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Joana Santos, Karine Frénal

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Dominique Soldati-Favre: Bringing *Toxoplasma gondii* to the Molecular World

Joana M. Santos[1]* *and Karine Frénal*[2]*

[1] Université Paris-Saclay, CEA, CNRS, Institute for Integrative Biology of the Cell (I2BC), Gif-sur-Yvette, France,
[2] Université Bordeaux, CNRS, Microbiologie Fondamentale et Pathogénicité, UMR 5234, Bordeaux, France

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***Correspondence:**
Joana M. Santos
joana.santos@i2bc.paris-saclay.fr
Karine Frénal
karine.frenal@u-bordeaux.fr

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FROM RNA PROCESSING TO PARASITE BIOLOGY

Anyone that knows Dominique, knows that she has a real passion for science and discovery. This passion includes parasitology so it might come as a surprise that she moved to the parasitology field almost by accident.

After doing a brilliant PhD in Zurich, Switzerland, in the Schümperli team, working on RNA processing, Dominique, with the support of a Swiss National Foundation postdoctoral grant and an EMBO fellowship, decided to join a lab in the US East Coast, but life decided otherwise and, in 1991, she joined John Boothroyd's team at Stanford University, in California. This was an outstanding team, with access to exceptional facilities, but it was transitioning from working on Trypanosomes to studying *Toxoplasma gondii*. Although *Toxoplasma* was easily cultured in the lab, it had yet to be genetically modified. At a time when the genome had yet to be sequenced and molecular biology was done without kits, Dominique, with her high energy level and swiss organization, showed that *Toxoplasma* could be transfected, a first for an intracellular parasite (Soldati and Boothroyd, 1993). She also showed, with other team members, that the transfected parasites could be drug selected and used for transgene expression, gene knockout and complementation (Kim et al., 1993; Soldati and Boothroyd, 1995; Black et al., 1995; Soldati et al., 1995). Her work did an enormous amount for the field and things became easier afterwards.

In 1995, Dominique finished her postdoctoral studies and moved to Germany to become an independent group leader. She was appointed Assistant Professor at the Center for Molecular Biology at the University of Heidelberg. There, she adapted the Cre-loxP system to *Toxoplasma* (Brecht et al., 1999) and revolutionized the field yet again by establishing the first inducible knockdown system for an Apicomplexa (Meissner et al., 2001; Meissner et al., 2002b). In 2001, Dominique moved her team to the Imperial College London, in the UK, where she held a position as a Senior Lecturer and Reader. In 2004, she became a Visiting Professor in parasitology at Imperial College and was appointed Associate Professor at the Faculty of Medicine of the University of Geneva, where her team is still based at, and where she became a Full Professor in 2010.

UNDERSTANDING *TOXOPLASMA* AT THE MOLECULAR AND STRUCTURAL LEVEL

Dominique's lab is one of the most celebrated teams in the Apicomplexa and parasitology field, known for combining technology with biology to answer specific questions, to be highly productive and for focusing on many different aspects of *Toxoplasma* biology with endless curiosity. Dominique never "fears to enter new territory and/or to challenge old dogma that might not be right". The Soldati team has contributed immensely to our understanding of parasite motility, host cell invasion and egress, protein trafficking, energy metabolism and even mice behavior. Two long-term research topics of the lab have been investigation of the actomyosin machinery powering gliding; and microneme composition, secretion and biogenesis. In the last decade, the Soldati lab has also explored the metabolism of both *Toxoplasma* and *Plasmodium*, as well as other molecular aspects of the malaria parasite.

Gliding motility and invasion of Apicomplexans were known to be active processes powered by a parasite actomyosin system (Dobrowolski and Sibley, 1996; Dobrowolski et al., 1997) but Dominique's lab was the first to identify its molecular components. In an impressive endeavor, her team characterized the kinetic and mechanical properties of the myosin heavy chain protein A (TgMyoA) with protein directly purified from tachyzoites (Herm-Götz et al., 2002), a first for a myosin. Simultaneously, they demonstrated that TgMyoA is critical for parasite motility and host cell invasion (Meissner et al., 2002b). Finally, the name "glideosome" was proposed by Dominique's lab to describe this new and unique actomyosin system (Opitz and Soldati, 2002). Together with other labs, the team then identified and functionally characterized the glideosome components (Gaskins et al., 2004; Frénal et al., 2010; Nebl et al., 2011; Williams et al., 2015; Jacot et al., 2016), as well as regulators of actin dynamics (Plattner et al., 2008; Mehta and Sibley, 2010; Daher et al., 2010; Yadav et al., 2011; Salamun et al., 2014; Jacot et al., 2016). Later, identification of Myosin H (TgMyoH), actin nucleator Formin 1 (TgFRM1) and the glideosome-associated connector (TgGAC) at the tachyzoites conoid showed how gliding motility is initiated at the parasite's apical tip (Graindorge et al., 2016; Jacot et al., 2016). Finally, very recently, the lab used expansion microscopy to explore the apical complex structure and function, including that of the enigmatic conoid (Dos Santos Pacheco et al., 2021).

In parallel, Dominique's lab has had a continued interest on micronemes, specialized parasite apical secretory organelles, storing adhesins and other effector molecules implicated in gliding motility, host cell attachment, invasion and egress. The lab has identified several of its components and protein complexes, and investigated their trafficking, structure and function during the parasite lytic cycle (Di Cristina et al., 2000; Ferguson et al., 2000; Reiss et al., 2001; Brecht et al., 2001; Meissner et al., 2002a; Huynh et al., 2003; Mital et al., 2005; Blumenschein et al., 2007; Kessler et al., 2008; Friedrich et al., 2010; Sheiner et al., 2010; Marchant et al., 2012; Sardinha-Silva et al., 2019). In recent years, the team ventured into discovering the mechanisms behind microneme biogenesis and exocytosis. In 2018, they identified Transporter Facilitator Protein 1 (TgTFP1) (Hammoudi et al., 2018), an essential protein for parasite survival due to its crucial role in microneme biogenesis and maturation. In 2016, the identification of the protein acylated pleckstrin homology domain-containing protein (TgAPH) as a phosphatidic acid sensor anchored at the surface of the micronemes (Bullen et al., 2016) prompted the lab to investigate the signaling cascade leading to microneme secretion and parasite egress (Bullen et al., 2016; Jia et al., 2017; Darvill et al., 2018; Bisio et al., 2019; Bisio et al., 2022) and, with other labs, to draw the picture we know today (Farrell et al., 2012; Brown and Sibley, 2018; Bisio and Soldati-Favre, 2019; Bullen et al., 2019; Yang et al., 2019).

Another topic frequently addressed by Dominique throughout the years has been parasite metabolism. She was one of the first in the field to propose that energy metabolism could be exploited therapeutically (Polonais and Soldati-Favre, 2010). Ever since, her team has defined the parasite metabolic needs and capabilities by using both *in silico* and *in vivo* approaches to investigate specific metabolic pathways (Limenitakis et al., 2013; Oppenheim et al., 2014; Kloehn et al., 2020; Kloehn et al., 2021) but also build metabolic models for *T. gondii* tachyzoite and bradyzoite stages (Tymoshenko et al., 2015; Krishnan et al., 2020).

The Soldati team has also ventured into studying *Plasmodium*, in collaboration with other teams but also solo, with as much success as with *Toxoplasma* (Pino et al., 2012; Chiappino-Pepe et al., 2017; Stanway et al., 2019; Bisio et al., 2020; Bertiaux et al., 2021). They have, for instance, identified a new multistage antimalarial inhibitor blocking both parasite invasion and egress (Pino et al., 2017) and investigated specific metabolic pathways of *P. berghei* intra-erythrocytic and liver stages (Oppenheim et al., 2014; Stanway et al., 2019).

RECOGNIZED BY HER PEERS

Parasitology is a small and relatively neglected field compared to others so even those who are exceptional are rarely praised. Even so, Dominique has been the recipient of multiple accolades, namely the Kar Asmund Rudolphi-Medal of the German Society for Parasitology in 2001, the Prize of the Gertrude von Meissner Foundation in 2009 and twice the Pfizer Prize for Basic Research in Infection, awarding specific lab publications, and the Cloëtta Foundation Prize in 2015 and the Alice and C. C. Wang Award in Molecular Parasitology in 2019, acknowledging Dominique's scientific career. She is a member of prestigious academies, including the Swiss Academy of Medical Sciences, the European Academy of Microbiology and EMBO, was an HHMI International Scholar and Senior Scholar in Infectious Diseases, and she has received a number of prominent grants, including a European Research Council (ERC) Advanced Grant, unarguably one of the most competitive European grants. She has also organized numerous parasitology meetings, including the Molecular Parasitology Meeting or the Gordon Research Conference on Host-Parasite Interactions, she is the Academic Editor of selected

publications for various journals (eLife, PLoS Pathogens, Traffic, Cell Host & Microbe, and others), she has been a contributor to the F1000 since 2006, and she has been a grant reviewer for national and international grant schemes and an expert for the ERC or the Wellcome Trust's Peer Review College.

Despite all the praises Dominique has received, and all the high impact papers she has published, many of the people we interviewed mentioned that they didn't actually know who Dominique was when they interviewed - it was "after talking to her in her little office that it became immediately clear to me that I absolutely wanted to join her lab - her personality and how she talked about science and her research inspired me from the minute I met her", it was "only after spending a few months in her lab that I realized how lucky I was!". This is a testament of Dominique's ability to never wanting to be the bigger person in the room and for always caring for the person in front of her - "she took a huge interest in my future career and supported me wherever she could", "I had always the freedom to make my own decisions and she would respect them".

"Dominique is firm when people want women to be nice", someone said. Indeed, Dominique is straightforward and says exactly what she thinks. Despite what some called a steep learning curve, everyone was unanimous in saying that Dominique masters the art of getting everyone to push themselves and be motivated. From the very beginning of her career as a mentor, Dominique was certainly demanding but never pressured people to work harder or gave the impression that she thought that way (even if she might…).

Dominique always let people do side projects, think for themselves. Her enthusiasm and energy are an unlimited source of motivation that pushed us all to work more and be better. Some of us even remember presenting to her results of experiments done behind her back and having Dominique being very encouraging and open for new, even crazy ideas. This is certainly a result of the lab good atmosphere, which has lasted, even though the team has moved internationally twice. As a postdoc, Dominique was known to have fun and even played some unforgettable jokes on the lab head. We can say this trait has continued. The lab beer o'clocks and the department dress up Christmas parties were always memorable.

REPRESENTATION AND EMPOWERMENT

This essay is written in the context of a special issue of Women in Parasitology. Dominique would be the first to say that she is not a woman scientist but a scientist that is also a woman. When she became a group leader, there were not many women in that position and Dominique herself has said that the low number of women in the field was one of the obstacles she found in her career. While the number of women in the field has increased, men still dominate, especially at high positions. Women we interviewed said that working with Dominique was empowering as a woman not because of something she said or did in particular but because just seeing another woman doing well in your field is empowering.

Throughout her career, Dominique underwent changes family-wise, going from being a mother of 2 during her postdoc, to having 3 and then 4 children as a lab head. To her, family was at the center of her choices without being a barrier and that showed us that it doesn't have to be one or another but we can do both and do it well. It was always motivating to observe her living for science even if we all knew she had a family life outside the lab.

Dominique has been an example not only to the people that worked/work with her but to anyone that has interacted with her at workshops, training courses or conferences. At the University of Geneva, she has been vice-dean for research at the Faculty of Medicine for 10 years, she is the head of the department of Microbiology and Molecular Medicine since 2020 and, since 2008, she is the director of the Graduate School Biomedical Sciences. She has also taught numerous workshops, including a Cell biology workshop in Mali in 2012 and the Biology of Parasitism (BoP) and Middle-Eastern BOP courses. During these courses, Dominique always took the time to discuss with every student and was keen to learn about their culture, career, and ambitions. Dominique is also a mentor for women outside science, as part of the Swiss-French network for mentoring women careers.

FINAL THOUGHTS

The words used by her supervisor, colleagues, former students and postdocs to describe Dominique's career, personality and research are shown on **Figure 1** but we think that more than anything we can write, some of what was shared with us better exemplify the impact she has had on all of us: "I looked for a good supervisor and

FIGURE 1 | Words used by former supervisor, colleagues, PhD students and post-docs to describe Dominique's personality, career and research.

mentor. Dominique was both from the very beginning", "I am proud to have been in her lab", "Dominique represents the person combining all the capacities to direct and lead research projects and above all the capacity to transmit these values", "Dominique has undoubtedly shaped my way of doing science", "Dominique has been the only PI who I felt really cared about her people in the lab and would ensure everyone was on the right track", "Dominique's work pushes us to do better science", "Dominique is an inspirational colleague, rigorous in her science".

We hope this essay highlights the pioneer and breakthrough work Dominique has done and continues to do but also what a role model she has been for all of us who have had the privilege to work with her. Both men and women see Dominique as a mentor and as an inspiration in the way she does science, shares her knowledge, runs the lab and is available even though she also has a family, travels frequently and has to attend to other professional obligations.

AUTHOR CONTRIBUTIONS

Both authors prepared, wrote and edited the manuscript and jointly made the figure.

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REFERENCES

Bertiaux, E., Balestra, A. C., Bournonville, L., Louvel, V., Maco, B., Soldati-Favre, D., et al. (2021). Expansion Microscopy Provides New Insights Into the Cytoskeleton of Malaria Parasites Including the Conservation of a Conoid. *PloS Biol.* 19, e3001020. doi: 10.1371/journal.pbio.3001020

Bisio, H., Chaabene, R. B., Sabitzki, R., Maco, B., Marq, J. B., Gilberger, T.-W., et al. (2020). The ZIP Code of Vesicle Trafficking in Apicomplexa: SEC1/Munc18 and SNARE Proteins. *mBio* 11, e02092-20. doi: 10.1128/mBio.02092-20

Bisio, H., Krishnan, A., Marq, J.-B., and Soldati-Favre, D. (2022). *Toxoplasma Gondii* Phosphatidylserine Flippase Complex ATP2B-CDC50.4 Critically Participates in Microneme Exocytosis. *PloS Pathog.* 18, e1010438. doi: 10.1371/journal.ppat.1010438

Bisio, H., Lunghi, M., Brochet, M., and Soldati-Favre, D. (2019). Phosphatidic Acid Governs Natural Egress in *Toxoplasma Gondii via* a Guanylate Cyclase Receptor Platform. *Nat. Microbiol.* 4, 420–428. doi: 10.1038/s41564-018-0339-8

Bisio, H., and Soldati-Favre, D. (2019). Signaling Cascades Governing Entry Into and Exit From Host Cells by *Toxoplasma Gondii*. *Annu. Rev. Microbiol.* 73, 579–599. doi: 10.1146/annurev-micro-020518-120235

Black, M., Seeber, F., Soldati, D., Kim, K., and Boothroyd, J. C. (1995). Restriction Enzyme-Mediated Integration Elevates Transformation Frequency and Enables Co-Transfection of *Toxoplasma Gondii*. *Mol. Biochem. Parasitol* 74, 55–63. doi: 10.1016/0166-6851(95)02483-2

Blumenschein, T. M. A., Friedrich, N., Childs, R. A., Saouros, S., Carpenter, E. P., Campanero-Rhodes, M. A., et al. (2007). Atomic Resolution Insight Into Host Cell Recognition by *Toxoplasma Gondii*. *EMBO J.* 26, 2808–2820. doi: 10.1038/sj.emboj.7601704

Brecht, S., Carruthers, V. B., Ferguson, D. J., Giddings, O. K., Wang, G., Jakle, U., et al. (2001). The Toxoplasma Micronemal Protein MIC4 is an Adhesin Composed of Six Conserved Apple Domains. *J. Biol. Chem.* 276, 4119–4127. doi: 10.1074/jbc.M008294200

Brecht, S., Erdhart, H., Soete, M., and Soldati, D. (1999). Genome Engineering of *Toxoplasma Gondii* Using the Site-Specific Recombinase Cre. *Gene* 234, 239–247. doi: 10.1016/S0378-1119(99)00202-4

Brown, K. M., and Sibley, L. D. (2018). Essential cGMP Signaling in *Toxoplasma* Is Initiated by a Hybrid P-Type ATPase-Guanylate Cyclase. *Cell Host Microbe* 24, 804–816.e6. doi: 10.1016/j.chom.2018.10.015

Bullen, H. E., Bisio, H., and Soldati-Favre, D. (2019). The Triumvirate of Signaling Molecules Controlling *Toxoplasma* Microneme Exocytosis: Cyclic GMP, Calcium, and Phosphatidic Acid. *PloS Pathog.* 15, e1007670. doi: 10.1371/journal.ppat.1007670

Bullen, H. E., Jia, Y., Yamaryo-Botté, Y., Bisio, H., Zhang, O., Jemelin, N. K., et al. (2016). Phosphatidic Acid-Mediated Signaling Regulates Microneme Secretion in *Toxoplasma*. *Cell Host Microbe* 19, 349–360. doi: 10.1016/j.chom.2016.02.006

Chiappino-Pepe, A., Tymoshenko, S., Ataman, M., Soldati-Favre, D., and Hatzimanikatis, V. (2017). Bioenergetics-Based Modeling of *Plasmodium Falciparum* Metabolism Reveals Its Essential Genes, Nutritional Requirements, and Thermodynamic Bottlenecks. *PloS Comput. Biol.* 13, e1005397. doi: 10.1371/journal.pcbi.1005397

Daher, W., Plattner, F., Carlier, M.-F., and Soldati-Favre, D. (2010). Concerted Action of Two Formins in Gliding Motility and Host Cell Invasion by *Toxoplasma Gondii*. *PloS Pathog.* 6, e1001132. doi: 10.1371/journal.ppat.1001132

Darvill, N., Dubois, D. J., Rouse, S. L., Hammoudi, P.-M., Blake, T., Benjamin, S., et al. (2018). Structural Basis of Phosphatidic Acid Sensing by APH in Apicomplexan Parasites. *Structure* 26, 1059–1071.e6. doi: 10.1016/j.str.2018.05.001

Di Cristina, M., Spaccapelo, R., Soldati, D., Bistoni, F., and Crisanti, A. (2000). Two Conserved Amino Acid Motifs Mediate Protein Targeting to the Micronemes of the Apicomplexan Parasite *Toxoplasma Gondii*. *Mol. Cell Biol.* 20, 7332–7341. doi: 10.1128/MCB.20.19.7332-7341.2000

Dobrowolski, J. M., Carruthers, V. B., and Sibley, L. D. (1997). Participation of Myosin in Gliding Motility and Host Cell Invasion by *Toxoplasma Gondii*. *Mol. Microbiol.* 26, 163–173. doi: 10.1046/j.1365-2958.1997.5671913.x

Dobrowolski, J. M., and Sibley, L. D. (1996). *Toxoplasma* Invasion of Mammalian Cells is Powered by the Actin Cytoskeleton of the Parasite. *Cell* 84, 933–939. doi: 10.1016/S0092-8674(00)81071-5

Dos Santos Pacheco, N., Tosetti, N., Krishnan, A., Haase, R., Maco, B., Suarez, C., et al. (2021). Revisiting the Role of *Toxoplasma Gondii* ERK7 in the Maintenance and Stability of the Apical Complex. *mBio* 12, e0205721. doi: 10.1128/mBio.02057-21

Farrell, A., Thirugnanam, S., Lorestani, A., Dvorin, J. D., Eidell, K. P., Ferguson, D. J., et al. (2012). A DOC2 Protein Identified by Mutational Profiling is Essential for Apicomplexan Parasite Exocytosis. *Science* 335, 218–221. doi: 10.1126/science.1210829

Ferguson, D. J., Brecht, S., and Soldati, D. (2000). The Microneme Protein MIC4, or an MIC4-Like Protein, Is Expressed Within the Macrogamete and Associated With Oocyst Wall Formation in *Toxoplasma Gondii*. *Int. J. Parasitol* 30, 1203–1209. doi: 10.1016/S0020-7519(00)00096-5

Frénal, K., Polonais, V., Marq, J.-B., Stratmann, R., Limenitakis, J., and Soldati-Favre, D. (2010). Functional Dissection of the Apicomplexan Glideosome Molecular Architecture. *Cell Host Microbe* 8, 343–357. doi: 10.1016/j.chom.2010.09.002

Friedrich, N., Santos, J. M., Liu, Y., Palma, A. S., Leon, E., Saouros, S., et al. (2010). Members of a Novel Protein Family Containing Microneme Adhesive Repeat Domains Act as Sialic Acid-Binding Lectins During Host Cell Invasion by Apicomplexan Parasites. *J. Biol. Chem.* 285, 2064–2076. doi: 10.1074/jbc.M109.060988

Gaskins, E., Gilk, S., DeVore, N., Mann, T., Ward, G., and Beckers, C. (2004). Identification of the Membrane Receptor of a Class XIV Myosin in *Toxoplasma Gondii*. *J. Cell Biol.* 165, 383–393. doi: 10.1083/jcb.200311137

Graindorge, A., Frénal, K., Jacot, D., Salamun, J., Marq, J. B., and Soldati-Favre, D. (2016). The Conoid Associated Motor MyoH Is Indispensable for *Toxoplasma Gondii* Entry and Exit From Host Cells. *PloS Pathog.* 12, e1005388. doi: 10.1371/journal.ppat.1005388

Hammoudi, P.-M., Maco, B., Dogga, S. K., Frénal, K., and Soldati-Favre, D. (2018). *Toxoplasma Gondii* TFP1 Is an Essential Transporter Family Protein Critical for Microneme Maturation and Exocytosis. *Mol. Microbiol.* 109, 225–244. doi: 10.1111/mmi.13981

Herm-Götz, A., Weiss, S., Stratmann, R., Fujita-Becker, S., Ruff, C., Meyhöfer, E., et al. (2002). *Toxoplasma Gondii* Myosin A and Its Light Chain: A Fast, Single-Headed, Plus-End-Directed Motor. *EMBO J.* 21, 2149–2158. doi: 10.1093/emboj/21.9.2149

Huynh, M.-H., Rabenau, K. E., Harper, J. M., Beatty, W. L., Sibley, L. D., and Carruthers, V. B. (2003). Rapid Invasion of Host Cells by *Toxoplasma* Requires Secretion of the MIC2-M2AP Adhesive Protein Complex. *EMBO J.* 22, 2082–2090. doi: 10.1093/emboj/cdg217

Jacot, D., Tosetti, N., Pires, I., Stock, J., Graindorge, A., Hung, Y. F., et al. (2016). An Apicomplexan Actin-Binding Protein Serves as a Connector and Lipid Sensor to Coordinate Motility and Invasion. *Cell Host Microbe* 20, 731–743. doi: 10.1016/j.chom.2016.10.020

Jia, Y., Marq, J.-B., Bisio, H., Jacot, D., Mueller, C., Yu, L., et al. (2017). Crosstalk Between PKA and PKG Controls pH-Dependent Host Cell Egress of *Toxoplasma Gondii*. *EMBO J.* 36, 3250–3267. doi: 10.15252/embj.201796794

Kessler, H., Herm-Gotz, A., Hegge, S., Rauch, M., Soldati-Favre, D., Frischknecht, F., et al. (2008). Microneme Protein 8–a New Essential Invasion Factor in *Toxoplasma Gondii*. *J. Cell Sci.* 121, 947–956. doi: 10.1242/jcs.022350

Kim, K., Soldati, D., and Boothroyd, J. C. (1993). Gene Replacement in *Toxoplasma Gondii* With Chloramphenicol Acetyltransferase as Selectable Marker. *Science* 262, 911–914. doi: 10.1126/science.8235614

Kloehn, J., Lunghi, M., Varesio, E., Dubois, D., and Soldati-Favre, D. (2021). Untargeted Metabolomics Uncovers the Essential Lysine Transporter in *Toxoplasma Gondii*. *Metabolites* 11, 476. doi: 10.3390/metabo11080476

Kloehn, J., Oppenheim, R. D., Siddiqui, G., De Bock, P.-J., Kumar Dogga, S., Coute, Y., et al. (2020). Multi-Omics Analysis Delineates the Distinct Functions of Sub-Cellular Acetyl-CoA Pools in *Toxoplasma Gondii*. *BMC Biol.* 18, 67. doi: 10.1186/s12915-020-00791-7

Krishnan, A., Kloehn, J., Lunghi, M., Chiappino-Pepe, A., Waldman, B. S., Nicolas, D., et al. (2020). Functional and Computational Genomics Reveal Unprecedented Flexibility in Stage-Specific *Toxoplasma* Metabolism. *Cell Host Microbe* 27, 290–306.e11. doi: 10.1016/j.chom.2020.01.002

Limenitakis, J., Oppenheim, R. D., Creek, D. J., Foth, B. J., Barrett, M. P., and Soldati-Favre, D. (2013). The 2-Methylcitrate Cycle is Implicated in the Detoxification of Propionate in *Toxoplasma Gondii*. *Mol. Microbiol.* 87, 894–908. doi: 10.1111/mmi.12139

Marchant, J., Cowper, B., Liu, Y., Lai, L., Pinzan, C., Marq, J. B., et al. (2012). Galactose Recognition by the Apicomplexan Parasite *Toxoplasma Gondii*. *J. Biol. Chem.* 287, 16720–16733. doi: 10.1074/jbc.M111.325928

Mehta, S., and Sibley, L. D. (2010). *Toxoplasma Gondii* Actin Depolymerizing Factor Acts Primarily to Sequester G-Actin. *J. Biol. Chem.* 285, 6835–6847. doi: 10.1074/jbc.M109.068155

Meissner, M., Brecht, S., Bujard, H., and Soldati, D. (2001). Modulation of Myosin A Expression by a Newly Established Tetracycline Repressor-Based Inducible System in *Toxoplasma Gondii*. *Nucleic Acids Res.* 29, E115. doi: 10.1093/nar/29.22.e115

Meissner, M., Reiss, M., Viebig, N., Carruthers, V. B., Toursel, C., Tomavo, S., et al. (2002a). A Family of Transmembrane Microneme Proteins of *Toxoplasma Gondii* Contain EGF-Like Domains and Function as Escorters. *J. Cell Sci.* 115, 563–574. doi: 10.1242/jcs.115.3.563

Meissner, M., Schlüter, D., and Soldati, D. (2002b). Role of *Toxoplasma Gondii* Myosin A in Powering Parasite Gliding and Host Cell Invasion. *Science* 298, 837–840. doi: 10.1126/science.1074553

Mital, J., Meissner, M., Soldati, D., and Ward, G. E. (2005). Conditional Expression of *Toxoplasma Gondii* Apical Membrane Antigen-1 (TgAMA1) Demonstrates That TgAMA1 Plays a Critical Role in Host Cell Invasion. *Mol. Biol. Cell* 16, 4341–4349. doi: 10.1091/mbc.e05-04-0281

Nebl, T., Prieto, J. H., Kapp, E., Smith, B. J., Williams, M. J., Yates, J. R., et al. (2011). Quantitative *In Vivo* Analyses Reveal Calcium-Dependent Phosphorylation Sites and Identifies a Novel Component of the *Toxoplasma* Invasion Motor Complex. *PloS Pathog.* 7, e1002222. doi: 10.1371/journal.ppat.1002222

Opitz, C., and Soldati, D. (2002). "The Glideosome": A Dynamic Complex Powering Gliding Motion and Host Cell Invasion by *Toxoplasma Gondii*. *Mol. Microbiol.* 45, 597–604. doi: 10.1046/j.1365-2958.2002.03056.x

Oppenheim, R. D., Creek, D. J., Macrae, J. I., Modrzynska, K. K., Pino, P., Limenitakis, J., et al. (2014). BCKDH: The Missing Link in Apicomplexan Mitochondrial Metabolism is Required for Full Virulence of *Toxoplasma Gondii* and Plasmodium Berghei. *PloS Pathog.* 10, e1004263. doi: 10.1371/journal.ppat.1004263

Pino, P., Caldelari, R., Mukherjee, B., Vahokoski, J., Klages, N., Maco, B., et al. (2017). A Multistage Antimalarial Targets the Plasmepsins IX and X Essential for Invasion and Egress. *Science* 358, 522–528. doi: 10.1126/science.aaf8675

Pino, P., Sebastian, S., Kim, E. A., Bush, E., Brochet, M., Volkmann, K., et al. (2012). A Tetracycline-Repressible Transactivator System to Study Essential Genes in Malaria Parasites. *Cell Host Microbe* 12, 824–834. doi: 10.1016/j.chom.2012.10.016

Plattner, F., Yarovinsky, F., Romero, S., Didry, D., Carlier, M.-F., Sher, A., et al. (2008). *Toxoplasma* Profilin is Essential for Host Cell Invasion and TLR11-Dependent Induction of an Interleukin-12 Response. *Cell Host Microbe* 3, 77–87. doi: 10.1016/j.chom.2008.01.001

Polonais, V., and Soldati-Favre, D. (2010). Versatility in the Acquisition of Energy and Carbon Sources by the Apicomplexa. *Biol. Cell* 102, 435–445. doi: 10.1042/BC20100005

Reiss, M., Viebig, N., Brecht, S., Fourmaux, M. N., Soete, M., Di Cristina, M., et al. (2001). Identification and Characterization of an Escorter for Two Secretory Adhesins in *Toxoplasma Gondii*. *J. Cell Biol.* 152, 563–578. doi: 10.1083/jcb.152.3.563

Salamun, J., Kallio, J. P., Daher, W., Soldati-Favre, D., and Kursula, I. (2014). Structure of *Toxoplasma Gondii* Coronin, an Actin-Binding Protein That Relocalizes to the Posterior Pole of Invasive Parasites and Contributes to Invasion and Egress. *FASEB J.* 28, 4729–4747. doi: 10.1096/fj.14-252569

Sardinha-Silva, A., Mendonça-Natividade, F. C., Pinzan, C. F., Lopes, C. D., Costa, D. L., Jacot, D., et al. (2019). The Lectin-Specific Activity of *Toxoplasma Gondii* Microneme Proteins 1 and 4 Binds Toll-Like Receptor 2 and 4 N-Glycans to Regulate Innate Immune Priming. *PloS Pathog.* 15, e1007871. doi: 10.1371/journal.ppat.1007871

Sheiner, L., Santos, J. M., Klages, N., Parussini, F., Jemmely, N., Friedrich, N., et al. (2010). *Toxoplasma Gondii* Transmembrane Microneme Proteins and Their Modular Design. *Mol. Microbiol.* 77, 912–929. doi: 10.1111/j.1365-2958.2010.07255.x

Soldati, D., and Boothroyd, J. C. (1993). Transient Transfection and Expression in the Obligate Intracellular Parasite *Toxoplasma Gondii*. *Science* 260, 349–352. doi: 10.1126/science.8469986

Soldati, D., and Boothroyd, J. C. (1995). A Selector of Transcription Initiation in the Protozoan Parasite *Toxoplasma Gondii*. *Mol. Cell Biol.* 15, 87–93. doi: 10.1128/MCB.15.1.87

Soldati, D., Kim, K., Kampmeier, J., Dubremetz, J.-F., and Boothroyd, J. C. (1995). Complementation of a *Toxoplasma Gondii* ROP1 Knock-Out Mutant Using Phleomycin Selection. *Mol. Biochem. Parasitology* 74, 87–97. doi: 10.1016/0166-6851(95)02487-5

Stanway, R. R., Bushell, E., Chiappino-Pepe, A., Roques, M., Sanderson, T., Franke-Fayard, B., et al. (2019). Genome-Scale Identification of Essential Metabolic Processes for Targeting the *Plasmodium* Liver Stage. *Cell* 179, 1112–1128.e26. doi: 10.1016/j.cell.2019.10.030

Tymoshenko, S., Oppenheim, R. D., Agren, R., Nielsen, J., Soldati-Favre, D., and Hatzimanikatis, V. (2015). Metabolic Needs and Capabilities of *Toxoplasma Gondii* Through Combined Computational and Experimental Analysis. *PloS Comput. Biol.* 11, e1004261. doi: 10.1371/journal.pcbi.1004261

Williams, M. J., Alonso, H., Enciso, M., Egarter, S., Sheiner, L., Meissner, M., et al. (2015). Two Essential Light Chains Regulate the MyoA Lever Arm to Promote *Toxoplasma* Gliding Motility. *MBio* 6, e00845-00815. doi: 10.1128/mBio.00845-15

Yadav, R., Pathak, P. P., Shukla, V. K., Jain, A., Srivastava, S., Tripathi, S., et al. (2011). Solution Structure and Dynamics of ADF From *Toxoplasma Gondii*. *J. Struct. Biol.* 176, 97–111. doi: 10.1016/j.jsb.2011.07.011

Yang, L., Uboldi, A. D., Seizova, S., Wilde, M.-L., Coffey, M. J., Katris, N. J., et al. (2019). An Apically Located Hybrid Guanylate Cyclase-ATPase Is Critical for

the Initiation of Ca2+ Signaling and Motility in *Toxoplasma Gondii*. *J. Biol. Chem.* 294, 8959–8972. doi: 10.1074/jbc.RA118.005491

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