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Title: *Plasmodium falciparum* impaired invasion of glucose-6-phosphate dehydrogenase deficient red blood cells due to underexpression of beta-spectrin

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Introduction

Malaria still is a major cause of death and morbidity worldwide and it has long been interacting with the human host. Malaria has been exerting a selective pressure on the human genome and helps to maintain higher-than-expected frequency of human red blood cell (RBC) polymorphisms. RBC variants such as sickle-cell anaemia and glucose-6-phosphate dehydrogenase (G6PD) deficiency have been shown to confer protection against severe malaria.

It is generally considered that these RBC polymorphisms confer protection mainly by causing impaired growth of parasites in the host RBC or due to enhanced removal of mutant RBCs in the spleen. However, studies have shown that parasite invasion might also be impaired, which was demonstrated in our lab: parasites invading and growing in G6PD-deficient RBCs revealed impaired invasion (maturation seemed to be normal).

Objectives

Our goal is to study the effect of G6PD-deficient RBCs on parasite development by:

1. Assessing parasite invasion and maturation of *P. falciparum* in deficient and normal RBCs;

2. Analysing proteomic profile of uninfected and infected RBCs as well as of parasites;

3. Comparing parasite invasion and maturation of normal and calpain-supplemented RBCs.

Methods

Our study analysed *P. falciparum in vitro* invasion and growth. Furthermore, we obtained quantitative proteomics data regarding parasite and host RBC proteomes.

We later maintained *P. falciparum* cultures in control RBCs and in RBCs incubated with CaCl2, in order to promote calpain activation (a Ca2+-dependent cysteine) and spectrin degradation. We also assessed parasite invasion and maturation in these cultures and compared parasite and RBC protein extracts by SDS-PAGE.

Results

Invasion and maturation assays indicated reduced parasite invasion of G6PD-def RBCs. Proteomics results seemed to show that important proteins of the RBC membrane (spectrin and ankyrin) are underexpressed and might be responsible for parasite impaired invasion.

Incubation of normal RBCs in CaCl2-supplemented medium also led to reduced parasite invasion.

Conclusion

We plan to validate these results with further studies and by obtaining complementary metabolomics information to better understand host-parasite dynamics and the mechanisms associated with RBC polymorphisms (particularly G6PD-deficiency) that provide protection against malaria.

References

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