ACT treatment failure and resistance gene variants in African Plasmodium falciparum

As we near the end of a second decade of widespread artemisinin combination therapy (ACT) use for treating human malaria, there are signs of waning efficacy in some African settings. Evidence to date suggests the parasite factors linked to ACT treatment failure in Asia, such as K13 variants and markers of piperaquine drug failure, have not themselves spread to Africa. Rather, a suite of variant *Plasmodium falciparum* loci, experimentally linked to reduced artemisinin susceptibility *in vitro*, are under scrutiny in African parasite populations. These include not only *pfk13* variants, but also variant alleles of *pfcoronin*, *pfk10*, *pfubp1* and *pfap2mu*. I will present recent molecular, epidemiological and *in vitro* data and attempt to provide some mechanistic insights that could help us understand the emerging complexity of the genetic polymorphisms underlying reduced artemisinin susceptibility. Finally, the importance of such variant loci in resistance surveillance will be considered.

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