BIOGRAPHICAL SKETCH

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NAME: John Charles Boothroyd

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POSITION TITLE: Professor (Emeritus-Active) of Microbiology and Immunology, Stanford School of Medicine

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, Montreal, Canada	B.Sc. (Hons)	06/1975	Cell/Mol/Dev Biology
Edinburgh University, Edinburgh, Scotland	Ph.D.	06/1979	Molecular Biology

A. Personal Statement

I have led a research group at Stanford since 1982 and during that time ~75 predoc or postdoc trainees have completed their training with me. Outside my own group, I have served as Senior Associate Dean for Research and Training in Stanford's School of Medicine which included oversight of the Office of Graduate Education and the Office of Postdoctoral Affairs. As Stanford's Associate Vice Provost for Graduate Education and Postdoctoral Affairs, I have helped create additional programs to help predocs and postdocs with their professional development, including development of a 10-week course entitled, "Preparing for Faculty Careers" that I have taught personally 9 of the past 10 years. I also work with faculty, especially more junior faculty, providing intensive workshops each year on mentoring. I put an emphasis on culturally aware mentoring and have collaborated with others on campus to create bespoke training in the biosciences on this topic.

I am personally committed to diversifying the scientific workforce because it is both the right thing to do and because it is necessary: diverse communities produce better science. I have worked toward that end as an individual PI, as an administrator at Stanford, and as a member of the National Academy of Sciences. I have helped launch and steer the Propel and PRISM diversity-oriented postdoctoral programs at Stanford and served as a mentor and instructor for Stanford's DARE program ("Diversifying Academia, Recruiting Excellence") which aims to diversify the academy through enabling outstanding PhD students from diverse backgrounds who aspire to faculty roles to acquire all they need to obtain and thrive in such a position. I have co-authored two NAS reports focused on training, one entitled, "The Next Generation of Biomedical Researchers: Breaking Through," and the other entitled, "Promising Practices for Addressing the Underrepresentation of Women in Science, Engineering and Medicine: Opening Doors."

In the realm of research, 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; Srinavasan 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 75 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 34 who have become independent investigators and added substantially to our understanding of *Toxoplasma, Trypanosoma* and other parasites.

B. Positions and Honors

B.1. Employment Positions

2018-date	Associate Vice-Provost for Graduate Education and Postdoctoral Affairs, Stanford University.
2015-date	Burt and Marion Avery Professor (Emeritus-Active since 2022), Dept. of Microbiology and Immunology, Stanford School of Medicine
2008-2018	Associate Vice-Provost for Graduate Education, Stanford University
2003-2005	Senior Associate Dean for Research and Training, Stanford University School of Medicine
2002-2003	Senior Associate Dean for Research, Stanford University School of Medicine
1999-2002	Chair, Department of Microbiology and Immunology, Stanford School of Medicine
1994-date	Professor, Dept. of Microbiology and Immunology, Stanford School of Medicine.
1988-1994	Associate Professor, Dept. of Microbiology and Immunology, Stanford School of Medicine
1982-1988	Assistant Professor, Department of Microbiology and Immunology (formerly Medical Microbiology), Stanford School of Medicine, Stanford, California
1979-1982	Scientist, Immunochemistry/Molecular Biology Department, Wellcome Research Laboratories, Beckenham, Kent, U.K.

B.2. Other Professional Positions and Service

2023-date	Chair, Academic Council, Schmidt Science Fellows
2021-2024	Member, Governing Council, National Academy of Sciences, USA
2020-2024	Member, Board of Directors, San José State University Research Foundation
2019-2023	Member, Academic Council, Schmidt Science Fellows
2018-2019	Member, Committee on Addressing the Underrepresentation of Women in Science, Engineering and Medicine, National Academies of Sciences, Engineering and Medicine
2016-2018	Member, Committee on Next Generation Researchers Initiative, National Academies of Sciences, Engineering and Medicine
2015-2019	Director, Stanford-San José State University IRACDA Program
2012-2016	Member (2012-2013) and Chair (2013-2016), Pathogenesis of Infectious Diseases Advisory Committee, Burroughs Wellcome Fund
2005-2009	Associate Editor (2005-2006) and Section Editor (2006-2009), PLOS Pathogens.
1999	Chair, Gordon Conference on Parasitism
1997-date	NIH Study Section Member, Eukaryotic Pathogens (PTHE: 10/93; 6/94; 6/97; 10/99; 2/02; 2/05; 10/10; 6/12; 7/14-6/20); and AIDS Opportunistic Infections and Cancer (AOIC: 7/06, 7/07, 8/08 (special emphasis))
1995-2001	Member (1995-1998) and Chair (1999-2001), Molecular Parasitology Advisory Committee, Burroughs Wellcome Fund
1992-1998	Editor, Microbiological Reviews (American Society of Microbiology
1991-1993	Director, MBL Summer Course in "Biology of Parasitism", Woods Hole
1987-date	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), mBio (2010-date)

B.3. Honors and Awards

2021	C.C. and Alice Wang Award in Molecular Parasitology, American Society of Biochemistry and Molecular Biology

2020 Bassford Lecturer, University of North Carolina
2016 Member, National Academy of Sciences, USA
2016 Outstanding Ally Award, Stanford University Postdoctoral Association
2015 Burt and Marion Avery Endowed Professor of Immunology, Stanford University
2015 Larsen Distinguished Lecturer, College of Veterinary Medicine, Washington State Univ.
2014 Ricketts Symposium Lecturer, University of Chicago
2013 Willison Lecturer, University of Michigan, Ann Arbor, MI
2013 Officers' Choice Recognition Award, Stanford University Postdoctoral Association
2012 Rose Lecturer, Columbia University, New York
2010 Noble Memorial Lecturer, University of Oklahoma
2010 Marian Koshland Lecturer, University of California, Berkeley
2008 Leuckart Medal, German Society of Parasitology
2007 Fellow, American Academy of Microbiology
2005 Meyer Lecturer, Univ. California San Francisco
2002 Ellison Medical Foundation Senior Scholar Award in Global Infectious Diseases.
1994 MERIT Award, NIH/NIAID
1994 Scaife Lecturer, University of Edinburgh
1986 Molecular Parasitology Award, Burroughs Wellcome Fund
1976 Overseas Research Scholarship, Royal Commission for the Exhibition of 1851

C. Other Contributions to Science (with 4 key publications each)

1. Molecular Biology of African Trypanosomes. Sleeping sickness is caused by the protozoan, *Trypanosoma brucei*. Trypanosome antigenic variation has been known to exist for over 100 years. I led a research group that played a key role in deducing the molecular basis underlying this phenomenon and in the process we co-discovered mRNA trans-splicing and polycistronic transcription, the first reports of such in eukaryotes. These findings presented a new paradigm for pathogenesis of an infectious disease and altered how people think of transcription and mRNA processing in eukaryotes.

a. 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.
b. Sutton, R.E. and Boothroyd, J.C. 1986. Evidence for Trans-splicing in Trypanosomes. **Cell** 47:527-535.
c. Muhich, M. and Boothroyd, J.C. 1988. Polycistronic Transcripts in Trypanosomes and their Accumulation during Heat Shock: Evidence for a Precursor Role in mRNA Synthesis. **Mol. Cell. Biol.** 8:3837-3846.
d. 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.

2. Diagnosis, Population Biology and Virulence of Toxoplasma gondii. *Toxoplasma* is an important human and animal parasite and it has long been known that infections vary in their intensity from mild to highly virulent. My group tested the hypothesis that this was due to strain-specific differences in virulence and discovered that, despite *Toxoplasma's* presumed reliance on sexual reproduction, its population structure is largely clonal and that just one mating event in the lab or nature could increase virulence of the parasites by several logs. We went on to provide evidence that these different strains have different impacts when infecting otherwise healthy humans. This led to rethinking what factors might predict the severity and outcome of an infection. We also developed the first PCR-based test for diagnosing human infection with this parasite.

a. 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.
b. Sibley, L.D. and Boothroyd, J.C. 1992. Virulent strains of *Toxoplasma gondii* are clonal. **Nature** 359:82-85.
c. 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.
d. 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.

3. Molecular Methods and Resources for Study of Toxoplasma. *Toxoplasma* is an obligate intracellular parasite making its genetic manipulation challenging. We have dedicated considerable effort to the development of many key resources for *Toxoplasma* research including transformation methods, genetic maps, bioluminescence imaging, engineering of parasites that inject Cre-recombinase and proteomic/transcriptomic analyses of the parasite and the infected host cell.

a. 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.
b. 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.
c. 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. PMC547072
d. Koshy, A.A., Fouts, A.E., Lodoen, M.B., Alkan, O., Blau, H.M. and Boothroyd J.C. 2010. *Toxoplasma gondii* secreting Cre recombinase: a new tool to study host-parasite interactions. **Nature Methods** 7:307-309. PMC2850821

4. Dissecting the Invasion Machinery of Apicomplexan Parasites. *Toxoplasma* and the related genus *Plasmodium* (the causative agents of malaria) invade by similar mechanisms that include formation of a "moving junction" at the ring of contact between the invading parasite and the host cell. We identified the components of the complex and showed that it involves linkage between a micronemal protein on the parasite surface, AMA1, and a set of rhoptry neck (RON) proteins that are injected into the host cell. We also showed that an orthologous complex exists in the malaria parasite, *Plasmodium falciparum*.

a. 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. PMC1262624
b. 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. PMC1489286
c. 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:e1001282. PMC3037364
d. Poukchanski, A., Fritz*, H.M., Tonkin*, M.L., Treeck, M., Boulanger, M.J., and Boothroyd, J.C. 2013. *Toxoplasma gondii* sporozoites invade host cells using two novel paralogues of RON2 and AMA1. **PLoS ONE** 8(8): e70637. PMC3734201. [* equal contributors]

5. Understanding the Dialogue with the Infected Host Cell. We extended our analysis of strain-specific virulence in *Toxoplasma* to identify the effectors involved and the mechanisms by which the different forms of these proteins mediate the host-pathogen interaction to produce more or less virulence. We showed that when Toxoplasma parasites infect a human cell, they inject polymorphic protein kinases and pseudokinases from their rhoptries (ROPs); these serve as key virulence factors and differences in their expression and/or sequence are responsible for differences in virulence. For example, the tyrosine kinase ROP16 mimics a key human enzyme (JAK2) in phosphorylating the crucial immune modulators, STATs. We further showed that only some strains of *Toxoplasma* recruit host mitochondria to the vacuole in which they grow inside a human cell, used this fact to identify the key parasite protein involved (MAF1) and showed that recruitment affects how the host responds to the infection. Lastly, we have put a major focus on how effectors are deliverd into the host cell, including discovery of a novel translocation system necessary for host c-Myc regulation ("MYR"). These many findings have transformed how we think about the ways that Toxoplasma interacts with the host cells it infects and provide many opportunities for novel therapeutic interventions.

a. Saeij*, J.P.J., Boyle*, J.P., Coller, 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]. PMC2646183
b. Pernas, L., Adomako-Ankomah, Y., Shastri, A., Ewald, S.E., 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
c. 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

d. Cygan*, A.M., Theisen*, T.C., Mendoza, A., Marino, N.D., Panas, M.W., and Boothroyd, J.C. 2020. Co-immunoprecipitation with MYR1 identifies three additional proteins within the Toxoplasma parasitophorous vacuole required for translocation of dense granule effectors into host cells. **mSphere** 5(1):e00858-19 [*equal contributors] PMC7031616

A complete list of my publications is available at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/john.boothroyd.1/bibliograpahy/41907506/public/?sort=date&direction=ascendi: PA-21-052g