

**BIOGRAPHICAL SKETCH**

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NAME: John Charles Boothroyd

eRA COMMONS USER NAME (credential, e.g., agency login): Boothroyd.John,

POSITION TITLE: Professor of Microbiology and Immunology

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
McGill University	B.Sc.(Hons)	1975	Cell/Mol/Dev Biology
Edinburgh University	Ph.D.	1979	Molecular Biology

**A. Personal Statement**

I believe my group has a track record of sustained accomplishment in research on parasites using whatever technology is needed to answer important questions. We have often done this through strategic collaborations with others. We studied the cell and molecular biology of *Trypanosoma brucei* from 1982-1999 and, since 1983, the cell biology and pathogenesis of the Apicomplexan parasite, *Toxoplasma gondii*. The group typically consists of ~8-10 investigators (typically 3-4 post-docs, 4-5 graduate students and a technician) and I would like to believe we have provided key contributions to the following discoveries:

- RNA is transcribed polycistronically and trans-spliced in trypanosomes (Campbell et al., Nature, 1984; Sutton and Boothroyd, Cell, 1986; Muhich et al., Mol. Cell. Biol. 1988; Bangs et al., 1992)
- *Toxoplasma* population structure is largely clonal (Sibley and Boothroyd, Nature, 1992) and dramatic virulence changes result from recombination (Grigg et al., Science, 2001; Boyle et al., PNAS, 2006)
- *Toxoplasma* injects polymorphic kinases and pseudokinases into the host cell that modulate the host-parasite interaction in a strain-specific manner (Saeij et al., Science, 2006; Saeij et al., Nature, 2007; Ong et al., J. Biol. Chem., 2010; Reese et al., PNAS, 2011; Fleckenstein et al., PLoS Biology, 2012; Pernas et al., PLoS Biology, 2014)
- the moving junction of invading Apicomplexan parasites is a stage-specific collaboration of several proteins from different secretory organelles (Alexander et al., PLoS Pathogens, 2005; Alexander et al., Eukaryotic Cell, 2006; Tyler and Boothroyd, PLoS Pathogens, 2010; Srinivasan et al., PNAS, 2011; Poukchanski et al., 2013)
- co-opting of the host cell is a complex process involving highly specific machinery and effectors, including ones mediating host mitochondrial association (Pernas et al., PLoS Biology, 2014; Kelly et al., mSphere, 2017) and ones reaching the host nucleus via an unusual translocation machinery dubbed the MYR complex (Franco et al., mBio, 2016, Marino et al., PLoS Pathogens, 2018).

I am most proud, however, of the fact that the >65 students and post-doctoral fellows who made these findings have gone on to establish their own successful careers in government, industry, non-profit and academia, including many who have become independent investigators who have added substantially to our understanding of *Toxoplasma* and other parasites.

**B. Positions and Honors****B.1. Employment Positions**

- 1979-1982      Scientist, Immunochemistry/Molecular Biology Department, Wellcome Research Laboratories, Beckenham, Kent, U.K.
- 1982-1988      Assistant Professor, Department of Microbiology and Immunology (formerly Medical Microbiology), Stanford University School of Medicine, Stanford, California.

1988-1994	Associate Professor, Dept. of Microbiology and Immunology, Stanford School of Medicine.
1994-2015	Professor, Dept. of Microbiology and Immunology, Stanford School of Medicine.
2015-date	Burt and Marion Avery Professor, Dept. of Microbiol. and Immunol., Stanford Medicine.
1994-1999	Co-Chair, Department of Microbiology and Immunology, Stanford School of Medicine.
1999-2002	Chair, Department of Microbiology and Immunology, Stanford School of Medicine.
2002-2003	Senior Associate Dean for Research, Stanford School of Medicine.
2003-2005	Senior Associate Dean for Research and Training, Stanford School of Medicine.
2008-2018	Associate Vice Provost for Graduate Education, Stanford University.
2018-date	Associate Vice Provost for Graduate Education and Postdoctoral Affairs, Stanford University.

## **B.2. Other Professional Positions and Service**

1987-date	Member, Editorial Board, <i>Exptl. Parasitol.</i> (1987-1994), <i>Mol. Biochem. Parasitol.</i> (1987-date), <i>J. Euk. Microbiol.</i> (1988-1995), <i>Ann. Rev. of Microbiol.</i> (1993-1997; 2006), <i>Trends in Parasitology</i> (2001-2006), <i>mBio</i> (2010-date)
1991-1993	Director, MBL Summer Course on "Biology of Parasitism", Woods Hole
1992-1998	Editor, <i>Microbiological Reviews</i> (American Society of Microbiology)
1995-2001	Member (1995-1998) and Chair (1999-2001), Molecular Parasitology Advisory Committee, Burroughs Wellcome Fund
1997-2017	NIH Study Section Member, Eukaryotic Pathogens (PTHE: 10/93; 6/94; 6/97; 10/99; 2/02; 2/05; 10/10; 6/12; 7/14-6/17); and AIDS Opportunistic Infections and Cancer (AOIC: 7/06, 7/07, 8/08 (special emphasis))
1999	Chair, Gordon Conference on Parasitism
2005-2009	Associate Editor (2005-2006) and Section Editor (2006-2009), <i>PLOS Pathogens</i> .
2010	Member, NIH "Distinguished Editorial Panel"; RC4 Review in <i>Infect. Dis. and Microbiol.</i>
2012-2016	Member (2012-2013) and Chair (2013-2016), Pathogenesis of Infectious Diseases Advisory Panel, Burroughs Wellcome Fund
2016-2018	Member, Committee on Next Generation Researchers Initiative, U.S. National Academies of Sciences, Engineering and Medicine
2018-2019	Member, Committee on Increasing Representation of Women in STEM, U.S. National Academies of Sciences, Engineering and Medicine
2019-2022	Member, Academic Council, Schmidt Science Fellows, in partnership with the Rhodes Trust

## **B.3. 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.
2005	Meyer Lecturer, Univ. California San Francisco
2007	Fellow, American Academy of Microbiology
2008	Leuckart Medal, German Society of Parasitology
2010	Noble Memorial Lecturer, University of Oklahoma
2010	Marian Koshland Lecturer, University of California, Berkeley
2012	Member, Inventor Hall of Fame, Stanford University
2012	Rose Lecturer, Columbia University, New York
2013	Willison Lecturer, University of Michigan, Ann Arbor, MI
2014	Ricketts Symposium Lecturer, University of Chicago
2014	Stanford Biosciences Excellence in Mentoring Award
2015	Burt and Marion Avery Professor of Immunology, Stanford University
2015	Larsen Distinguished Lecturer, College of Veterinary Medicine, Washington State Univ.
2015	Centenary Speaker, Walter and Eliza Hall Institute, Melbourne, Australia
2016	Member, National Academy of Sciences, USA
2016	Outstanding Ally Award, Stanford University Postdoctoral Association

## **C. Selected Key Publications (223 total):**

- Boothroyd, J.C., Cross, G.A.M., Hoeijmakers, J.H.J. and Borst, P. 1980. A variant surface glycoprotein of *Trypanosoma brucei* synthesized with a C-terminal hydrophobic "tail" absent from purified glycoprotein. **Nature** 288:624-626.
- Boothroyd, J.C., Highfield, P.E., Cross, G.A.M., Rowlands, D.J., Lowe, P.A., Brown, F. and Harris, T.J.R. 1981. Molecular cloning of the Foot and Mouth Disease Virus genome and nucleotide sequence of the structural protein genes. **Nature** 290:800-802.
- Campbell, D.A., Thornton, D.A. and Boothroyd, J.C. 1984. Apparent discontinuous transcription of *Trypanosoma brucei* variant surface antigen genes. **Nature** 311:350-355.
- Sutton, R.E. and Boothroyd, J.C. 1986. Evidence for trans-splicing in trypanosomes. **Cell** 47:527-535.
- Bangs, J.D., Crain P.F., Hashizume, T., McCloskey J.A. and Boothroyd, J.C. 1992. Mass Spectrometry of mRNA Cap 4 from trypanosomatids reveals two novel nucleosides. **J. Biol. Chem.** 267: 9805-9815.
- Sibley, L.D. and Boothroyd, J.C. 1992. Virulent strains of *Toxoplasma gondii* are clonal. **Nature** 359:82-85.
- 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.
- 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.
- 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.
- 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. PMC118016
- Alexander, D.L., Mital, J., Ward, G.E., Bradley, P.J. and Boothroyd, J.C. 2005. Identification of the moving junction complex of an Apicomlexan parasite, *Toxoplasma gondii*: collaboration between two distinct secretory organelles. **PLOS Pathogens** 1:137-149.
- 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.
- 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].
- 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].
- Ong, Y.-C., Reese, M.L. and Boothroyd, J.C. 2010. *Toxoplasma* ROP16 subverts host function by direct phosphorylation of STAT6. **J. Biol. Chem.** 285:28731-28740. PMC2937901
- Tyler, J.S. and Boothroyd, J.C. 2011. The C-terminus of *Toxoplasma* RON2 provides the crucial link between AMA1 and the host-associated invasion complex. **PLoS Pathogens** 7(2):e1001282. PMC3037364
- Reese, M.L., Zeiner, G., Saeij, G., Boothroyd, J.C. and Boyle, J.P. 2011. A polymorphic family of injected pseudokinases is paramount in *Toxoplasma* virulence. **Proc. Natl. Acad. Sci. USA** 108:9625-9630. PMC3111280.
- Treeck, M., Sanders, J., Elias, J.E. and Boothroyd, J.C. 2011. The phosphoproteomes of *Plasmodium falciparum* and *Toxoplasma gondii* reveal unusual adaptations within and beyond the parasites' boundaries. **Cell Host and Microbe** 10:410-419. PMC3254672.
- Fritz, H.M., Buchholz, K.R., Chen, X., Durbin-Johnson, B., Rocke, D.M., Conrad, P. and Boothroyd, J.C. 2012. Transcriptomic analysis of *Toxoplasma* development reveals many novel functions and structures specific to oocysts. **PLoS ONE** 7(2): e29998. PMC3278417
- Fleckenstein\*, M.A., Reese\*, M.L., Konen-Waisman, S., Boothroyd, J.C., Howard, J.C and Steinfeldt, T. 2012. A *Toxoplasma gondii* pseudokinase inhibits host IRG resistance GTPases. **PLoS Biology** 10(7): e1001358 [\* equal contributors]. PMC3393671
- Koshy, A., Dietrich, H. Melehani, J.H., Shastri, A.J. and Boothroyd, J.C. 2012. *Toxoplasma* co-opts host cells it does not invade. **PLoS Pathogens** 8(7): e1002825. PMC3406079.
- Ewald, S.E., Chavarria-Smith, J. and Boothroyd, J.C. 2014. NLRP1 is an inflammasome sensor for *Toxoplasma gondii*. **Infection and Immunity** 82:460-468. PMC3911858.

- Pernas, L., Adomako-Ankomah, Y., Shastri, A., Ewald, S., Treeck, M., Boyle, J.P. and Boothroyd, J.C. 2014. *Toxoplasma* effector MAF1 mediates recruitment of host mitochondria and impacts the host response. **PLoS Biology** 12(4): e1001845. PMC4004538.
- Treeck, M., Sanders, J.L., Arrizabalaga, G., Elias, J.E., and Boothroyd, J.C. 2014. Phosphoproteomic analysis of *Toxoplasma gondii* mutants reveals a pleiotropic role for calcium-dependent protein kinase 3. **PLOS Pathogens** 10(6):e1004197. PMC 4063958
- Reese, M.L., Shah, N. and Boothroyd, J.C. 2014. The *Toxoplasma* pseudokinase ROP5 is an allosteric inhibitor of the immunity-related GTPases. **J. Biol. Chem.** 289(40):27849-58. PMC 4183189
- Franco\*, M., Panas\*, M.W., Marino\*, N.D., Lee, W.M.-C., Buchholz, K.R., Kelly, F.D., Bednarski, J.J., Sleckman, B.P., Pourmand, N., and Boothroyd, J.C. 2016. A novel secreted protein, MYR1, is central to *Toxoplasma*'s manipulation of host cells. **mBio** 7:e02231-15 [\* equal contributors]. PMC4742717
- Guiton, P.S., Sagawa, J., Fritz, H.M. and Boothroyd, J.C. 2017. An *in vitro* model of intestinal infection reveals a developmentally regulated transcriptome of *Toxoplasma* sporozoites and a NF- $\kappa$ B-like signature in infected host cells. **PLoS ONE** 12(3): e173018 PMC5376300
- Kelly, F., Wei, B., Cygan, A.M., Tonkin, M., Boulanger, M., and Boothroyd, J.C. 2017. *Toxoplasma gondii* MAF1b binds the host cell MIB complex to mediate mitochondrial association. 2017. **mSphere** 2(3) e000183-17. PMC 5444011
- Nakamoto, M.A., Lovejoy, A.F., Cygan, A.M. and Boothroyd, J.C. 2017. mRNA pseudouridylation affects RNA metabolism in the parasite *Toxoplasma gondii*. **RNA** 062794.117. PMC 5689004
- Marino, N.D., Panas, M.W., Franco, M., Theisen, T.C., Naor, A., Rastogi, S., Buchholz, K.R., Lorenzi, H.A. and Boothroyd, J.C. 2018. Identification of a novel protein complex essential for effector translocation across the parasitophorous vacuole membrane of *Toxoplasma gondii*. **PLoS Pathogens** 14(1): e1006828. PMC 5794187.
- Pernas, L., Boothroyd, J.C. and Scorrano, L. 2018. Mitochondria limit *Toxoplasma* growth by competing for fatty acids. **Cell Metabolism** 27:886-897. PMID 29617646 (PMC in process)

**A complete list of my publications is available at:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/john.boothroyd.1/bibliography/41907506/public/?sort=date&direction=ascending>

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**D. Research Support**

**Current:**

RO1 AI021423 (P.I. John C. Boothroyd) 07/1/14 - 06/30/20

NIH/NIAID

“*Toxoplasma* Rhoptry Function.”

This is a competing renewal for the above-mentioned grant concerning how rhoptry proteins are introduced into the host cell during invasion and what changes those injected proteins cause within an infected host cell *in vivo*.

RO1 AI129529-01 (P.I.: John C. Boothroyd) 08/09/18-07/31/22

NIH/NIAID

“Identifying the machinery that translocates *Toxoplasma* effectors into the host cell.”

The major goals of this project are to identify the machinery used to translocate dense granule effectors across the parasitophorous vacuole membrane into the host cell.

Intercampus Initiative (P.I. Wah Chiu) 10/15/18-10/14/21

Chan-Zuckerberg Biohub

Project Leader: John C. Boothroyd

“Integrated Imaging to Understand Complex Biological Machines in Context”

This is a collaborative effort between Stanford, UCSF and UC Berkeley to use cryo-electron tomography to image the invasion machinery used by *Toxoplasma* when entering a cell.