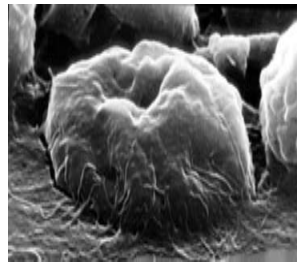

Genetic identification of *Plasmodium falciparum* parasite virulence markers

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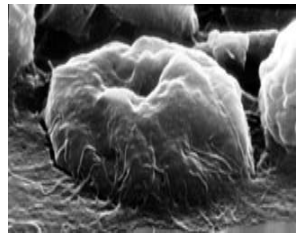
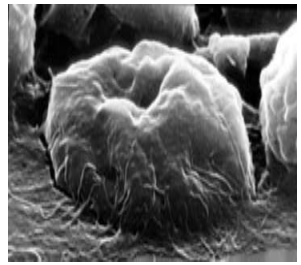
Objectives



- Our aim is to identify loci, gene(s) and genotypes of *P. falciparum* associated with pathogenicity and severe malaria.

- Chart parasite genotypes - clinical phenotypes association and identify one or more parasite genetic markers of pathogenicity

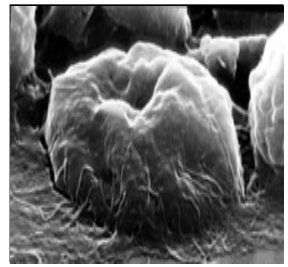
Methods (1)



- A combined epidemiological, clinical and genetic analysis of *P. falciparum* isolates from uncomplicated clinical malaria (UCM) and different severe clinical malaria (SM) cases.

- UCM and SM cases will be recruited in three countries (Mali, Cameroon and Gabon) according to the WHO criterias.

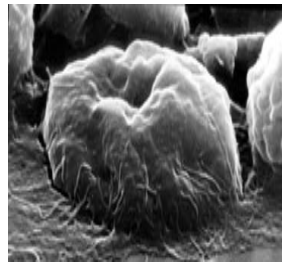
Methods (2)



- *P. falciparum* genotypes will be compared according to severity and clinical presentation.

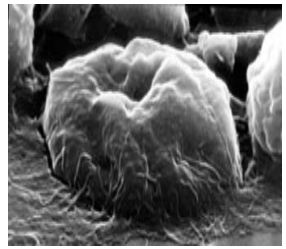
- Parasite loci associated with pathogenicity will be identified using a genome wide gene mapping approach.

Results (1)



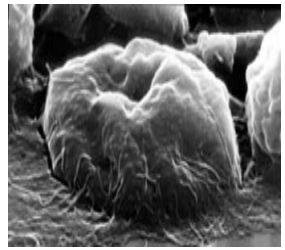
- Association test between clinical status and parasite genotypes (covariates: human genetic factors, drug use and parasite drug sensitivity).
- Identification of some genes and their genotypes.
- Characterization of parasite genetic factors involved in the pathogenesis of human SM.

Results (2)



- The polymorphism is causative or likely in Linkage disequilibrium (LD) with a causative mutation.
- Determination of LD blocks and susceptibility haplotypes.
- Thus, only associated polymorphims independently the ones of the others will give an association which will remain significant.

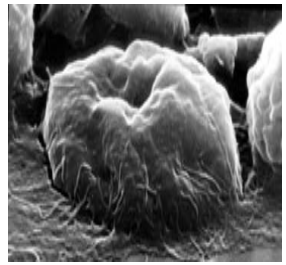
Discussion & Conclusions



- The research findings (a prognosis factor) may benefit clinical decision-making process in allowing early identification of mild clinical cases that are more susceptible to become severe.

- They may also benefit decision-making process for drug or vaccine development: parasite genetic factors significantly associated to pathogenesis should be taken into account in efficacy analysis of drug/vaccine clinical trials to avoid misleading conclusions, e.g. rejecting malaria vaccines or treatments that are effective against some parasite strains and not others.

Future perspectives



- To see if the identified genes and their genotypes have also an impact on immunological phenotypes outcome to better understand the physiopathological mechanisms of disease and to set up the new targets for therapeutic intervention through the development of new tools such as vaccine and to adjust the efficacy analysis of drug/vaccine clinical trials for parasite genetic factors