BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
John C. Boothroyd	Professor of Microbiology and Immunology
eRA COMMONS USER NAME Boothroyd.John	

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

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

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 Apixomplexan parasite, *Toxoplasma gondii*. The group typically consists of ~12 investigators (typically 7 post-docs and 5 graduate students) 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)
- 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)

I am most proud, however, of the fact that many of the students and post-doctoral fellows who have helped make these findings have gone on to establish their own groups that have, in turn, added substantially to our understanding of *Toxoplasma* and other eukaryotic parasites.

B. POSITIONS:

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), Chair (1999-2002), Dept. of Microbiology and Immunology, Stanford University
2002-2003: Senior Associate Dean for Research, Stanford University School of Medicine
2003-2005: Senior Associate Dean for Research and Training, Stanford University School of Medicine
2008-date: Associate Vice Provost for Graduate Education, Stanford University

C. 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
2010: Noble Memorial Lecturer, University of Oklahoma
2010: Marian Koshland Lecturer, University of California, Berkeley
2012: Inductee, Inventor Hall of Fame, Stanford University
2012: Rose Lecturer, Columbia University, New York
2012: Keynote Speaker, Molecular Parasitology Meeting, Woods Hole, MA
2013: Willison Lecturer, University of Michigan, Ann Arbor, MI
2013: Outstanding Service to Graduate Students, Stanford School of Medicine

D. 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 (2006-2009), 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), mBio (2010-date)
NIH Study Section Member, Eukaryotic Pathogens (PTHE; 10/93; 6/94; 6/97; 10/99; 2/02; 2/05; 10/08 (special emphasis); 10/10; 6/12); and AIDS Opportunistic Infections and Cancer (AOIC; 7/06, 7/07, 8/08 (special emphasis))
Member (1995-1998) and Chair (1999-2001), Molecular Parasitology Committee, Burroughs Wellcome Fund
Chair, Gordon Conference on Parasitism. Rhode Island (1999).
Member, NIH “Distinguished Editorial Panel”; RC4 Review in Infectious Diseases and Microbiology (6/10)
Member (2012-2013) and Chair (2013-2015), Pathogenesis of Infectious Diseases Advisory Committee, Burroughs Wellcome Fund

E. SELECTED KEY PUBLICATIONS (209 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.

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.

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.

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. [* equal contributors].

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., 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].

Saeij*, J.P.J., Coller*, 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].

Vyas, A., Kim, S.-K., Giacomini, N., Boothroyd, J.C. and Sapolsky, R.M. 2007. Behavioral changes induced by *Toxoplasma* infection of rodents are highly specific to cat odors. **Proc. Natl. Acad. Sci. USA** 104:6442-6447.

Kafsack, B.F.C., Pena, J.D.O., Coppens, I., Ravindran, S., Boothroyd, J.C. and Carruthers, V.B. 2008. Rapid membrane disruption by a perforin-like protein facilitates parasite egress from host cells. **Science** 323:530-533.

Koshy, A.A., Fouts, A.E., Lodoen, M.B., Alkan, O., Blau, H.M. and Boothroyd J.C. 2010. *Toxoplasma* secreting Cre recombinase for analysis of host-parasite interactions. **Nature Methods** 7:307-309. PMC2850821

Zeiner, G.M., Norman, K., Thomson, J.M., Hammond, S.M. and Boothroyd, J.C. 2010. *Toxoplasma* infection specifically increases the levels of key host microRNAs. 2010. **PLoS ONE** 5(1):e8742. PMC2806928

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.

Srinivasan, P., Beatty, W.L., Diouf, A., Herrera, R., Ambroggio, X., Moch, J.K., Tyler, J.S., Narum, D.L., Pierce, S.K., Boothroyd, J.C., Haynes, J.D. and Miller, L.H. 2011. Binding of Plasmodium merozoite surface protein AMA1 to RON2 triggers junction formation and invasion. **Proc. Natl. Acad. Sci. USA** 108:13275-13280. PMC3156155.

Reese, M.L. and Boothroyd, J.C. 2011. A conserved noncanonical motif in the ROP5 pseudoactive site mediates its effect on Toxoplasma virulence. **J. Biol. Chem**. 286:29366-29375. PMC3190742

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.

Garrison*, E., Treeck*, M., Ehret, E., Oswald, B.P., Settles, M., Boothroyd, J.C. and Arrizabalaga, G. 2012. A forward genetic screen reveals calcium-dependent protein kinase 3 regulates egress in Toxoplasma. **PLoS Pathogens** 8(11): e1003049. PMC3510250. [* equal contributors]

Caffaro, C.E., Koshy, A., Liu, L., Zeiner, G., Hirschberg, C.B. and Boothroyd, J.C. 2013. A nucleotide sugar transporter (NST1) involved in glycosylation of the Toxoplasma tissue cyst wall is required for efficient persistence of bradyzoites. **PLoS Pathogens** 9(5): e1003331 PMC3642066

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]

Child, M.A., Hall, C.I., Abrow, V.E., Beck, J.R., Bowyer, P.W., Bradley, P.J., Boothroyd, J.C., Powers, J.C., Weerapana, E., and Bogyo, M. 2013. Small-molecule inhibition of a depalmitoylase enhances Toxoplasma host-cell invasion. **Nature Chemical Biology** 9:651-656. PMC Journal – in process

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. PMC Journal – in process

Franco, M., Shastri, A.S., and Boothroyd, J.C. 2014. Specific induction of host c-Myc by Toxoplasma gondii contributes to the dramatic host transcriptional changes seen upon infection. 2014. **Eukaryotic Cell** (accepted).

Pernas, L., Adomako-Ankomah, Y., Shastri, A., Boyle, J.P. and Boothroyd, J.C. 2014. Toxoplasma effector MAF1 mediates recruitment of host mitochondria and impacts the host response. **PLoS Biology** (accepted).

Pernas, L.F., Ramirez, R., Holmes, T., Montoya, J.G. and Boothroyd, J.C. 2014. Immune-profiling of pregnant Toxoplasma-infected US and Colombia patients reveals surprising impacts of infection on peripheral blood cytokines. **J. Inf. Dis.** (accepted)

D. RESEARCH SUPPORT:

ACTIVE:

R01 AI21423 (P.I. John C. Boothroyd) 7/1/09-6/30/14
NIH/NIAID
"Toxoplasma rhoptry function."
This grant concerns the process by which Toxoplasma rhoptry proteins facilitate the invasion and co-opting of a host cell.

RO1 AI73756 (P.I. John C. Boothroyd) 07/01/12-06/30/17
NIH/NIAID
"Strain-specific Host-Pathogen Interactions in Toxoplasmosis."
This grant uses genetics and microarrays to map and identify genes that are responsible for Toxoplasma strain-specific differences in virulence and co-opting of host transcription.

PENDING:

R01 AI21423-29 (P.I. John C. Boothroyd) 7/1/14-6/30/19
NIH/NIAID
"Toxoplasma rhoptry function."
This is a competing renewal for a grant that concerns the process by which Toxoplasma rhoptry proteins facilitate the invasion and co-opting of a host cell.
(recently reviewed and received a 3.0 percentile score so funding is assured)

R21 AI R21 AI112962-01 (P.I. John C. Boothroyd) 7/1/14-6/30/16
NIH/NIAID
"Role of c-Myc up-regulation in Toxoplasma infection"
This grant is to identify the mechanism by which Toxoplasma infection up-regulates host c-Myc.