Abstract 1

Modeling malaria genomics reveals transmission decline and rebound in Senegal

We sampled over 1,000 malaria parasites from Senegal between 2006 and 2013 using the molecular barcode. We found many monoinfections in this population and several clonal parasite infections. These data indicate that we can use molecular barcode to look for highly related parasites. We then looked at the genetic signatures among the population and found that there were highly related samples among the population. We also did a linkage analysis and showed that there were distinct networks of parasite types in the sample population. We also noticed an increase in the frequency of highly related networks present in later years, indicating that malaria transmission had decreased. These findings match other data from the National Malaria Control Program in Senegal that indicate malaria transmission is decreased. Thus, our data can be used to model malaria transmission patterns in many different malaria endemic settings. We will present our findings during the scientific session showing how the molecular barcode can model malaria transmission.

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Abstract 2

Modeling malaria genomics reveals transmission decline and rebound in Senegal

We examined a set of 1,007 *Plasmodium falciparum* samples collected in Thiès, Senegal between 2006 and 2013 in order to study the effects of malaria-control interventions on parasite population genomics. We genotyped these parasite samples using our 'molecular barcode' of 24 single-nucleotide polymorphisms and observed that about 35% of the single-genome samples grouped into subsets with identical barcodes, varying in size by year and even persisting across dry seasons. The barcodes also formed networks of related groups that were similar to those also identified by analysis of 164 completely sequenced parasites that revealed extensive sharing of genomic regions. In at least two cases we found first-generation recombinant offspring of parents whose genomes were similar or identical to genomes also present in the sample. We applied an epidemiological model that tracks parasite genotypes and reproduced these patterns of barcode subsets. Quantification of likelihoods in the model strongly suggests reduced transmission from 2006-2010, with a significant rebound in Thiès in 2012-2013. The reduced transmission and rebound was directly confirmed by incidence data from Thiès and was not found in Senegal overall. These findings imply that intensive intervention to control malaria results in rapid and dramatic changes in parasite population genomics. The results also suggest that genomics combined with epidemiological modeling may afford prompt and continuous tracking of progress toward malaria elimination.

Abstract 3

Modeling malaria genomics reveals transmission decline and rebound in Senegal

We genotyped over 1,000 malaria infections collected from patients in Senegal between 2006 and 2013 for both drug resistance markers and for signatures of population structure. Over this time we found a decrease in MOI and increase in clonality, but no evidence of K13 mutations that are associated with drug resistance. Mutations in pfcrt (K76T) were either the same or increased over time, but there were differences in pfmdr1 mutations with a decrease in the N86Y and N1042D mutations and an increase in the Y184F mutation. The K76T mutation was associated with amodiaquine and chloroquine reistance as well as artemisinin sensitivity. The N86Y and N1042D mutations were associated with decreased artemisinin sensitivity, but did not change in response to amodiaquine and chloroquine. At the same time these changes in drug resistance were occurring, the population structure was decreasing, and there were more genetically related parasites. While there was no evidence of K13 mutations related to artemisinin resistance found among these parasites, we were able to identify a number of mutations including the A578S mutation. We think that the decrease in population structure indicates that interventions like use of antimalarial drugs are still effective. This is consistent with finding no evidence of K13 mutations associated with artemisinin resistance since the main drug used to treat malaria in Senegal is Coartem, which contains artemisinin. We are testing the samples collected in 2014 and 2015 and will present our updated data on drug resistance marker typing and population structure typing.