

**20th Molecular Parasitology Meeting
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The Molecular Parasitology Meeting is held annually at Woods Hole, MA. This year the conference was organised for the 20th time between September 13th and 17th. This meeting is one of the leading general parasitology meetings in the world, covering aspects of parasite molecular biology, cell biology, biochemistry, genetics and genomics, focusing on protozoan parasites.

Young post-docs and PhD students are especially encouraged to present at the meeting, so that they are given an opportunity to present their results, which are usually unpublished. This fact creates a possibility to discuss and constructively criticise the presented data and future experiments in a creative, friendly environment of students, post-docs and field experts.

The meeting consisted of ten sessions. The "Illicit trafficking" session was arguably the one of highest interest, since the work presented on *Plasmodium* and *Toxoplasma* parasite species revealed some facts about the transport machinery of the Apicomplexan parasites. The so called translocon is of particular notice since it enables the parasites for surface localisation of pathogenicity-related antigens and receptors initiating signaling cascades crucial for proper function of all cellular processes occurring in the parasite. The surface molecules are therefore important for parasite pathology and survival, as well as to "sensing" the host environment conditions and interaction with host cell receptors. Recent studies showed that most *Plasmodium* proteins exported to the host red blood cell (RBC) contain the *Plasmodium* export element (PEXEL). Identification of exported proteins might also be based on the presence of one or more transmembrane domains (TMs) targeting a particular protein to membrane structures such as parasitophorous vacuole (PV) or RBC membrane. One study presented at the MPM meeting by Christof Gruring has shown that a TM domain from a previously characterised membrane protein does not necessarily confer membrane localisation to another protein, as shown by fusion studies. This finding indicates that the translocon system is more complex than previously believed, and involves several levels of regulation.

The MPM meeting provided an excellent opportunity for me to present my data. Upon submitting an abstract I have been selected to give an oral presentation on the unexpected essential function of uniformly conserved sirtuin protein SIR2A in the mosquito stage of *Plasmodium berghei* life cycle. I have received several interesting comments and suggestions about my work. Several other presented data inclined me to perform additional experiments which might be helpful in understanding the specific function of SIR2A, which has so far been elusive. I have made contact with several research groups, asking for useful antibodies and protocols for further experiments.

An unexpected role of SIR2A in the life cycle of malaria parasites

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Malaria parasites are able to evade the host immune system through altering the surface antigen repertoire expressed primarily from subtelomeric locations. The process of shuffling the surface molecules, called antigenic variation, contributes to parasite survival in their hosts. Regulation of antigenic variation includes epigenetic mechanisms such as post-translational modifications. In *Plasmodium falciparum* a widely conserved SIR2 (PfSIR2-13 or PfSIR2A) histone deacetylase plays a crucial role in the regulation of multigene families (e.g. *var* genes) involved in antigenic variation. A second, more diverged SIR2 orthologue, SIR2B, exists in *P. falciparum*. Targeted deletion of either *Pfsir2a* or *Pfsir2b* caused transcriptional up-regulation of distinct types of *var* genes in the early asexual blood stages. SIR2A and SIR2B orthologues exist in all sequenced *Plasmodium* species, including the rodent model malaria parasite *P. berghei*. We have generated *P. berghei* lines lacking expression of either PbSIR2A or PbSIR2B and uniquely mutants lacking expression of both proteins. *In vivo*, in the mouse model, no gross alterations were observed in asexual blood stage growth, multiplication and virulence of all 3 mutants. Global transcriptome analysis of asexual blood stages of the double deletion mutant (*Pbsir2a-/Pbsir2b-*) exhibited deregulation of members of subtelomeric gene families (*bir*, *Pb-fam*) implicated in the process of antigenic variation. Unexpectedly, development of parasites lacking PbSIR2A was completely blocked in the mosquito host at the ookinete-to-oocyst transition level. Using mutant parasites expressing a GFP-tagged PbSIR2A protein we found an unexpected peripheral localisation at the apical end of the ookinete. Moreover, light microscopy analysis of ookinetes suggests an aberrant apical complex formation. These results imply that SIR2A might play a role during invasion/traversal of the ookinete of the midgut wall. Currently we are analysing the critical role for *Pbsir2a* during ookinete motility, midgut barrier traversal and early oocyst formation.