Name	MORITZ TREECK
Position	Group Leader (2nd 6)
Year joined *(Crick or founder institute)*	2014

Career History

2009 - Phd, Bernhard Nocht Institute, Hamburg, Germany
2009 – 2014- Postdoc, Stanford University

Major Awards, Honours and Prizes

Membership of external committees, editorial boards, review panels, SABs etc

External advisor for Wellcome Trust Strategic Award, 2019

Lab Name	***Signalling in Apicomplexan Parasites Laboratory***

Research programme and achievements

My research group focuses on the interaction of two related parasites (Plasmodium falciparum and Toxoplasma gondii) with their human or animal host cell. We study how parasites exit, invade and remodel the host cells they are required to infect. We have developed novel technologies that allow us to investigate these questions in higher throughput.

Using these novel tools, we have been able to overcome major hurdles in the field. We have shown that the species-specific expansion and remodelling of human red blood cells is mediated by parasite-secreted kinases in the most virulent malaria-causing parasite, have identified for the first time that most virulence factors of Toxoplasma in a mouse act on the cell-autonomous immune response, and demonstrated that a key Toxoplasma regulator of host cell interaction is acting in a non-cell autonomous manner, leading to a new appreciation of the control of the systemic immune response by the parasite. We showed that myristoylation of a parasite-secreted protein is required for the entry into host cell; to our knowledge this is the first myristoylated protein entering the secretory pathway in any eukaryote.

In the future we will investigate how Toxoplasma is one of the most successful parasites on earth, using the CRISPR technologies we have developed to identify all virulence factors, and their genetic interactions in various hosts and cell types. We will measure how these factors influence the immune system.

For the malaria-causing parasite, we will investigate in detail how the kinases we identified modulate disease outcome on the molecular level, and investigate their function in host-pathogen interaction in endemic countries through the analysis of field isolate data and studies on infected red blood cells directly from patients.

Research outputs

Broncel, M., Dominicus, C., Vigetti, L., Nofal, S. D., Bartlett, E. J., Touquet, B. et al. & Treeck M. (2020) ***Profiling of myristoylation in Toxoplasma gondii reveals an N-myristoylated protein important for host cell penetration*****. Elife 9:e57861. DOI: 10.7554/eLife.57861**
In this study we describe the Toxoplasma myristoylated proteome, validate inhibitors of P. falciparum N-Myristoyl-transferases to be potent against Toxoplasma and identify N-Myristoylation on a parasite-secreted protein. This is the first description of myristoylation on a secreted protein important for cell-cell interaction.

Davies, H., Belda, H., Broncel, M., Ye, X., Bisson, C., Introini, V. et al. & Treeck M. (2020) ***An exported kinase family mediates species-specific erythrocyte remodelling and virulence in human malaria*****. Nat Microbiol 5, 848-863. DOI: 10.1038/s41564-020-0702-4**
We demonstrate species-specific remodelling of red blood cells by the most virulent malaria-causing parasite, mediated by a species-specific expansion of an exported kinase family. Systematic deletion of all 20 members and quantitative phosphoproteomics identifies the kinase targets and supports their role in pathogenesis.

Hunt, A., Russell, M. R. G., Wagener, J., Kent, R., Carmeille, R., Peddie, C. J. et al. & Treeck M. (2019) ***Differential requirements for cyclase-associated protein (CAP) in actin-dependent processes of Toxoplasma gondii*****. Elife 8:e50598. DOI: 10.7554/eLife.50598**
Toxoplasma, as many other related pathogens, has a limited set of actin regulators. Here we demonstrate that complex actin regulation can be achieved by partially overlapping functions of actin regulators. We demonstrate a role for the actin regulator CAP in host cell invasion and maintenance of parasite integrity during division.

Tiburcio, M., Yang, A. S. P., Yahata, K., Suarez-Cortes, P., Belda, H., Baumgarten, S. et al. & Treeck M. (2019) ***A novel tool for the generation of conditional***

***knockouts to study gene function across the Plasmodium falciparum life cycle*. mBio 10(5):e01170-19. DOI: 10.1128/mBio.01170-19**
We generate the first malaria parasite line that enables conditional gene deletions across the full lifecycle. This is a major advance to probe the "dark boxes" of parasite biology in the mosquito host and human liver stages and paves the way for drug target validation and production of attenuated parasites for vaccination studies.

Young, J., Dominicus, C., Wagener, J., Butterworth, S., Ye, X., Kelly, G. et al. & Treeck M. (2019) *A CRISPR platform for targeted in vivo screens identifies Toxoplasma gondii virulence factors in mice*. Nature communications 10, 3963. DOI: 10.1038/s41467-019-11855-w
We devised a flexible CRISPR platform to generate mutant Toxoplasma pools for tailored genetic screens and used it in vivo for the first time to identify novel effector proteins that ensure parasite survival. We show that known virulence factors are separated by their function in this screen.