda Gates Foundation Grant      Dobson (PI)      2007-2012

Supplemental Lymphatic Filariasis Vector Intervention in the South Pacific

The goal of this study was to develop and deliver tools based on *Wolbachia* to accomplish population suppression and/or replacement of *Aedes polynesiensis*, a major vector of filarial worms in large regions of the South Pacific

Role: Co-Investigator