BORIS STRIEPEN

CURRENT ADDRESS:

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EDUCATION AND TRAINING:

University of Pennsylvania, Philadelphia, PA. Post-doctoral Fellow, November 1995 - December 1999. Field of research: Cell biology and molecular genetics of *Toxoplasma gondii*.

Philipps-Universität, Marburg, Germany. Dr. *rerum naturum*, October 1995. Field of research: Glycolipid biochemistry.

Philipps-Universität, Marburg, Germany. Diplom (MS) in Biology, July 1991.

Rheinische Friedrich Wilhelms Universität, Bonn, Germany. Vordiplom in Biology, November 1987.

PROFESSIONAL EXPERIENCE:

2005-	Associate Professor with tenure, University of Georgia
2004-	Adjunct Professor, Department of Microbiology, University of Georgia
2000-	Assistant Professor, Center for Tropical and Emerging Global Diseases & Department of Cellular Biology, University of Georgia. Cell and molecular biology of apicomplexan parasites.
1995 - 1999	Postdoctoral Fellow, University of Pennsylvania. Protein targeting in the protozoan parasite *Toxoplasma gondii*, with Dr. David S. Roos.
1991 - 1995	Doctoral student, Philipps-Universität. Worked on the structure and biosynthesis of glycolipid membrane anchors in the laboratory of Dr. Ralph T. Schwarz.
1994	Lecturer in parasitology, Philipps-Universität
1991	Parasitological field work at the *Centre de Recherche sur les Trypanosomoses Animales*, Bobo Dioulasso, Burkina Faso, with Dr. Peter Clausen.
1987 - 1988	Undergraduate research on the histology and ultra-structure of parasitic flat worms, with Dr. Hans Komnick, Universität Bonn.

FELLOWSHIPS, HONORS & SERVICE:

Undergraduate fellow of the Friedrich-Ebert-Foundation, Germany, 1988-90.
Dissertation fellowship, Friedrich-Ebert-Foundation, Germany, 1991-94.
Dissertation *'Summa cum laude'* Phillips-University Marburg
Postdoctoral fellowship, Deutsche Forschungsgemeinschaft (DFG), Germany 1996-98.
University of Georgia Creative Research Medal, 2007

Marine Biological Laboratories summer course Biology of Parasitism, Woods Hole, MA, lecturer (8/01, 8/02, 7/03, 8/04, 8/05), faculty for a 2 week experimental module (7/06, 7/07), reviewer of applicants (2/05, 2/06).
Member NIH study section AOIC, AIDS associated Opportunistic Infections and Cancer (2005-09)
Ad Hoc Member NIH study section AARR4, Opportunistic Infections and Malignancies in AIDS (7/01, 7/02, 11/02, 8/03, 11/03)
Ad Hoc Member NIH study section TMP, Tropical Medicine and Parasitology (2/03).
Reviewer for DOD-EPSCOR (7/04)
Chair Coccidiosis Conference, held in conjunction with the ASP meeting in Mobile, Al, 7/05 (cancelled due to hurricane)
Organizer of the International Congress on Toxoplasmosis, together with Mike White and Silvia Moreno, Chico Hot Springs, MT, 6/07
Member of the Editorial Board of: Molecular Microbiology (2005-), International Journal of Parasitology (2007-).
Reviewed manuscripts for: PLOS Pathogens, Molecular and Biochemical Parasitology, Journal of Cell Biology, Infection and Immunity, Journal of Biological Chemistry, Experimental Parasitology, Journal of Cell Science, Journal of Parasitology, Molecular Microbiology, Nucleic Acid Research, Microbes and Infection, Microscopy and Microanalysis, Cellular Microbiology, Journal of Molecular Evolution, International Journal of Parasitology, Biochimica et Biophysica Acta, Current Drug Targets, Trends in Parasitology, Molecular Biology of the Cell, and Nature.

FUNDING:

Postdoctoral training grant, The molecular biology of protein transport in *Toxolasma gondii*, Deutsche Forschungsgemeinschaft (German Research Council), 1996-98, **PI: Boris Striepen**, $70,000 total direct cost

UGA Research Foundation Junior Faculty Grant, 2000, Isolation of secretory mutants in *Toxoplasma gondii*, $6500 total direct cost, **PI: Boris Striepen**

Merck Research Laboratories, 2000-01, Genetic techniques for apicomplexan parasites, $40,000 total direct cost, **PI: Boris Striepen**

NIH RO1 AI 48475, Protein targeting and secretion in *Toxoplasma*, 2001-05, **PI: Boris Striepen**, $700,000 direct total cost.

NIH RO1 AI 55268, IMPDH as drug target in *Cryptosporidium*, 2003-08, **PI: Boris Striepen**, $1,250,000 direct total cost

NIH RO1 AI 64671, Biology of the Apicomplexan Plastid, 2005-10, **PI: Boris Striepen**, $1,000,000 direct total cost.

NIH T32 Training Grant AI060546-01, Training in Tropical and Emerging Global Diseases, 2004-2009, **PI: Daniel Colley**. $197,000 direct annual cost.

Support for the Coccidiosis Conference, Mobile, Al, 7/2004, **PI: Boris Striepen**, Burroughs Welcome Fund, $5,000, Merck Research Laboratories, $2000.

NIH R13 AI074299, Ninth International Congress on Toxoplasmosis, 2007, **PI: Boris Striepen**, $20,000 total direct cost, **pending**

NIH RO1, Purine and Pyrimidine Salvage Pathways of *Cryptosporidium parvum*, 2007-2012, **PI: Buddy Ullman**, $750,000 total direct cost for the UGA subcontract, **pending**

NIH UO1, Development of IMPDH-Targeted Drugs against *Cryptosporidium parvum*, 2007-2011, **PI: Liz Hedstrom**, $ 700,000 total direct cost for the UGA subcontract, **pending**.

NSF Major Research Instrumentation, A High-throughput imaging facility for the University of Georgia, 2007, **PIs: Jacek Gaertig and Boris Striepen**, $282,000 total direct cost, **pending**

NIH/Fogarty Center, Parasitic Diseases Research at the IIB (collaborative training grant with Argentina), 2007-2012, **PI: Roberto Docampo**, **pending**

TEACHING:

Courses directed:
Tropical Medicine and Parasitology (1994), Philipps-Universität Marburg
Biology of Parasitism CBIO 8500 (2001, 03, 05, 07), UGA
Medical Parasitology CBIO 4500/6500L (2002, 04, 06), UGA
Infection, FRES 1020 (2002, 03), UGA
The Cellular Biology of Infection, CBIO 4990 (2005)
Research Seminar in Cellular Biology, CBIO 8070 (2005) UGA,
(Visit http://webs.cb.uga.edu/~striepen/teaching.html for links to course web sites for further detail)

Organizer of the CTEGD biweekly Journal Club (2000 – to date)

Other teaching at UGA:
Medical Parasitology, CBIO 4500/6500L (2000), 1 lecture
Advanced Techniques in Molecular Parasitology PARA 8080L (2000, 02), 1 lecture, 1 lab day
People, Plagues and Parasites PARA/CBIO 3100 (2001, 02, 03, 04, 05, 06, 07), 2 lectures
Introduction to Research in Cellular Biology, Biology CBIO 6130 (2000, 01, 02, 03, 04, 05, 06), 1 lecture
Research Seminar in Cellular Biology, CBIO 8070 (2001), 2 seminars
Parasitic Protozoa, PARA 8090 (2002), 1 lecture
Principles of Biology, Bio1107H, (2003) 1 lecture
Molecular and Biochemical Parasitology CBIO 8250 (2004, 06) 2 lectures

PUBLICATIONS:

1. **Striepen, B.**, Tomavo, S., Dubremetz, J.F., and Schwarz, R.T. (1992) Identificaiton and characterization of glycosyl-inositolphospholipids in *Toxoplasma gondii*, *Biochem. Soc. Tans.* 20: 296

2, Azzouz, N., **Striepen, B.**, Gerold, P., Capdeville, Y., and Schwarz, R.T. (1995) Glycosyl-inositol-phosphoceramide in the free-living protozoan *Paramecium primaurelia:* Modification of core glycans by mannosyl phosphate. *EMBO J.* 14**:**4422-1433.

3. Gerold, P., **Striepen, B.**, Reitter, B., Geyer, H., Geyer, R., Reinwald, E., Risse, H.J., and Schwarz, R.T. (1996) Glycosyl-phosphatidylinositols of *Trypanosoma congolense*: two common precursors but a new protein-anchor. *J. Molec. Biol.* 261**:**181-94.

4. **Striepen, B.**, Zinecker, C.F., Damm, J.B.L, Melgers, P.A.T., Gerwig, G.J., Koolen, M., Vliegenthart, J.F.G., Dubremetz, J.F., and Schwarz, R.T. (1997) Molecular structure of the "low molecular weight antigen" of *Toxoplasma gondii*: a glucose α1-4 *N*-acetylgalactosamine makes free glycosyl-phosphatidylinositols highly immunogenic. *J. Molec. Biol.* 266**:**797-813.

5. Roos, D.S., Sullivan, W.J., **Striepen, B.**, Bohne, W. and Donald, R.G.K. (1997) Tagging genes and trapping promoters in *Toxoplasma gondii* by insertional mutagenesis. *Methods* 13: 112-122

6. **Striepen, B.**, He, C.Y., Matrajt, M., Soldati, D. and Roos, D.S. (1998) Expression, selection and organellar targeting of the green fluorescent protein in *Toxoplasma gondii*. *Mol. Biochem. Parasitol.* 92:328-338.

7. Waller, R.F., Keeling, P.J., Donald, R.G.K, **Striepen, B.**, Handman, E., Lang-Unasch, N., Cowman, A.F., Besra, G.S., Roos, D.S., McFadden, G.I. (1998) Nuclear-encoded proteins target to the plastid in *Toxoplasma gondii* and *Plasmodium falciparum*. *Proc. Natl. Acad. Sci. USA* 95: 12352-12357

8. Zinecker, C.F., **Striepen, B.**, Tomavo, S., Dubremetz, J.F., and Schwarz, R.T. (1998) The dense granule antigen, GRA2 of *Toxoplasma gondii* is a glycoprotein containing O-linked oligosaccharides. *Mol. Biochem. Parasitol.* 97: 241-246

9. **Striepen, B.**, Dubremetz, J.F., and Schwarz, R.T. (1999) Glucosylation of glycosyl-phosphatidylinositols: Identification of Uridine-Diphosphate-Glucose as the direct donor for side chain modification in *Toxoplasma gondii* using carbohydrate analogs. *Biochemistry* 38:1478-1487

10. Chaturvedi, S., Qi, H., Coleman, D., Rodriguez, A., Hanson, P.S., **Striepen, B.**, Roos, D.S., and Joiner, K.A. (1999) Constitutive calcium independent release of *Toxoplasma gondii* dense granules occurs through the NSF/SNAP/SNARE/Rab machinery. *J. Biol. Chem.* 274: 2424-2431

11. Roos, D., Crawford, M.J., Donald, R.G.K., Kissinger, J.C., Klimczak, L.J., and **Striepen, B.** (1999) Origin, targeting, and function of the apicomplexan plastid. *Curr. Microbiol. Opinion* 2: 426-432

12. Hager, K.M., **Striepen, B**., Tilney, L.G., Roos, D.S. (1999) The nuclear envelope serves as an intermediary between the ER and golgi comples in the intracellular parasite *Toxoplasma gondii*. *J. Cell Sci* 112:2631-2638

13 Roos, D., Crawford, M.J., Donald, R.G.K., Fohl, L.M., Hager, K.M., Kissinger, J.C., Reynolds, M.G., **Striepen, B.**, and Sullivan, W.J. (1999) Transport and trafficking: *Toxoplasma* as a model for *Plasmodium*. *Novartis Fdn. Symp.* 266, 266:176-95

14. **Striepen, B.**, Crawford, M.J. Shaw, M.K., Tilney, L.D., Seeber, F., and Roos, D.S. (2000) The plastid of *Toxoplasma gondii* is divided by association with the centrosomes. *J. Cell Biol*. 151: 1423-1434.

15. He, C.Y, Shaw, M.K., Pletcher, C.H., **Striepen, B**., Tilney, L.G. and Roos, D.S. (2001) A plastid segregation defect in the protozoan parasite *Toxoplasma gondii*. *EMBO J*. 20: 330-339

16. **Striepen, B.**, Soldati, N., Garcia-Reguet, Dubremetz, J.F., and Roos, D.S. (2001) Targeting of soluble proteins to the rhoptries and micronemes in *Toxoplasma gondii*, *Mol. Biochem. Parasitol* 113: 45-53

17. Wille, U., Villegas, E.N., **Striepen, B.**, Roos, D.S., and Hunter, C.A. (2001) IL-10 does not contribute to the pathogenesis of a virulent strain of *Toxoplasma gondii*. (2001), *Parasit. Immunol*. 23: 291-296

18. Radke, J.R., **Striepen, B**., Guerini, M., Jerome, M.E., Roos, D.S., White, M.W. (2001) Defining the cell cycle of the tachyzoite stage of *Toxoplasma gondii*, *Mol. Biochem. Parasitol*. 115: 165-175

19. He, C.Y., **Striepen, B.**, Pletcher, C.H, Murray, J.M., and Roos, D.S. (2001) Targeting and processing of nuclear-encoded apicoplast proteins in plastid segregation mutants of *Toxoplasma gondii*. *J. Biol. Chem*. 276: 28436-28442.

20. Zinecker, C.F., **Striepen, B**., Geyer, H., Geyer, R., Dubremetz, J.F., and Schwarz, R.T. (2001) Two Glycoforms are present in the GPI-Membrane Anchor of the Surface Antigen 1 (P30) of *Toxoplasma gondii*. *Mol. Biochem. Parasitol*.116: 127-134.

21. Roos, D.S., Crawford, M.J., Donald, R.G., Fraunholz, M., Harb, O.S., He, C.Y., Kissinger, J.C., Shaw, M.K., **Striepen, B**. (2002) Mining the *Plasmodium* genome database to define organellar function: what does the apicoplast do? *Philos. Trans. R. Soc. Lond. B. Biol. Sci.* 357: 35-46.

22. Hu, K., Mann, T., **Striepen, B.**, Beckers, C.J.M., Roos, D.S., Murray, J.M. (2002) Daughter cell assembly in the protozoan parasite *Toxoplasma gondii*. *Mol. Biol. Cell*. 13: 593-606

23. **Striepen, B.**, White, M.W., Li, C., Guerrini, M., Malik, S.B., Logsdon, J.M., Liu, C., Abrahamsen, M.S. (2002) Genetic complementation in apicomplexan parasites. *Proc. Natl. Acad. Sci. USA* 99: 6304-6309

24. Neudeck, A., Stachelhaus, S., Nischik, N., **Striepen, B.**, Reichmann, G., and Fischer, H.G. (2002) Expression variance, biochemical and immunological properties of *Toxoplasma gondii* dense granule protein GRA7. *Microb. Infect*. 4: 581-590

25. Drozdowicz Y.M., Shaw M., Nishi M., **Striepen B.**, Liwinski H.A., Roos D.S., Rea P.A. (2002) Isolation and functional characterization of TgVP1, a type I vacuolar H+-translocating pyrophosphatase from *Toxoplasma gondii*: The dynamics of its subcellular localization and the cellular effects of a diphosphonate inhibitor. *J. Biol. Chem*. 278:1075-1085

26. Gubbels, M.J., Li, C., and **Striepen, B.** (2003) High throughput growth assay for *Toxoplasma gondii* using yellow fluorescent protein, *Antimicrob. Agents Chemother*. 47: 309-316

27. Hoane, J.S., Carruthers, V.B., **Striepen, B.**, Morrison, D.P., Entzeroth, R., and Howe, D. (2003) Analysis of the *Sarcocystis neurona* microneme protein SnMIC10: protein characteristics and expression during intracellular development. *Int. J. Parasitol*. 33: 671-679

28. Wojczyk, B.S, Hagen, F.K., **Striepen, B.**, Hang, H.C., Bertozzi, C.R., Roos, D.S. and Spitalnik, S.L. (2003) cDNA Cloning and Expression of UDP-N-acetyl-D-galactosamine:

Polypeptide N-Acetylgalactosaminyltransferase T1 from *Toxoplasma gondii*, *Mol. Biochem. Parasitol.* 131: 93-107

29. Gubbels, M.J., and **Striepen, B.** (2004) Studying the cell biology of apicomplexan parasites using fluorescent proteins. *Microscop. Microanal.* 10: 568-579.

30. Radke, J.R., Gubbels, M.J., Jerome, M.E., Radke, J.B., **Striepen, B.**, and White, M.W. (2004) Identification of a sporozoite-specific member of the Toxoplasma SAG superfamily via genetic complementation. *Mol. Microbiol.* 52: 93-105

31. **Striepen, B**., Pruijssers, J.P., Huang, Li, C., Gubbels, M.J., Umejiego, N.N., Hedstrom, L, and Kissinger, J.C (2004) Genetransfer in the evolution of parasite nucleotide biosynthesis. *Proc. Natl. Acad. Sci. USA.* 101: 3154-3159.

32. **Striepen, B.** and Kissinger, J.C. (2004) Genomics meets trangenics in the search for the elusive *Cryptosporidium* drug target. *Trends Parasitol.* 20:355-358.

33. **Striepen, B.** (2007) Drug resistance and emerging targets in the opportunistic pathogens *Toxoplasma gondii* and *Cryptosporidium parvum,* Mayers, D., Lerner, S., Ouellette, M and Sobel, J. (Eds.) Antimicrobial Drug Resistance: Principles and Practice for the Clinic and Bench. Humana Press. In Press.

34. Gubbels, M.J., Wieffer, M., and **Striepen, B.** (2004) Fluorescent protein tagging in *Toxoplasma gondii*: identification of a novel inner membrane complex component conserved among Apicomplexa. *Mol. Biochem. Parasitol.* 137: 99-110.

35. Rogers, M.B., Achibald, J.M., Field, M., Li, C., **Striepen, B.**, and Keeling, P.J. (2004) Plastid-Targeting Peptides from the Chlorarachniophyte *Bigelowiella natans*. *J. Eukaryot. Microbiol.* 51:529-535

36. Umejiego, N.N., Riera, T., Li, C., Hedstrom, L., and **Striepen, B.** (2004) *Cryptosporidium parvum* IMP dehydrogenase: Identification of functional, structural and dynamic properties that can be exploited for drug design. *J. Biol. Chem.* 279: 40320-40327.

37. Howe, D.K., Gaji, R.Y., Mroz-Barret, M., Gubbels, M.J., **Striepen, B.**, and Stamper, S. (2005) *Sarocystis neurona* merozoites espress a family of immunogenic surface antigens that are orthologs of the SAG/ARS surface antigens in *Toxoplasma gondii*. *Infect. Immun.* 73: 1023-33.

38. Gubbels, M.J., **Striepen, B.**, Shastri, N., Turkoz, M., and Robey, E.A. (2005) Class I MHC presentation of antigens secreted into the parasitophorous vacuole by *Toxoplasma gondii*. *Infect. Immun.* 73: 703-11.

39. White, M.W., Jerome, M. E., Vaishnava, S., Guerini M., Behnke, M. and **Striepen, B.** (2005) Studies of a mitotic mutant yield evidence for cell cycle coordination in *Toxoplasma gondii*. *Mol. Microbiol.* 55: 1060-71.

40. Sullivan, W.J., Dixon, S.E., Li, C., **Striepen, B.,** Queener, S.F. (2005) Cloning and characterization of inosine 5'-monophosphate dehydrogenase from *Toxoplasma gondii* *Antimicrob. Agents Chemother.* 49: 2172-9.

41. Vaishnava, S., Morrison, D., Gaji, R.Y., Entzeroth, R.K., Howe, D.L., and **Striepen, B.** (2005) Plastid segregation and cell division in the apicomplexan parasite *Sarcocystis neurona*. *J. Cell Sci.* 118: 3397-3407.

42. Egan, C.E., Dalton, J.E., Andrew, E. M., Smith, J.E., Gubbels, M.J, **Striepen, B**. and Carding, S.R. (2005) A requirement for the V1 subset of peripheral T cells in the control of the systemic growth of *Toxoplasma gondii* and infection-induced pathology. *J. Immonol.* 175*:* 8191-8199

43. Gubbels, M.J., Vaishnava, S., Boot, N., Dubremetz, J.F. and **Striepen, B.**, (2006) A MORN-repeat protein is a dynamic component of the *Toxoplasma gondii* cell division apparatus. *J. Cell Sci.* 119, 2236-2245.

44. Golanzka, J., **Striepen, B.,** and Ullman, B. (2006) Adenosine kinase from *Cryptosporidium parvum*. *Mol. Biochem. Parasitol.* 149: 223-30.

45. Gubbels, M.J., Mazumdar, J., vanDooren, G., and **Striepen, B.** (2007) Genomic manipulation of *Toxoplasma gondii*. In The biology of *Toxoplasma gondii*. Soldati, D. and Ajioka, J. (Eds.), Human Press. In press.

46. **Striepen, B.** and Soldati, D. (2007) Genetic engineering of *Toxoplasma gondii*. In *Toxoplasma gondii*: The Model Apicomplexan - Perspective and Methods. Weiss, L.D. and Kim, K. (Eds.) Elsevier. In press.

47. Gaji, R.Y., Zhang, D. Breathnach, C.C. Vaishnava, S., **Striepen, B.,** and Howe, D.K. (2006) Molecular genetic transfection of the coccidian parasite *Sarcocystis neurona*. *Mol. Biochem. Parasitol.* 150: 1-10.

48. Andrade, R.M., Wessendarp, M, Gubbels, M.J., **Striepen, B.,** and Subauste, C.S. (2006) CD-40 induces macrophage anti-microbial activity by triggering authophagy-dependent fusion of pathogen-containing vacuoles and lysosomes. *J. Clin. Invest.* 116: 2366-77.

49 Dalton, J.A., S.M. Cruickshank, C.E. Egan, R. Mears, D.J. Newton, E.M. Andrew, B. Lawrence, G. Howell, K.J. Else, M.-J. Gubbels, **B. Striepen**, J. Smith, S.J. White, and S.R. Carding. 2006. Intraepithelial gamma-delta positive lymphocytes maintain the integrity of intestinal epithelial tight junctions in response to infection. Gastroenterology, 131: 818-29

50. Mazumdar, J., Wilson, E., Masek, K., Hunter, C and **Striepen, B** (2006) Apicoplast fatty acid synthesis is essential for organelle biogenesis and survival in *Toxoplasma gondii*. *Proc. Natl. Acad. Sci.* 103: 13192–13197.

51. Vaishnava, S. and **Striepen, B.** (2006) The cell biology of endosymbiosis – How parasites build, divide and segregate the apicoplast. *Mol. Microbiol.* 61: 1380–1387.

52. **Striepen, B.** (2006) Criticism: what to do about science's bad public image? (Correspondence) *Nature* 444: 265

53. **Striepen, B.**, Jordan, C.M., Reiff, S., and van Dooren, G. (2007) Building the perfect parasite: Apicomplexan cell division. *PLOS Pathogens*, submitted.

53. Mazumdar, J. and **Striepen, B.** (2007) Parasite fatty acid and lipid metabolism. *Euk. Cell*, invited review, in preparation

54. Gubbels, M.J., Muthalagi, M., Parrot, B., Brooks, C.F., White, M.W., and **Striepen, B** (2007) Forward genetics in *Toxoplasma gondii*: NimA is essential for parasite cell cycle progression, in preparation

55. van Dooren, G.G., Muthalagi, M., Brooks C.F., Jordan, C.M., and **Striepen, B.** (2007) A high throughput recombineering pipeline for conditional knock outs in parasites, in preparation

56. Hedstrom, L. Umejiego, N., Riera, T., and **Striepen, B.,** (2007) High-throughput screening against a horizontally transferred bacterial IMPDH identifies novel anti-parasitic inhibitors for *Cryptosporidium*, in preparation

57. Nair, S. and **Striepen, B.** (2007) The cell biology and metabolism of the apicomplexan plastid. Exp. Parasitol., invited review, in preparation

PATENTS:

European Patent T/95161 ALG, *Toxoplasma gondii* glycoconjugates (*T. gondii* glycolipid antigens for the diagnosis of toxoplasmosis, in collaboration with Intervet BV, Azko Nobel, Boxtel, The Netherlands).

U.S. Provisional Patent Application No.: 60/810,276. Compounds and Methods for Treating Mammalian Gastrointestinal Parasitic Infections (IMPDH inhibitors for the treatment of Cryptosporidium, in collaboration with Liz Hedstrom, Brandeis University).

INVITED CONFERENCE TALKS & SEMINARS :

1. Laboratory of Parasitic Diseases, NIH, Bethesda, MD, 12/96
2. Molecular Parasitology Meeting VII, Woods Hole, MA 9/96
3. Department of Veterinary Molecular Biology, Montana State University, Bozeman, MT, 7/97
4. Department of Infection and Immunity, Harvard School of Public Health, Boston, MA, 9/98
5. 18th Meeting of the German Society of Parasitology, Dresden, Germany, 3/98
6. Center for Molecular Biology, Heidelberg, Germany, 3/98
7. The Rockefeller University, New York, NY, 9/98
8. IX Molecular Parasitology Meeting IX, Woods Hole, MA 9/98
9. Department of Microbiology, University of Kenntucky, Lexington, KY, 2/99
10. School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, 2/99
11. Department of Biochemistry, Imperial College, London, UK, 3/99
12. London School of Tropical Medicine and Hygiene, London, UK, 3/99
13. Department of Cellular Biology, University of Georgia, Athens, GA, 4/99
14. 5th International Conference on Toxoplasmosis, Marshall, CA, 5/99
15. Center for Infectious Diseases, Universität Würzburg, Würzburg, Germany, 5/99
16. Center for Hygiene and Medical Microbiology, Phillips-Universität, Marburg, Germany 5/99
17. Annual Meeting of the American Society of Parasitology, Monterey, CA, 7/99
18. Molecular Parasitology Meeting X, Woods Hole, MA 9/99
19. Merck Research Laboratories, Rahway, NJ 10/99
20. Department of Medical Microbiology and Parasitology, University of Georgia, Athens, GA 4/00
21. X Parasitology and Vector Biology Symposium, University of Georgia, Athens, GA, 5/00
22. XI Parasitology and Vector Biology Symposium, University of Georgia, Athens, GA, 5/01
23. Center of Marine Biotechnology, University of Maryland, Baltimore, MD 5/01
24. 6th International Congress on Toxoplasmosis, Freising, Germany, 5/01
25. XI International Congress on Protozoology, Salzburg, Austria, 7/01
26. MBL course Biology of Parasitism, Woods Hole, MA, 7/01
27. Molecular Parasitology Meeting XII, Woods Hole, MA 9/01 (cancelled)
28. Department of Biochemistry and Molecular Biology, University of Georgia, Athens, GA, 10/01

29. ASM Regional Meeting, University of Alabama, Birmingham, AL, 11/01
30. British Society of Parasitology Spring Meeting, Salford, UK, 4/02
31. Center for Food Safety, University of Georgia, Griffin, GA, 7/02
32. MBL course Biology of Parasitism, Woods Hole, MA, 8/02
33. XII Parasitology and Vector Biology Symposium, University of Georgia, Athens, GA, 5/03
34. 7th International Conference on Toxoplasmosis, New York, NY, 5/03
35. MBL course Biology of Parasitism, Woods Hole, MA, 8/03
36. School of Biology and Bioengineering, Georgia Institute of Technology, Atlanta, GA, 8/03
37. Department of Cell and Structural Biology, University of Illinois at Urbana-Champaign, IL, 11/03
38. Department of Plant Biology, University of Georgia, Athens, GA, 12/03
39. Zoologisches Institut, Technische Universität Dresden, Dresden, Germany, 12/03
40. Zentrum für Hygiene und Infektionsbiologie, Philipps-Universität Marburg, Germany, 12/03
41. Distinguished Scientists Series, University of South Alabama Medical Center, Mobile, Al, 2/04
42. Department of Biochemistry, Brandeis University, Waltham, MA, 3/04
43. Department of Infection and Immunity, Harvard School of Public Health, Boston, MA, 3/04
44. Department of Microbiology, University of Georgia, Athens, GA, 5/04
45. Gordon Conference on Biology of Host-Parasite Interactions, Newport, RI, 6/04
46. MBL course Biology of Parasitism, Woods Hole, MA, 7/04
47. Department of Cellular Biology, University of Georgia, Athens, GA, 9/04
48. Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, MD 10/04
49. Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, 11/04
50. Department of Genetics, University of Munich, Munich, Germany, 11/04
51. Department of Tropical Medicine, University of Heidelberg, Heidelberg, Germany, 11/04
52. Department of Genetics, University of Georgia, Athens, GA, 12/04
53. Department of Mol. Microbiol. & Immunology, Johns Hopkins University, Baltimore, MD, 1/05
54. Department of Parasitology, NYU Medical School, New York, NY, 2/05
55. Department of Molecular Microbiology, Washington University, St. Louis, MO, 3/05
56. Department of Pathobiology, University of Pennsylvania, Philadelphia, PA, 4/05
57. Department of Pharmacology &Toxicology, Indiana University, Indianapolis, IN, 5/05
58. Department of Microbiology & Molecular Genetics, Unviersity of Vermont, Burlington, VT 5/05
59. 8th International Conference on Toxoplasmosis, Ajaccio, France, 6/05
60. MBL course Biology of Parasitism, Woods Hole, MA, 7/05
61. Coccidosis Conference held concurrent with the 80th annual ASP meeting, Mobile, AL, 7/05
62. Athens Regional Hospital, Athens, GA, 8/05
63. 9th Internatioanl Coccidosis Conference, Iguassu Falls, Brazil, 9/05
64. Department of Biology, Georgetown University, Washington, DC, 11/05
65. Department of Molecular Biology and Biochemistry, University of California, Irvine, CA, 11/05
66. Center for Drug Design, University of Minnesota, Minneapolis, MN, 03/06

67. Seattle Biomedical Research Institute, Seattle, WA, 04/06
68. NIH-NIAID Rocky Mountains Laboratories, Hamilton, MT, 04/06
69. COST 857, Apicomplexan Biology in the Post-Genomic Era, Dresden, Germany, 5/06
70. MBL course Biology of Parasitism, Woods Hole, MA, 6/06
71. Gordon Conference on Biology of Host-Parasite Interactions, Newport, RI, 6/06
72. Department of Microbiology, Cornell University, Ithaca, NY, 9/06
73. Meeting of the American Society of Tropical Medicine and Hygiene, Atlanta, GA, 11/06
74. Department of Biology, Haverford College, Haverford, PA, 2/07
75. Department of Pathobiological Sciences, Louisiana State University, Baton Rouge, LA, 4/07

TRAINEES:

Postdoctoral Fellows:
Dr. Marc-Jan Gubbels, 01- 05, now Assistant Professor, Department of Biology, Boston College, Boston, MA
Dr. Lisa Sharling, 04- to date
Dr. Giel van Dooren, 04- to date

Laboratory Technicians:
Catherine Li, Research Technician, 00-04, now lab coordinator in Department of Molecular Biology, UC Irvine,
Mani Muthalagi, Research Technician, 04-06
Nwakaso Umejiego, Research Technician, 04, now medical student Harvard Medical School, Boston, MA
Carrie Brooks, Lab Coordinator, 06-date

Graduate Students:
Shipra Vaishnava, PhD student, 01- 06, post doc with Dr. Laura Hooper, UT Southwestern Medical School, Dallas, TX
Jolly Mazumdar, PhD student, 01- 06, HHMI postdoctoral fellow with Dr. Celeste Simon, HHMI & University of Pennsylvania, Philadelphia, PA
Chitra Thadhani, MS student, 01- 05, now lab coordinator, University of Pennsylvania Medical School
David Morrison, MS student, 02-06, now Peace Corps, AIDS prevention in Jamaica
Marnix Wieffer, 01-02, spent 9 month in the lab in partial fulfillment of his MS from University of Nijmejen, now PhD student with Dr. Peter van der Sluijs, Univ. Utrecht, The Netherlands
Nico Boot, 03, visiting grad student from Free University, Amsterdam, The Netherlands, spend 8 month in partial fulfillment of his MS thesis, now PhD student at the Fungal Disease Laboratory, Free University of Amsterdam
Andrea Pruijssers, 03, visiting grad student from Wageningen University, Wageningen, The Netherlands, spend 9 month in partial fulfillment of her MS thesis now PhD student with Dr. Mike Strand, Department of Entomology, University of Georgia
Sethu Nair, PhD student, 06- to date
Carlie Jordan, PhD student, 06- to date
Sarah Reiff, PhD student, 07- to date
Swati Agrawal, PhD student, 07- to date

Rotation Students:
Quighao Xu (00), Cristine Scheel (00), Frank Hardin, (00), Jolly Mazumdar (01), Shipra Vaishnava, (01), Chitra Thadhani (01), David Morrison (02), Shining Wang (02), Josh Kotner (03), Noreen Lyell (05), Swapna Bhat (05), Sethu Nair (05), Carlie Jordan (05), Ben Parrot (06), Sarah Reiff (06), Swati Agrawal (07)

Undergraduate Researchers:
Nwakaso Umejiego, now medical student Harvard Medical School, Boston, MA
Nkomo Butts
Adam Huntley
Brad Lindell
Sebastian Romano
Manise Pierre

Sabbatical Visitors:
Dr. Michael White, 01, Professor, Department of Veterinary Molecular Biology, Montana State University, Bozeman, MT
Dr. Rudolf Entzeroth, Professor, Department of Biology, Technische Universität Dresden, Dresden, Germany
Dr. Martin Gastens, 02, PhD student with Dr. H.G. Fischer, Heinrich Heine Universität, Düsseldorf, Germany.

AWARDS & FUNDING TO TRAINEES RELATED TO RESEARCH IN PI'S LAB:

Dr. Marc-Jan Gubbels:
2 year postdoctoral fellowship from the American Heart Association, 02-04
1 year competitive renewal from the American Heart Association, 04-05
Speaker Award, Molecular Parasitology Meeting XIII, Woods Hole, MA, 2003
Speaker Award, Molecular Parasitology Meeting XV, Woods Hole, MA, 2005

Dr. Giel VanDooren:
CJ Martin Overseas Biomedical Fellowship from the Australian National Health and Medical Research Council. 2 years of funding for work in the PI's lab in the CTEGD and 2 years of additional funding for work with Dr. Malcom McConville at the University of Melbourne. 2005

Shipra Vaishnava:
Support to present at the 2002 Molecular Evolution Meeting, Vancouver, Canada, from Burroughs Welcome Fund & Graduate School UGA
Support to attend the Marine Biological Laboratories Advanced Microscopy course, Woods Hole, MA, Graduate School UGA
Speaker Award, Molecular Parasitology Meeting XIV, Woods Hole, MA, award included invitation to present at a special session for molecular parasitology at the Annual Meeting of the American Society of Tropical Medicine and Hygiene in Miami 2004

Jolly Mazumdar:
First Price for Poster, BHSI annual meeting, 2004

Poster Award, Molecular Parasitology Meeting XV, Woods Hole, MA, 2005
Robert C. Anderson Memorial Award, 2007. The highest honor for graduate students at the University of Georgia, This outstanding thesis award is given to only two students each year, usually one from the humanities and one from the sciences.

Nwakaso Umejiego:
UGA CURO Biomedical Research Summer Fellowship 2002
Support to present work at Molecular Parasitology Meeting XIV, Woods Hole, MA from Center of Undergraduate Research Opportunities, Biomedical & Health Sciences Institute and Department of Cellular Biology
Support to present at the Annual Biomedical Research Conference for Minority Students, San Diego, CA, 03, from the Center for Undergraduate Research Opportunities. Selected as one of two students to represent UGA.

Adam Huntley:
UGA CURO Biomedical Research Summer Fellowship 2004

REFERENCES:

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RESEARCH STATEMENT – BORIS STRIEPEN

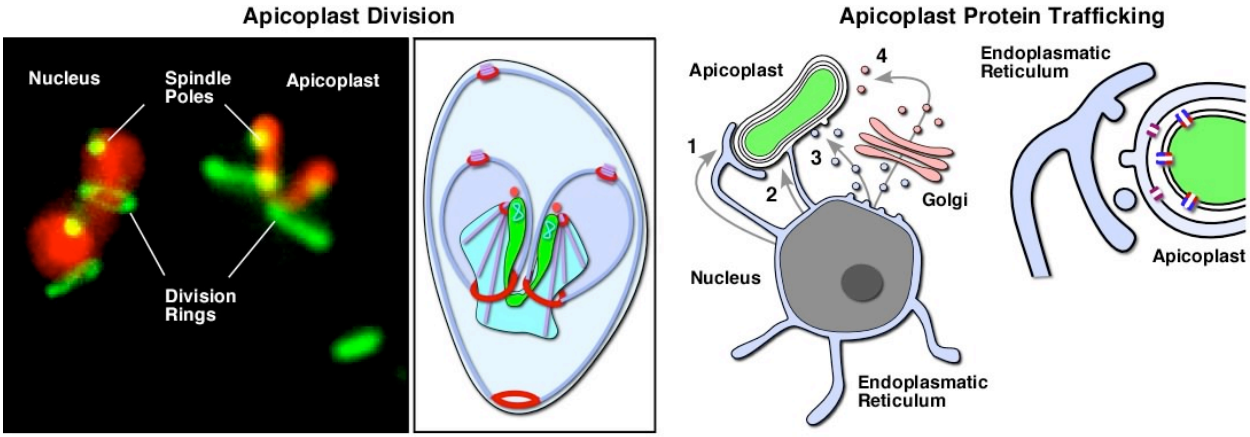
My laboratory studies the biology of parasitism. Our work has been focused on *Toxoplasma gondii* and *Cryptosporidium parvum,* two apicomplexan protozoa that cause severe disease in immunocompromized patients and small children. The spore like oocyst stage found in the life cycle of both organisms is highly resistant to water chlorination. Due to this resistance they cause (at times massive) waterborne outbreaks, a fact that has let to their listing as potential agents of bio-terrorism (appendix B). My laboratory uses a broad range of modern genetic, genomic, biochemical, and cell biological approaches to study fundamental parasite biology and uses this knowledge to identify targets for antiparasitic drug treatment. Specific areas of investigation that we are currently actively pursuing include:

The function and cell biology of the apicomplexan plastid

Protozoan parasites of the phylum Apicomplexa harbor a chloroplast-like organelle, the apicoplast. Genomic analyses suggest the biosynthesis of fatty acids, isoprenoids and heme as putative functions of the apicoplast. These pathways are of cyanobacterial origin and therefore offer attractive targets for the development of parasite specific drugs for the treatment of malaria and toxoplasmosis. However, the parasite genomes appear to encode potentially redundant pathways for the synthesis and/or uptake of some of these metabolites. Using a rigorous genetic approach we are validating each potential target pathway. By conditional knock out we have recently demonstrated that the type II fatty acid synthesis pathway localized to the apicoplast is essential for the survival and growth of *Toxoplasma gondii* in culture (*Proc. Natl. Acad. Sci.* 103: 13192–13197). Furthermore, *in vivo* down regulation of the FAS II pathway cured mice from a lethal challenge infection validating the target. Biochemical analysis of the mutant suggests that the main role of this pathway might not be bulk fatty acid synthesis but the synthesis of lipoic acid precursors. Currently we are engineering additional mutants in the heme and isoprenoid pathways (see below).

From a basic science perspective the apicoplast also provides a unique system to study the cell biology of endosymbiosis. The apicoplast is the product of secondary endosymbiosis, a ménage a trois of a cyanobacterium and two auxotrophic eukaryotes. This origin has let to a fascinating set of novel cellular mechanisms that are clearly distinct from those employed by the plant chloroplast (the product of a single endosymbiosis event). We are studying two fundamental cell biological problems in which the endosymbiont organelle and the 'host' had to develop cooperation at the cellular level: organelle replication and the trafficking of nuclear encoded proteins. While plant and algal chloroplasts employ a bacterial type FtsZ division ring for their replication this machinery appears to have been lost in apicomplexans (*Mol. Microbiol*. 61: 1380–1387). Using transgenic parasites and *in vivo* microscopy we have found that apicomplexans have replaced the prokaryotic machinery with a genuinely eukaryotic structure – the apicoplast physically associates with the poles of the mitotic spindle (*J. Cell Biol.* 151: 1423-1434, *J. Cell Sci.* 118: 3397-3407). Recently we have also identified a novel contractile ring that plays a critical role in the budding of the daughter parasites (*J. Cell Sci.* 119, 2236-2245). Time-lapse imaging strongly supports a role for this ring also in apicoplast fission (*Mol. Microbiol*. 61: 1380–1387, see figure on next page). Current work is aimed to put this model to a rigorous genetic and cell biological test. To identify further genes and proteins critical for the mechanism we are using comparative genomic as well as a forward genetic approaches.

While the apicoplast maintains its own genome the bulk of its ~500 proteins are nuclear encoded. Thus proteins have to be imported. As this organelle boasts four surrounding membranes this is no simple feat. Previous work by us and others has demonstrated that targeting occurs through the secretory pathway and that luminal apicoplast proteins are synthesized with a bipartite leader comprised of an ER signal peptide and an apicoplast specific targeting sequence which is removed upon import. How the proteins are routed from the ER to the apicoplast and how they cross multiple membranes remains poorly understood. We have recently identified a protein with modest primary sequence similarity to the chloroplast import channel Tic20. We have demonstrated that like Tic 20 this protein is a four pass integral membrane protein and localizes to the innermost apicoplast membrane. We have isolated a conditional knock out in this gene and learned that it is essential for parasite survival and that its loss results in morphological defects of the apicoplast (in preparation). We are currently conducting biochemical and cell biological studies to link this phenotype to loss of plastid protein import. We have identified additional candidates for a second protein channel, which we hypothesize will allow passage of the outer membrane(s) that we have begun to study. Lastly, we have embarked on a systematic analysis of *Toxoplasma* synthaxin homologs to identify an apicoplast specific SNARE responsible for ER to plastid routing. Based on our initial success with Tic20 (and Tic 22) and a new streamlined process to isolate mutant parasites (see below) we believe that these studies will quickly result in a detailed mechanistic model of protein trafficking to secondary plastids. Our studies on apicoplast cell biology are currently funded through NIH RO1 AI 64671.



Horizontal gene transfer and novel targets for the treatment of Cryptosporidiosis

The protozoan parasite *Cryptosporidium* is an important human pathogen causing severe disease in AIDS patients and young children. Neither vaccines nor fully effective drugs are available for this disease. We are studying the nucleotide metabolism of *Cryptosporidium parvum* in an effort to identify and develop new drug targets. Our genomic and experimental analyses have demonstrated that the parasite depends entirely on salvage from the host cell for its purine and pyrimidine needs. To our surprise we also discovered that two key genes in the salvage pathways were obtained through horizontal genetransfer from proteobacteria (*Proc. Natl. Acad. Sci. USA* 99: 6304-6309, *Proc. Natl. Acad. Sci. USA.* 101: 3154-3159, *Trends Parasitol.* 20:355-358). Our studies further demonstrate that one these transferred enzymes, inosine-monophosphate-dehydrogenase (IMPDH) is essential for parasite growth and survival. IMPDH from bacteria and eukaryotes differ considerably in their structure, kinetics and inhibitor susceptibility. This holds

great promise for IMPDH as a target for the treatment of cryptosporidiosis (IMPDH is the target of several currently used drugs and the human enzyme is very well studied). Using recombinant *Cryptosporidium* IMPDH we have shown that this enzyme indeed has all the kinetic hallmarks of a bacterial IMPDH and is clearly distinct from the human enzyme (*J. Biol. Chem.* 279: 40320-40327). In collaboration with the National Screening Laboratory (NSRB) at Harvard Medical School we have screened 45,000 compounds for their ability to inhibit *Cryptosporidium* IMPDH. All strong hits were purchased or resynthesized and subjected to kinetic analysis using both parasite (bacterial type) and human IMPDH. This work resulted in the identification of ten principal hits that specifically inhibit the parasite but not the human enzyme (in preparation and U.S. Provisional Patent Application #60/810,276). Two compounds in particular show very promising activity against parasites in a tissue culture model. This work is funded through NIH RO1 AI 55268. Current work is focused on the further optimization of the principal hits into a preclinical drug candidate. This is a significant effort and requires contributions from medicinal chemists, synthetic chemists, biochemists and parasitologists. Under the leadership of our long-term collaborator Liz Hedstrom we have assembled a multi-disciplinary research team including investigators from UGA, Brandeis, Harvard and Emory and have submitted a NIH UO1 program proposal to secure funds for this serious drug development effort. This effort should be greatly helped by the crystal structure of the enzyme, which we have recently solved (in preparation). Why did *Cryptosporidium* pick up bacterial genes, and why were those selected favorably over the eukaryotic genes. We are very interested in the biological role of transferred genes in *Cryptosporidium* and our efforts in this direction are currently focused on a bacterial TrypB tryptophan synthase gene that is surprisingly present in the parasite genome. TrypB is an intensely studied pathogenesis factor in *Chlamydia* and has been shown to be essential for persistence in the presence of Interferron gamma induced and IDO mediated tryptophan starvation. Our studies indicate that the enzyme is active and expressed in intracellular parasite stages (in preparation). Currently we are testing a potential role in parasite pathogenesis and persistence. Interestingly, the *Chlamydia* pathogenesis island that contains the TrypB gene also contains a purine salvage enzyme.

***Toxoplasma* as a model parasite – new tools for efficient forward and reverse genetics**

Over the last two decades protozoan parasites have turned from 'notoriously hard to study' into respectable genetic models. This technical breakthrough has triggered a marvelous renaissance of parasitology and has spurned a series of important discoveries. *Toxoplasma* is clearly one of the experimentally most accessible parasites and often used as a model for the malaria parasite *Plasmodium*. We strongly believe that pushing the envelope on genetic tools is crucial for the continued progress of our research. We have focused our efforts on two problems: how can we build forward genetic mutant screens and how can we construct gene specific knock-out strains more efficiently. In the course of this work we have developed protocols for chemical mutagenesis and the isolation of temperature sensitive mutants. Our first screen employed a 384 well plate replica assay for ts growth (*Antimicrob. Agents Chemother*. 47: 309-316). This resulted in the isolation of 70 independent mutants (in preparation). We have generated several libraries to achieve phenotypic complementation of these mutants (*Proc. Natl. Acad. Sci. USA.* 101: 3154-3159; *Mol. Microbiol*. 55: 1060-71). Our most recent library is based on a modified cosmid backbone. This reagent allows high efficiency complementation and we and our collaborator Michael White have successfully complemented a number of mutants identifying key genes in *Toxoplasma* cell division and cell cycle progression (in preparation). In addition we

have used modified libraries for expression cloning using antibodies (*Mol. Microbiol*. 52: 93-105) and GFP tags (*Mol. Biochem. Parasitol.* 137: 99-110) to identify genes based on their subcellular localization and life cycle stage specific expression.
Robust complementation in hand the main challenge has become to build better and more specific mutant screens. Currently we are working on high-throughput fluorescence microscopy and FACS based screens to identify mutants in apicoplast biogenesis and division.

Conditional gene targeting is feasible in *Toxoplasma* using a tet-regulated promoter element yet the procedure is relatively inefficient and very time consuming. Introducing a positive/negative selection scheme we have dramatically reduced the number of clones we have to screen (*Proc. Natl. Acad. Sci.* 103: 13192–13197). To further streamline this procedure we have turned to the cosmid library that we constructed for complementation. The *Toxoplasma* genome project has end-sequenced 5000 cosmids (half from our library and half from a library generated by David Sibley's group). The sequenced cosmids have been arrayed and mapped onto the *Toxoplasma* genome. The coverage is excellent and more than 85% of the genome is represented, often in multiple cosmids. Using this array we have essentially every parasite gene in a large insert clone in hand. We have adapted recombination cloning in *E. coli* lambda RED strains to modify *Toxoplasma* cosmids using a straightforward PCR based procedure. We can render a cosmid into a positive negative selectable construct to establish a conditional mutant in a single step in less than two weeks now (we can also epitope or GFP tag the locus). This process allows us to target large numbers of genes in a high-throughput parallel fashion. We are currently targeting a pilot set of genes involved in apicoplast metabolism and biogenesis. We feel that this approach has tremendous potential and could allow us a large-scale 'genetic assault' on parasite biology and metabolism well beyond the apicoplast. How parasites interact with their host cells at the metabolic level remains poorly understood and *Toxoplasma* offers a unique model to investigate this question. We are exploring the possibility of a program project that will use our new KO pipeline to tag each of the parasites metabolic pathways with a conditional mutant. This will establish which pathways are essential and validate potential drug targets. New tools and reagents will allow us considerably more sophisticated analysis. We will score changes in the parasite and host cell transcriptome to pin point interactions between individual pathways and cells. We are also eager to recruit a metabolomics expert to this project who could biochemically test the effects of the loss of certain pathways on parasite and host metabolite levels. We expect this to deliver a precise metabolic interaction map and will pilot our initial work on lipids and isoprenes for which both synthesis and uptake have been demonstrated in *Toxoplasma*.

TEACHING STATEMENT

I have extensive teaching experience both at the graduate and undergraduate level. Over the last seven years I have directed numerous lecture, seminar and lab course mostly focused on infectious diseases and parasite biology (please refer to my CV and see http://webs.cb.uga.edu/~striepen/teaching.html for detailed information on the courses I teach including syllabi and lecture notes).
I also teach a two-week module of the MBL summer course 'Biology of Parasitism' in Woods Hole, MA (http://www.mbl.edu/education/courses/summer/course_bio_para.html).

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February 28, 2007

David L. Sibley
Department of Molecular Microbiology
Washington University School of Medicine
660 S. Euclid Ave.
St. Louis MO 63110-1093

Dear Prof. Sibley,

I am writing in the strongest possible support of **Boris Striepen**'s application for an appointment in your department. I believe Boris is a rising young star in the parasitology community who will ascend all the more quickly with access to the stronger students and broader scientific community that a top-flight research institution can provide. I also believe Boris possesses an instinct for important problems together with the creativity, resourcefulness and rigor necessary to solve such problems. Factor in his good humor and collegiality, and I am confident that he will make any department both stronger and a better place to be.

I admire most scientists who attack problems by whatever means necessary. While Boris's strong suits are genetics and cell biology, he does not shy away from problems that require other expertise and can be quite relentless in convincing others to share his vision. That's how I came to meet him. Among other things, my laboratory has investigated the mechanism of IMP dehydrogenase (IMPDH), a critical enzyme in the biosynthesis of guanine nucleotides. We have characterized IMPDHs from a many different sources over the years, so when Boris approached me about characterizing IMPDH from *C. parvum*, I was hardly excited to measure the values of kcat and Km for yet another IMPDH from some obscure organism. Boris convinced me that *Cryptosporidium* is a parasite to be reckoned with. The IMPDH project has proceeded as close to seamlessly as one could hope. We have validated the target, showing the parasite is sensitive to IMPDH inhibitors and incapable of xanthine/guanine salvage in a cell culture system. The parasite enzyme has very different properties than the host and we discovered some specific inhibitors of the parasite enzyme that have modest antiparasitic activity in a cell culture model. We have also recently solved the structure of this enzyme. I believe we are now positioned to launch a full-fledged drug development project. Along the way, Boris noticed that the purine and pyrimidine pathways of *Cryptosporidium* include many genes obtained by horizontal gene transfer. This curious observation may provide important clues into how Apicomplexan parasites

evolved. On the practical drug development side, these enzymes are highly diverged from their host counterparts, and may therefore be potential targets. I should note that Boris had the insight to tackle *Cryptosporidium* early on, before the bio-warfare funding became available. Now many other laboratories are jumping in, following Boris's lead and targeting the same pathways. In fact, Boris has been in front of the pack in several other areas- fluorescent strains of *Toxoplasma gondii*, apicoplast function and mechanisms of cell division, to name a few.

Where many scientists seem to burrow into a comfy niche, Boris attacks difficult problems- e.g., target identification in *Cryptosporidium* (where genetic tools are nonexistent and biochemistry next to impossible). He has the right combination of attitude and people skills to succeed in any size pond- he will take advantage of resources in hand and find ways around obstacles. To cite an example from civilian life, where the move from the bright lights/big city of Philadelphia to Athens might well cripple a lesser person, rather than bemoan the absence of Thai food and film houses, Boris bought a canoe and became an avid paddler. He brings this same approach to his science- he finds new opportunities where others despair. I've followed/dabbled in the parasite field since my postdoctoral years with CC Wang at UCSF and I believe that Boris has the breadth, depth and creativity to rise to the very top.

You may wonder why I am not trying to recruit Boris to Brandeis. The thought has surely crossed my mind on more than one occasion, but, though it would be great to have him here, there is no community in parasitology or infectious disease, so it would be a really bad move for him- unlike a move to Washington University. I would love to see him in a place where he can take full flight, and I urge you to give him that opportunity.

with best regards,

Lizbeth Hedstrom, Ph.D.
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SCHOOL OF BOTANY

THE UNIVERSITY OF MELBOURNE

Wednesday, March 7, 2007

Prof David Sibley,
Search Committee
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Box 8230
Department of Molecular MicrobiologyWashington University School of Medicine
660 South Euclid Avenue
St. Louis, MO 63110-1093
USA

Dear David,

I write in support of Dr Boris Striepen's application for the Faculty Position at University of Wahsington. Dr Striepen is a dynamic, independent researcher with an extraordinarily strong track record. I first met Dr Striepen in 1997 after his PhD supervisor (Prof David Roos) had undertaken a sabbatical in Melbourne. During Prof Roos' sabbatical we began a collaboration, and Dr Striepen (then a grad student) performed some key experiments using GFP labelling to the relict chloroplast (the apicoplast) of *Toxoplasma* parasites with some gene sequences that we were investigating here in Melbourne. This GFP targeting data became a central plank of a paper that we published in PNAS that year. I was greatly impressed with Dr Striepen's contribution to the paper and I have since developed a strong respect for his scientific approach. He has since gone on to develop a very strong, independent line of research into the cell biology, molecular evolution and biochemistry of apicomplexan parasite. He has produced a suite of groundbreaking papers in major, high impact international journals such as J Cell Biology and PNAS. His genetic knockout paper in PNAS last year was a seminal milestone in the field of apicoplast biology.

During summers past I selected Dr Striepen as Faculty for the elite Biology of Parasitism course at Woods Hole MA. The Biology of Parasitism course is a high level laboratory-based course in parasitology aimed at kick starting young scientists in the field of parasitology. I directed a module in the course and was responsible for selecting 9-10 faculty each year to deliver the latest developments in parasitology to a high achieving cohort of students selected from a global pool. Dr Striepen was an outstanding performer in the teaching of this course. His enthusiasm with students is always extraordinary and his lectures and laboratory materials have always been truly excellent. Each year the

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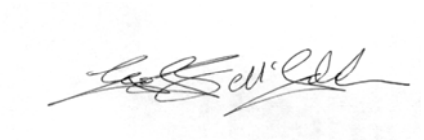
student feedback singled out Dr Striepen as one of the high points of my module. Over the last two years he has run his own module in the course focusing on apicoplast cell biology, and I have chimed in with a lecture, thus reversing our roles. Dr Striepen's modules were highly successful and acclaimed by the students and course organisers. He is a gifted teacher.

Dr Striepen is taking what I believe to be some of the most innovative lines in research into apicomplexan cell biology and metabolism. The identification of a relict plastid in apicomplexan parasites has proffered new approaches to treating very serious diseases such as malaria and toxoplasmosis. Whereas many researchers become increasingly narrow in their focus, Dr Striepen is expanding his view and taking a broad tack to understanding fundamental problems. He is devising some extraordinarily clever genetic screens to approach problems that seem to be otherwise at a technical impasse. His novel and energetic approach is most welcome, particularly at this point in time. I am tremendously impressed by his research into the apicoplast. He's definitely one of the up-and-coming stars in parasitology.

I particular appreciate Dr Stiepen's depth of approach and the array of techniques he utilises. He has successfully attracted funding and also assembled a high power group since starting up in Georgia. One of my own students, Dr Giel van Dooren, joined the Striepen lab as a postdoc and the direct feedback from Giel has been all very positive as regards the lab and Dr Striepen's supervision. Dr Striepen also has an eye for the aesthetic, which makes for great microscopy. He's interested in everything about the natural world, which makes him a real biologist and not overly blinkered like so many scientists these days. On a personal note, I very much enjoy Dr Striepen's company and admire the balance he strikes in life between hard work and participating in the rest of the world around him. I think this philosophy serves him and those around him extremely well.

In summary, I give Dr Striepen my utmost endorsement for your faculty position. He is an outstanding researcher, an inspiring teacher and would be an extremely worthy colleague; I'd like him in my department. He has made a key contribution to understanding the cell biology and metabolism of the apicomplexan parasite plastid, which is emerging as a key drug target for major global diseases. I have no doubt that his ingenious genetic approaches will open new doors for therapy, and his research represents a bold new direction in an area set to expand immensely. If you have any queries, please do not hesitate to contact me.

Yours sincerely,



Geoff McFadden *PhD FAA*
ARC Federation Fellow, Howard Hughes International Scholar

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Cc: David Roos <droos@sas.upenn.edu>
From: David Roos <droos@sas.upenn.edu>
Subject: *** reference for faculty applicant Boris Striepen
Date: Wed, 14 Mar 2007 05:19:39 -0400
To: sibley@borcim.wustl.edu (Sibley, David)

NOTE: THIS LETTER IS BEING SEND BY E-MAIL ONLY. PLEASE ADVISE IF YOU WOULD ALSO LIKE A PAPER COPY, WITH LETTERHEAD, TO BE SENT BY FAX OR MAIL

Dear David, Steve, and members of the faculty search committee:

I am writing in reference to Dr. Boris Striepen, a tenured Associate Professor of Cell Biology at the University of Georgia, whom I understand has applied for a faculty position in the Department of Molecular Microbiology at Washington University. This letter can be brief, because I can be so positive: Boris is outstanding. Indeed, I can think of no better mid-career candidate in the entire field of cell and molecular parasitology.

Striepen was a graduate student with Ralph Schwarz in Marburg Germany, where he was responsible for solving the structure of the T. gondii GPI anchor on parasite surface antigens. He joined my lab as a post-doc, in order to gain experience in molecular genetics and cell biology. In this, he was quite successful, engineering the first GFP expression in T. gondii, and exploiting this tool to study organellar replication in living cells, to map targeting signals to various compartments (dense granules, rhoptries, micronemes, apicoplast, plasma membrane, parasitophorous vacuole, etc), and as a selectable marker for genetic screens. I will not dwell on this work, much of which is no doubt familiar to you already, except to point out that it clearly demonstrated several of Boris' strengths: his scientific insight in designing experiments that are both scientifically informative and technically accessible, his enthusiasm for adopting or developing new technologies that expand the boundaries of what is achievable, and his hard work and troubleshooting expertise that ensures the successful implementation of new technologies.

In his own lab at the University of Georgia, Boris has been even more productive. In addition to a long list of solid publications (ranging from biochemical studies on IMPDH, to cell biological studies on MORN-domain proteins, to the development of immunological tools, to studies bringing Sarcocystis into the modern era) he has pursued three avenues of research that I would cite as being of major significance. Extending his postdoctoral work on the apicoplast, Boris has been one of many seeking to define the metabolic function(s) that this essential organelle contributes to apicomplexan parasites. Several investigators have focused on lipid metabolism, and a series of papers published over the past year leads to the surprising conclusion that apicoplast fatty acid synthesis may be required only for the synthesis of lipoic acid for internal housekeeping functions within the organelle itself. While both my lab and Sean Prigge's group at Johns Hopkins have pursued biochemical approaches, Boris' lab engineered a conditional knock-out ... a far more innovative and informative strategy. Striepen's work on horizontal gene transfer in Cryptosporidium (a collaboration with Jessica Kissinger) constitutes a second major contribution. In addition to highlighting several promising targets for drug development, this research has also been instrumental in educating the broader genomics community as to the frequency and significance of such events in (unicellular) eukaryotes. Finally, Striepen's development of complementation technology is the most important intellectual and technical advance for Toxoplasma molecular genetics in a decade; his most recent (as yet unpublished) data demonstrates the utility of this work through identification of numerous genes involved in cell cycle regulation.

It should be clear from the above that I hold Boris in very high regard, but

I fear that I may have failed to convey his most significant strengths: his wide-ranging intellectual curiosity, and his scientific collegiality. Boris is intelligent, imaginative, hard-working, an excellent teacher and mentor, and a responsible citizen, but most of all, he is perpetually excited by Science. There is no one that I would rather sit with over a beer to mull over a challenging intellectual problem. While Boris has several colleagues at Georgia who help to provide an adequate intellectual community, and he has been successful in attracting good post-docs, he would clearly benefit from a bigger pond ... and especially from a stronger pool of students. He is clearly thinking about moving on to a more stimulating environment; I wish that we had a position to offer him here!

Please do not hesitate to contact me if there is any further information that I can provide.

Best regards -- David

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