

BIOGRAPHICAL SKETCH

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NAME John C. Boothroyd	POSITION TITLE Professor of Microbiology and Immunology		
eRA COMMONS USER NAME Boothroyd.John			
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
McGill University	B.Sc. (Hons)	1975	Cell/Mol/Dev Biology
Edinburgh University	Ph.D.	1979	Molecular Biology

PROFESSIONAL EXPERIENCE:

1979-1982: Scientist, Molecular Biology Dept., Wellcome Research Laboratories, Beckenham, U.K.

1982-date: Assistant Professor (1982-1988), Associate Professor (1988-1994), Professor (1994-date), Dept. of Microbiology and Immunology, Stanford University School of Medicine, Stanford, California.

HONORS AND AWARDS:

1976-1978 Sir Arthur Sims Memorial Scholarship, Royal Society of Canada.
 1976-1979 Overseas Research Scholarship, Royal Commission for the Exhibition of 1851.
 1986-1991: Molecular Parasitology Award, Burroughs Wellcome Fund
 1994: Scaife Lecturer, University of Edinburgh
 1994-2004 MERIT Award, NIH/NIAID
 2002: Ellison Medical Foundation Senior Scholar Award in Global Infectious Diseases.
 2002: Dunlevie Family University Fellow in Undergraduate Education, Stanford University
 2005: Meyer Lecturer, Univ. California San Francisco
 2007: Fellow, American Academy of Microbiology
 2008: Leuckart Medal, German Society of Parasitology

OTHER PROFESSIONAL ACTIVITY:

Director, MBL Summer Course in "Biology of Parasitism", Woods Hole (1991-1993, inclusive)
 Editor, Microbiological Reviews (American Society of Microbiology) (1992-1998)
 Associate Editor (2005-2006) and Section Editor (2006-date), PLOS Pathogens.
 Member, Editorial Board, Exptl. Parasitol. (1987-date), Mol. Biochem. Parasitol. (1987-date), J. Euk. Microbiol. (1988-1994), Ann. Rev. of Microbiol. (1993-1997; 2006), Trends in Parasitology (2001-2006)
 Ad Hoc NIH Study Section Member, Eukaryotic Pathogens (PTHE; 10/93; 6/94; 6/97; 10/99; 2/02; 2/05); and AIDS Opportunistic Infections and Cancer (AOIC; 7/06, 7/07)
 Member (1995-2001) and Chair (1999-2001) Molecular Parasitology Committee, Burroughs Wellcome Fund
 Chair, Gordon Conference on Parasitism. Rhode Island (1999).
 Co-Chair (1994-1999) and Chair (1999-2002), Dept. Microbiology & Immunology, Stanford University.
 Senior Associate Dean for Research (2002-2005) and Training (2003-2005), Stanford School of Medicine.
 Associate Vice Provost for Graduate Education (2008-2010), Stanford University

PUBLICATIONS (156 TOTAL; SELECTED SHOWN PRE-2002; ALL SHOWN 2002 TO PRESENT):

Burg, J.L., Perelman, D., Kasper, L.H., Ware, P.L. and Boothroyd, J.C. 1988. Molecular analysis of the gene encoding the major surface antigen of *Toxoplasma gondii*. **J. Immun.** 141:3584-3591.
 Nagel, S.D. and Boothroyd, J.C. 1989. The Major Surface Antigen, p30, of *Toxoplasma gondii* is Anchored by a Glycolipid. **J. Biol. Chem.** 264:5569-5574.
 Grover, C.M., Thulliez, P., Remington, J.S. and Boothroyd, J.C. 1990. Rapid Prenatal Diagnosis of Congenital Toxoplasma Infection from Amniotic Fluid by Polymerase Chain Reaction. **J. Clin. Micro.** 28:2297-2301.

- Kasper, L.H., Khan, I.A., Ely, K.H., Buelow, R. and Boothroyd, J.C. 1992. Antigen specific (P30) mouse CD8+ T cells are cytotoxic against *Toxoplasma gondii* infected peritoneal macrophages. **J. Imm.** 148:1493-1498.
- Sibley, L.D. and Boothroyd, J.C. 1992. Virulent strains of *Toxoplasma gondii* are clonal. **Nature** 359:82-85.
- Sibley, L.D., LeBlanc, A., Pfefferkorn, E.R. and Boothroyd, J.C. 1992. Generation of a restriction fragment length polymorphism linkage map for *Toxoplasma gondii*. **Genetics** 132:1003-1015.
- Soldati, D. and Boothroyd, J.C. 1993. Transient transfection of the obligate intracellular parasite, *Toxoplasma gondii*. **Science** 260: 349-352.
- Kim, K., Soldati, D. and Boothroyd, J.C. 1993. Gene replacement in *Toxoplasma gondii* with chloramphenicol acetyl transferase as selectable marker. **Science** 262:911-914.
- Soldati, D and Boothroyd, J.C. 1995. A selector of transcription initiation in the protozoan parasite, *Toxoplasma gondii*. **Mol. Cell Biol.** 15:87-93.
- Knoll, L.J. and Boothroyd, J.C. 1998. Isolation of developmentally regulated genes from *Toxoplasma gondii* using a gene trap with the positive and negative selectable marker hypoxanthine-xanthine-guanine phosphoribosyltransferase. **Mol. Cell Biol.** 18:807-814.
- Manger, I.D.*, Hehl, A.*, Parmley, S., Sibley, L.D., Marra, M., Hillier, L., Waterston, R. and Boothroyd, J.C. 1998. Expressed Sequence Tag Analysis of the Bradyzoite Stage of *Toxoplasma gondii*: Identification of Developmentally Regulated Genes. **Infection and Immunity** 66:1632-1637. [*equal contribution].
- Ortega-Barria, E.O. and Boothroyd, J.C. 1999. A *Toxoplasma* lectin-like activity specific for sulfated polysaccharides is involved in host cell infection. **J. Biol. Chem.** 274:1267-1276.
- Hehl, A.B., Lekutis, C., Grigg, M., Dubremetz, J.-F., Ortega-Barria, E., Bradley, P. and Boothroyd, J.C. 2000. A *Toxoplasma gondii* homologue of the *Plasmodium* Apical Membrane Antigen 1 is involved in invasion of host cells. **Infection and Immunity** 68:7078-7086. [note first two authors are joint "first" authors].
- Black, M.W., Arrizabalaga, G. and Boothroyd, J.C. 2000. Ionophore-resistant mutants of *Toxoplasma gondii* reveal host-cell permeabilization as an early event in egress. **Mol. Cell Biol.** 20:9399-9408.
- Blader, I.J., Manger, I.D. and Boothroyd, J.C. 2001. Microarray analysis reveals previously unknown changes in *Toxoplasma gondii* infected human cells. **J. Biol. Chem.** 276:24223-24231.
- Knoll, L.J., Furie, G.L. and Boothroyd, J.C. 2001. Adaptation of signature-tagged mutagenesis for *Toxoplasma gondii*: a negative screening strategy to isolate genes that are essential in restrictive growth conditions. **Mol. Biochem. Parasitol.** 116:11-16.
- Camps, M. and Boothroyd, J.C. 2001. *Toxoplasma gondii*: Selective killing of extracellular parasites by oxidation using pyrrolidine dithiocarbamate. **Expt. Parasitol.** 4:206-214.
- Grigg, M.E., Ganatra, J., Boothroyd, J.C. and Margolis, T. 2001. Unusual abundance of atypical strains associated with ocular toxoplasmosis in humans. **J. Inf. Dis.** 184:633-639.
- Grigg, M.E., Suzuki, Y. and Boothroyd, J.C. 2001. Success and virulence in the AIDS pathogen *Toxoplasma* as the result of sexual recombination between two distinct ancestries. **Science** 294:161-165.
- Camps, M., Arrizabalaga, G. and Boothroyd, J.C. 2002. An rRNA mutation identifies the apicoplast as the target for clindamycin in *Toxoplasma gondii*. **Mol. Microbiol.** 43:1309-1318.
- Singh, U., Brewer, J.L. and Boothroyd, J.C. 2002. Genetic analysis of tachyzoite to bradyzoite differentiation mutants in *Toxoplasma gondii* reveals a hierarchy of gene induction. **Mol. Microbiol.** 44:721-733.
- Cleary, M., Blader, I.J., Singh, U., Brewer, J. and Boothroyd J.C. 2002. Gene expression during *Toxoplasma* development: Identification of distinct classes of regulated genes. **Eukaryotic Cell** 1:329-340.
- He, X.-L., Grigg, M.E., Boothroyd, J.C. and Garcia, K.C. 2002. A structural framework for host cell attachment revealed by the crystal structure of SAG1, the immunodominant surface antigen of *Toxoplasma gondii*. **Nature Structural Biology** 9:606-611.
- Bradley, P.J., Hsieh, C. and Boothroyd, J. C. 2002. Processing of *Toxoplasma* proROP1 is not necessary for targeting and release upon invasion. **Mol. Biochem. Parasitol.** 125: 155-158.
- Kong, J.-T., Grigg, M.E., Uyetake, L., Parmley, S. and Boothroyd, J.C. 2003. Serological Strain-Typing of Human Toxoplasmosis Using Synthetic Peptides. **J. Inf. Dis.** 187:1484-1496.
- Miller, M. A., Grigg, M. E., Kreuder, C, Melli, A.C., Crosbie, P.R., Jessup, D.A., Boothroyd, J.C., Brownstein, D. and Conrad, P.A. 2004. An unusual genotype of *Toxoplasma gondii* is common in Californian sea otters (*Enhydra lutris nereis*) and is a cause of high mortality. **Int. J. Parasitol.** 34:275-284.

- Arrizabalaga, G., Ruiz, F., Moreno, S. and Boothroyd J.C. 2004. Ionophore-resistant mutant of *Toxoplasma gondii* reveals involvement of a sodium/hydrogen exchanger in calcium regulation. **J. Cell Biol.** 165:653-662.
- Bradley, P.J., Li, N., and Boothroyd, J.C. 2004. A GFP-based motif-trap reveals a novel rhoptry targeting sequence in the *Toxoplasma* ROP4 protein. **Mol. Biochem. Parasitol.** 137:111-120.
- Rachinel, N., Dutta, C., Buzoni-Gatel, D., Mennechet, F.J.D., Grigg, M.E., Boothroyd, J.C. and Kasper, L.H. 2004. The induction of acute ileitis by a single microbial antigen of *Toxoplasma gondii*. **J. Immunol.** 173:2725-2735.
- Saeij, J.P.J., Boyle, J.P., Grigg, M.E., Arrizabalaga, G. and Boothroyd, J.C. 2005. Bioluminescence imaging of *Toxoplasma* infection in living mice reveals dramatic differences between strains. **Infection and Immunity** 73:695-702.
- Cleary, M., Meiering, C. Jan, E., Guymon, R. and Boothroyd, J.C. 2005. Biosynthetic Labeling of RNA via Uracilphosphoribosyltransferase Allows Cell-specific Microarray Analysis of mRNA Synthesis and Decay. **Nature Biotechnology** 23:232-237.
- Karasov, A.O., Boothroyd, J.C. and Arrizabalaga, G. 2005. Identification and disruption of a rhoptry localized sodium hydrogen exchanger in *Toxoplasma gondii*. **Int. J. Parasitol.** 35:285-291.
- Kim, S.-K. and Boothroyd, J.C. 2005. Stage-specific expression of surface antigens by *Toxoplasma gondii* as a mechanism that facilitates parasite persistence. **J. Immunol.** 174:8038-8048.
- Khan, A., Taylor, S., Su, C., Mackey, A.J., Boyle, J., Cole, R., Glover, D., Tang, K., Paulsen, I., Berriman, M., Boothroyd, J.C., Pfeifferkorn, E.R., Dubey, J.P., Roos, D.S., Ajioka, J.W., Wootton, J.C. and Sibley, L.D. 2005. A genome map for *Toxoplasma gondii*. **Nucl. Acids Res.** 33:2980-2992.
- Schwarz, J., Fouts, A.E., Ferguson, D and Boothroyd, J.C. 2005. A novel bradyzoite-specific rhoptry protein in *Toxoplasma gondii*. **Mol. Biochem. Parasitol.** 144:159-166.
- Bradley, P.J., Ward, C., Cheng, S.J., Alexander, D.L., Collier, S., Coombs, G.H., Dunn, J.D., Ferguson, D.J., Sanderson, S.J., Wastling, J.M. and Boothroyd, J.C. 2005. Proteomic analysis of *Toxoplasma* rhoptries reveals many novel constituents for host-parasite interaction. **J. Biol. Chem.** 280: 34245-34258.
- Vanchinathan, P., Brewer, J.L., Harb, O.S., Boothroyd, J.C. and Singh, U. 2005. Disruption of a locus encoding a nucleolar zinc finger protein inhibits tachyzoite to bradyzoite differentiation in *Toxoplasma gondii*. **Infection and Immunity** 73:6680-6688.
- Alexander, D.L., Mital, J., Ward, G.E., Bradley, P.J. and Boothroyd, J.C. 2005. Identification of the moving junction complex of an Apicomplexan parasite, *Toxoplasma gondii*: collaboration between two distinct secretory organelles. **PLOS Pathogens** 1:137-149.
- Coppens, I., Dunn, J.D., Romano, J.D., Pypaert, M., Zhang, H., Boothroyd, J.C. and Joiner, K.A. 2006. *Toxoplasma gondii* sequesters lysosomes from mammalian hosts in the vacuolar space. **Cell** 125:261-274.
- Boyle, J.P., Rajasekar, B., Saeij, J.P.J., Ajioka, J., Berriman, M., Paulsen, I., Roos, D.S., Sibley, L.D., White, M. and Boothroyd, J.C. 2006. Just one cross appears capable of dramatically altering the population biology of a eukaryotic pathogen like *Toxoplasma gondii*. **Proc. Natl. Acad. Sci. USA** 103:10514-10519.
- Alexander, D.L., Arastu-Kapur, S., Dubremetz, J.-F., and Boothroyd, J.C. 2006. *Plasmodium falciparum* AMA1 (PfAMA1) binds a rhoptry neck protein homologous to TgRON4, a component of the moving junction in *Toxoplasma*. **Eukaryotic Cell** 5:1169-1173.
- Saeij*, J.P.J., Boyle*, J.P., Collier, S.C., Taylor, S., Sibley, L.D., Brooke-Powell, E.T., Ajioka, J.W. and Boothroyd, J.C. 2006. Polymorphic secreted kinases are key virulence factors in toxoplasmosis. **Science** 314:1780-1783. [* equal contributors].
- Gilbert, L.A., Ravindran, S., Turetzky, J.M., Boothroyd, J.C. and Bradley, P.J. 2007. *Toxoplasma gondii* targets a protein phosphatase to the nucleus of infected host cells. **Eukaryotic Cell** 6:73-83.
- Saeij*, J.P.J., Collier*, S., Boyle, J.P., Jerome, M. White, M. and Boothroyd, J.C. 2007. *Toxoplasma* co-opts host gene expression by injection of a polymorphic kinase homologue. **Nature** 445:324-327. [* equal contributors].
- Fouts, A.E. and Boothroyd, J.C. 2007. Infection with *Toxoplasma* bradyzoites has a diminished impact on host transcript levels relative to tachyzoite-infection. **Infection and Immunity** 75:634-642.
- Boyle, J. P., Saeij, J.P.J. and Boothroyd, J.C. 2007. *Toxoplasma gondii*: Inconsistent dissemination patterns following oral infection in mice. **Experimental Parasitology** 116:302-305.

- Kim, S.-K., Fouts, A. and Boothroyd, J.C. 2007. *Toxoplasma gondii* dysregulates IFN- γ -inducible gene expression in human fibroblasts: insights from a genome-wide transcriptional profiling. **J. Immunol.** 178:5154-5165.
- Vyas, A., Kim, S.-K., Giacomini, N., Boothroyd, J.C. and Sapolsky, R.M. Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to cat odors. **Proc. Natl. Acad. Sci. USA** 104:6442-6447.
- Kim, S.-K., Karasov, A.O. and Boothroyd, J.C. 2007. Bradyzoite-specific surface antigen SRS9 plays a role in maintaining *Toxoplasma gondii* persistence in the brain and shaping a protective host response in the intestine. **Infection and Immunity** 75:1626-1634.
- Tam, T.V., Kim-S.-K., Camps, M., Boothroyd, J.C. and Knoll, L.J. 2007. Identification of the *Toxoplasma gondii* Surface Antigens Recognized by the Bradyzoite-Specific P36 Monoclonal Antibody. **Intl. J. Parasitol.** 37:877-885.
- Saeij, J.P., Arrizabalaga, G. and Boothroyd, J.C. 2008. A cluster of four surface antigen genes specifically expressed in bradyzoites, SAG2CDXY, plays an important role in *Toxoplasma gondii* persistence. **Infection and Immunity** 76: 2402-2410.
- Boyle, J.P., Saeij, J.P.J., Harada, S.Y. and Boothroyd, J.C. 2008. Expression QTL mapping of *Toxoplasma* genes reveals multiple mechanisms for strain-specific differences in gene expression. **Eukaryotic Cell** 7: 1403-1414.

RESEARCH PROJECTS ONGOING OR COMPLETED DURING THE LAST THREE YEARS:

Completed:

RO1 AI45057 (P.I. John C. Boothroyd) 3/1/99-2/28/06

NIH/NIAID

“Genetics of Invasion and Egress in *Toxoplasma*.”

The major goals of this work are to study invasion and egress using mutants and complementation to identify the genes involved. It also includes studies of the role of calcium and micronemal proteins (e.g., AMA1) in these processes.

Ellison Medical Foundation (P.I. John C. Boothroyd) 11/1/02-10/31/06

Senior Scholar Award in Global Infectious Disease

“Evolution of Virulence in Parasitic Protozoa.”

The major goals of this work are to examine genetic crosses of parasites to map and identify genes involved in virulence. This grant ended 10/31/06 and was non-renewable.

Ongoing:

RO1 AI41014 (P.I. John C. Boothroyd) 12/1/06-11/30/11

NIH/NIAID

“Developmental Biology of *Toxoplasma*”

The major goals of this project are to identify key genes involved in the differentiation of *Toxoplasma gondii* tachyzoites to bradyzoites. This is the grant currently being considered.

R01 AI21423 (P.I. John C. Boothroyd) 5/1/04 - 4/30/09

NIH/NIAID

“Host-Pathogen Interaction in *Toxoplasma*.”

The major goals of this project are to identify the role of *Toxoplasma* proteins that facilitate invasion into the host cell, especially surface antigens and rhoptry neck proteins, and to determine how these influence the host response to infection.

RO1 AI-73756 (P.I. John C. Boothroyd) 07/01/07 – 06/30/12

NIH/NIAID

“Strain-specific Host-Pathogen Interactions in Toxoplasmosis.”

This grant uses genetics and microarrays to map and identify genes that are crucial in *Toxoplasma* virulence and co-opting of host transcription.