BIOGRAPHICAL SKETCH

NAME: Marc-Jan Gubbels

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Agricultural University Wageningen, The Netherlands	BS	08/1991	Molecular Sciences
Agricultural University Wageningen, The Netherlands	MS	08/1994	Molecular Sciences
University of Utrecht, The Netherlands	PhD	06/2000	Parasitology
University of Georgia, USA	Post-doc	08/2005	Parasitology, Cell Biology

Positions and Honors

Positions

1995 – 1996 Community Service, Utrecht University (The Netherlands), Lab. for Physiological Chemistry.
2000 Post-Doc University Utrecht (the Netherlands) and Co-organizer of a laboratory workshop at the University of Pretoria, (South Africa). With Drs. Frans Jongejan and Albert W.C.A. Cornelissen.
2001 - 2005 Post-Doc/Assistant Research Scientist at the Center for Tropical and Emerging Global Diseases, University of Georgia (USA). With Dr. Boris Striepen
2005 - 2011 Assistant Professor at the Department of Biology, Boston College (USA)
2011 - 2012 Sabbatical: Visiting Scientist at the Max Planck Institute for Infection Biology, Berlin, Germany (Humboldt fellowship; host: Dr. Kai Matuschewski).
2011 - 2015 Associate Professor at the Department of Biology, Boston College (USA)
2015 - date Professor at the Department of Biology, Boston College (USA)
Fall of 2018 Sabbatical: Visiting Scientist at the Harvard T.H Chan School of Public Health, Department of Immunology and Infectious Diseases (host: Dr. Manoj Duraisingh)

Professional Activities

Journal reviewer

Antimicrobial Agents and Chemotherapy, BBA Molecular Cell Research, Biotechnology Journal, BMC Biology, BMC Genomics, Cell Host and Microbe, Cellular Microbiology, Cytoskeleton, eLife, Eukaryotic Cell, FASEB J, Frontiers in Bioscience, Infection and Immunity, International Journal of Biological Sciences, International Journal for Parasitology, International Journal for Parasitology: Drugs and Drug Resistance, Journal of Applied Acarology, Journal of Biological Chemistry, Journal of Cell Biology, Journal of Cell Science, Journal for Clinical Microbiology, Journal of Eukaryotic Microbiology, mBio, Microscopy and Microanalysis, Molecular and Biochemical Parasitology, Molecular Microbiology, mSphere, Nature Communications, Nature Microbiology, Parasitology, PLoS Biology, PLoS Genetics, PLoS ONE, PLoS Pathogens, Traffic, Trends in Parasitology

Grant reviewer

2018 - 2022 Permanent member NIH Study Section “Pathogenic Eukaryotes (PTHE)
NIH PTHE study section (ad hoc June 2018), NIH Special Emphasis Panels ZRG1 IDM-M (02) M, PAR-14-080, ZGM1 RCB-7 (SC), ZRG1 IDM-P (02) M K-awards-MID-B, ZRG1 IDM-P (02), ZRG1 AARR-K(04), ZRG1 IDM-M (03), ZRG1 IDM-B (03), ZRG1 AARR-E (02), ZRG1 AARR-K (02) ZRG1 IDM-M (03) M, the American Heart Association (Microbiology section), National Science Foundation (Molecular and Cell Biology section), Wellcome Trust (UK), Canada Foundation for Innovation, and the European Research Council (EU), Human Frontier Science Program, Biotechnology and Biological Sciences Research Council (BBSRC) (UK), Swiss National Science Foundation (CH), Agence Nationale de la Recherche (F).

Editorial boards

2010 - 2018 Editorial Board member on the journal Infection and Immunity
2010 - 2015 Editorial Board member on the journal Experimental Parasitology
2014 - 2016 Editorial Board member on the journal Eukaryotic Cell
2014 - Reviews Editor for the journal PLoS Pathogens

Other professional Service

2009 - 2011 Advisory committee member for the *Toxoplasma gondii* genome website portal, ToxoDB.org
2013 - 2015 President, New England Association for Parasitologists (NEAP)
2014 - 2015 Chair of Division AA (free-living, symbiotic, and parasitic protists) of the American Society for Microbiology (ASM)
2017 - 2019 Scientific Working Group (SWG) member for the Eukaryotic Pathogen Genomics Resource, EuPathDB.org

Honors and Awards

2006 New Investigator Award from the Smith Family Foundation
2008 March of Dimes Basil O'Connor Starter Award
2011 American Cancer Society Research Scholar Award
2011 Humboldt Foundation Fellowship Award for Experienced Researchers

C. Contribution to Science *(in chronological order)*

1. Development of a Reverse Line Blot (RLB) assay to simultaneously diagnose *Theileria* spp. and *Babesia* spp. infection. My PhD research revolved around *Theileria annulata*, a tick-borne apicomplexan parasite causing tropical theileriosis in cattle and spanned a variety of aspects [1-4]. By way of background, besides *T. annulata* several other benign and pathogenic tick-transmitted *Theileria* and *Babesia* spp. infect cattle, causing a lot of confusion. I generated a RLB assay to simultaneously diagnose and identify these apicomplexan parasites [1]. A variable region of the 18S rRNA gene was amplified using conserved primers and subsequently hybridized perpendicular on a blot with species-specific probes with a line blotter. This sensitive and versatile assay revealed many missed- and mis-diagnosis made in the past. RLB has since been widely applied in the field to a wide variety of studies, (e.g. goat & sheep [4], dogs and to measure parasitemia). After my PhD I co-organized a RLB workshop in South Africa to train a group of African researchers, a course that continued in later years under the EMBO banner.

1. **Gubbels, J.M.,** A.P. de Vos, M. van der Weide, J. Viseras, E. de Vries, L.M. Schouls and F. Jongejan. 1999. Simultaneous detection of bovine *Theileria* and *Babesia* species using reverse line blot hybridization. *J. Clin. Microbiol*. 37: 1782-1789. PMC84950
2. **Gubbels, M.-J.,** H. Yin, M. van der Weide, Q. Bai, I.J. Nijman, G. Liu and F. Jongejan. 2000. Molecular and biological characterisation of the *Theileria buffeli/orientalis* group*. Int. J. Parasitol.* 30: 943-952. 10927085
3. **Gubbels, M.-J.,** F. Katzer, B.R. Shiels and F. Jongejan. 2001. Study of *Theileria annulata* population structure during bovine infection and following transmission to ticks. *Parasitology* 123: 553-561. 11814042
4. Schnittger, L., H. Yin, B. Qi, **M.-J. Gubbels,** D. Beyer, S. Niemann, F. Jongejan and J. S. Ahmed. 2004. Simultaneous detection and differentiation of *Theileria* and *Babesia* parasites infecting small ruminants by reverse line blotting. *Parastiol. Res.* 92: 189-196. 14652747

2. Development of forward genetics for *Toxoplasma gondii.* Over 50% of the predicted genes in *Toxoplasma* have no homology with any gene outside the Apicomplexa. Especially processes unique to the parasite are expected to employ unique genes, which will be hard to discover by comparative biology. To identify genes based on their function rather than on their identity, the goal of my post-doc in Boris Striepen's lab was to develop forward genetics for *Toxoplasma*. Although chemical mutagenesis had been established in the 1970s, identifying the mutated gene was impossible by classical genetic crosses (cat infections are unproductive with *in vitro* adapted strains). To overcome this challenge we developed different genetic complementation approaches using cDNA and genomic DNA libraries. High efficiency genomic complementation was achieved with a cosmid library with 35+ kb inserts [1]. Hence, this approach was a major breakthrough and identified the causative mutations and genes in >2 dozen growth mutants [1]. Furthermore, I pioneered whole-genome re-sequencing by Illumina short reads in collaboration with the bioinformatics expertise of Dr. Gabor Marth [2], which was applied in collaboration with others (e.g. [3]). Raising the impact of this breakthrough was the novelty of the causative gene in this invasion/egress mutant, underscoring the power of forward genetics. We evaluated and optimized chemical mutagenesis protocols and analyzed the nature of the DNA damage [4]. In recent years

we applied our methods toward *in vitro* lab evolution experiments of *Toxoplasma*, which project is providing exciting new insights as changes over 1000+ generations occur quickly on the RNA expression level rather than on genomic mutations fixing in the evolving populations.

1. **Gubbels, M.-J.,** C.F. Brooks, M. Muthalagi, T. Szatanek, J. Flynn, B. Parrot, B. Striepen and M.W. White. 2008. Forward Genetic Analysis of the Apicomplexan cell and division cycle in *Toxoplasma gondii*. *PLoS Pathogens*. 4(2): e36 (0001-0015). *(Editor's Pick).* PMC2242837
2. Farrell, A. S. Thirugnanam, A. Lorestani, J.D. Dvorin, K.P. Eidell, B.R. Anderson-White, D.J.P. Ferguson, Duraisingh, G.T. Marth, and **M.-J. Gubbels.** 2012. A DOC2 protein identified by mutational profiling is essential for apicomplexan parasite exocytosis. *Science*. 335:218-221. (*Editor's choice).* PMC3354045
3. Brown, K.M., E. Suvorova, **A. Farrell,** A. McLain, A. Dittmar, G.B. Wiley, G.T. Marth, P.M. Gaffney, **M.-J. Gubbels,** M. White, and I.J. Blader. 2014. Forward genetic screening identifies a small molecule that blocks *Toxoplasma* growth by inhibiting both host- and parasite-encoded kinases. *PLoS Path.* 10(6): e1004180. PMC4055737
4. Farrell, A., B.I. Coleman, B. Benenati, K.M. Brown, I. Blader, G.T. Marth, and **M.-J. Gubbels.** 2014. Whole genome profiling of spontaneous and chemical mutagenesis induced mutations in *Toxoplasma gondii*. *BMC Genomics.* 15: 354. PMC4035079

3. Dissection of *Toxoplasma gondii* cell division by endodyogeny. In humans *Toxoplasma* divides asexually through endodyogeny, wherein two daughter cells bud inside a mother. We study this unique process to identify new drug targets. We have demonstrated that the daughter cytoskeletons initiate around the duplicated centrosomes [1] and subsequently elongate to serve as the scaffold for organelle partitioning. Furthermore, we have shown that a family of intermediate filament-like IMC proteins is sequentially assembled in the daughter bud [reviewed in 4]. This work resolved developmental steps at an unprecedented level, which has since been applied in the analysis of division mutants (e.g. [2, 3]). A big open question we are pursuing is how the cytoskeleton tapers toward the end. We have shown that a contractile force assembles on the basal end of the buds (e.g. [3]). This basal complex is the functional ortholog of the mammalian contractile ring, but its exact mechanism of constriction is still not very clear. In addition, we still lack mechanism on how the various steps are controlled and coordinated. To this end my lab is addressing kinases and phosphatases operating on endodyogeny. We have also successfully applied proximity-based biotinylation (BioID2) to dissect the proteome and architecture of the cytoskeleton [e.g. 3]. Overall, our work has deciphered key events at in daughter budding, which has filled a toolbox to dissect both endodyogeny as well as other apicomplexan division modes [4].

1. Chen, C.-T. and **M.-J. Gubbels.** 2013. The *Toxoplasma gondii* centrosome is the platform for internal daughter budding as revealed by a Nek1 kinase mutant. *J. Cell Sci.* 126:3344-3355. PMC3730244
2. Chen, C.-T. and **M.-J. Gubbels.** 2019. TgCep250 is dynamically processed through the division cycle and essential for structural integrity of the *Toxoplasma* centrosome. *MBoC* 30:1160-1169. PMC6724518
3. Engelberg, K., C.-T. Chen, T.J. Bechtel, V. Sánchez Guzmán, A. Drozda, S. Chavan, E. Weerapana, and **M.-J. Gubbels.** 2020. The apical annuli of *Toxoplasma gondii* are composed of coiled-coil and signaling proteins embedded in the IMC sutures. *Cell. Micro.* 22:e13112 PMC6925623
4. **Gubbels, M.-J.,** C.D. Keroack, S. Dangoudoubiyam, H.L. Worliczek, A.S. Paul, C. Bauwens, B. Elsworth, K. Engelberg, D.K. Howe, I. Coppens, M.T. Duraisingh. 2020. Fussing about fission: defining variety among mainstream and exotic apicomplexan cell division modes. *Front Cell Infect Microbiol*. 10: 269. PMC7289922

4. Dissection of *Toxoplasma gondii* host cell invasion and egress. Invasion and egress are inherently part of the parasitic life style and are essential steps in completing the lytic cycle. Host cell egress and invasion are completely controlled by the parasite and therefore these processes are viable drug targets. Egress and invasion are closely related and rely on shared processes such as secretion of micronemes, activation of actin-myosin based motility and conoid extrusion, all of which are controlled by the release of Ca^{2+} in the cytoplasm. Using our forward genetic mutant system we identified a new protein, TgDOC2, which we demonstrated to control Ca^{2+}-dependent microneme secretion and is essential for egress and invasion [1]. This exciting work started to uncover the inner workings of Ca^{2+}-mediated secretion by focusing on Ca^{2+} sensors, which in *Toxoplasma* comprise 3 ferlin genes. One of these surprisingly controlled rhoptry secretion [4], whereas another one controls microneme trafficking and secretion [5]. Lastly, we looked into other aspects of microneme secretion (e.g. calcineurin [2] and phosphoglucomutases [3]).

1. Farrell, A. S. Thirugnanam, A. Lorestani, J.D. Dvorin, K.P. Eidell, B.R. Anderson-White, D.J.P. Ferguson, Duraisingh, G.T. Marth, and **M.-J. Gubbels.** 2012. A DOC2 protein identified by mutational profiling is essential for apicomplexan parasite exocytosis. *Science*. 335:218-221. (*Editor's choice).* PMC3354045

2. Paul, A.S., S., Saha, K. Engelberg, R.Y. Jiang, B.I. Coleman, A.L. Kosber, C.-T. Chen, M. Ganter, N. Espy, T.-W. Gilberger, **M.-J. Gubbels*,** and M.T. Duraisingh*. 2015. Apicomplexan calcineurin regulates specific attachment of free parasites to host cells for infection. *Cell Host Microbe.* 18, 1–12. *co-corresponding author. PMC4506782
3. Saha, S., B.I. Coleman, R. Dubey, I.J. Blader, and **M.-J. Gubbels.** Two phosphoglucomutase paralogs facilitate ionophore-triggered secretion of the *Toxoplasma* micronemes. *mSphere.* 2: e00521-17. PMC5705807
4. Coleman, B.I., S. Saha, S. Sato, K. Engelberg, D.J.P. Ferguson, I Coppens, M. Lodoen, and **M.-J. Gubbels.** 2018. A member of the ferlin calcium sensor family is essential for *Toxoplasma gondii* rhoptry secretion. *mBio* 9: e01510-18. PMC6168857
5. Tagoe, D.N.A., A. A. Drozda, I. Coppens, B.I. Coleman, and **M-J. Gubbels.** *Toxoplasma* ferlin1 is a versatile and dynamic mediator of microneme trafficking and secretion. bioRxiv: https://biorxiv.org/cgi/content/short/2020.04.27.063628v1

A complete list of peer-reviewed publications can be found in the following link:
https://www.ncbi.nlm.nih.gov/myncbi/marc-jan.gubbels.1/bibliography/public/