**Presentation title:** Decoding the code of duty: “Ring stage *Plasmodium falciparum* alters microRNA/mRNA of brain and lung endothelium”

**Corresponding Author name:** Nahla Galal Metwally

**Affiliation:** Bernhard Nocht Institute for Tropical Medicine

**Email ID’s:** metwally@bnitm.de

**Presentation type:** Oral presentation

**Abstract:**

**Decoding the code of duty: “Ring stage *Plasmodium falciparum* alters microRNA/mRNA of brain and lung endothelium”**

Nahla Galal Metwally1,8,\*,⊗, Maria del Pilar Martinez Tauler1,⊗, Hanifeh Torabi1,⊗, Johannes Allweier⊗, Sara Mohamed1, Maryèva Bessemoulin1&5, Philip Bouws1, Fatima Al Shaikh1, Yifan Wu1, Milad Temori1, Tabea Schell1, Maximillian Rakotonerinalalao1, Katharina Höhn2, Dániel Cadar3, Thomas Jacobs4,Holger Heine6 and Iris Bruchhaus1&7

1 Research group Host Parasite Interaction, 2Cellular Parasitology Department, 3 Arbovirology Department, 4 Research group Protozoa Immunology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany. 5University of Strasbourg and CNRS, Strasbourg, France, 6Research Center Borstel, Leibniz Lung Center, Borstel, Germany, 7 Biology Department University ofHamburg, Hamburg, Germany

8Lead author

\*Correspondence

⊗These authors contributed equally

Malaria infection is known to severely compromise endothelial cells (EC). The pathogenic consequences of ECs activation might lead to organ failure and death. The organ-specific response of the endothelium has not been described in detail. It is not known whether microRNAs play a specific role in the complications of severe malaria, although microRNAs control 60% of the genes expressed in the human body.

In this study, we report microRNA candidates that are specifically expressed in both ECs types and their secreted extracellular vesicles (EVs). We were able to show that shear stress plays a role in the switching on of variable signaling pathways in brain ECs, such as IL-8 signaling and tight junctions. Specific miRNAs that we found to be differentially expressed in the ECs seem to control these pathways. Incubation with ring stage infected red blood cells (iRBCs) results in activation of endocytic pathways in brain ECs. In contrast, in lung cells, the most prominent activated pathway was the electron transport pathway which was found to be activated in immune cells during inflammation. Data analysis showed that endocytosis and electron transport pathways were targeted by some miRNA candidates. These miRNAs were significantly altered after 8 hours of coincubation with ring stage iRBCs at a shear stress of 1.5 dyne/cm2.

We hypothesize that EC dysfunction is a precursor to severe malaria complications. This disrupts the balance between vasoconstriction and vasodilation, predisposing to cytoadhesion of iRBCs, endothelial proliferation and blood brain barrier leakage. Certain miRNA candidates may be involved in the control of these events within ECs. Through cell-to-cell communication between iRBCs and ECs, these miRNAs can sense the presence of iRBCs and thus stimulate the initiating signaling pathways to respond to infection. Thus, we consider the miRNAs to be “*the code of duty*” for the initial immune response in the cells.