



Anopheles gambiae species complex and gene transfer

What is gene flow?

Gene flow is the introduction of genetic material (by interbreeding) from one population of a species to another, or between different species. Cross-mating between species (hybridisation) does not necessarily lead to gene flow unless fertile hybrids are found in the progeny.

What is the *Anopheles gambiae* species complex?

- The *Anopheles gambiae* species complex is a group of closely related species: *An. gambiae*, *An. coluzzii*, *An. arabiensis*, *An. melas*, *An. merus*, *An. bwambae*, *An. quadriannulatus* and *An. amharicus*. Collectively these are known as *An. gambiae* s.l.
- Target Malaria only works with *An. gambiae*, *An. coluzzii* and *An. arabiensis*, which are the most important malaria vectors in the complex. These are the only *An. gambiae* s.l. species that are found at the field sites where we are working in Burkina Faso, Mali and Uganda.
- *An. melas* and *An. merus* are also vectors of malaria, but have lower vectorial capacity, and are only found along coastal regions of west and east Africa respectively.

- *An. bwambae* is a malaria vector but has a very small geographical distribution: it is only found in hot springs in Uganda.
- *An. quadriannulatus* and *An. amharicus* are not malaria vectors, and mainly bite animals.
- It is not possible to visually distinguish among species of *An. gambiae s.l.*, so genetic methods are used to identify the species.

Can you have hybridisation between species?

- In the laboratory, all *An. gambiae s.l.* species will cross-mate and produce viable eggs. Egg hatching rate is lower than for matings within the same species, and some combinations of species result in a skewed sex ratio towards males. With the exception of *An. gambiae* x *An. coluzzii*, male hybrid offspring are sterile. Female hybrids are fertile but typically have reduced fertility compared with the parent female.
- *An. gambiae* and *An. coluzzii* mate freely under laboratory conditions and produce fertile offspring of both sexes.

Do the species hybridise in the wild?

- In nature there are pre-mating barriers (such as single-species swarms and different habitat preferences) that restrict hybridisation. In addition, some species (*An. melas*, *An. merus*, *An. quadriannulatus*, *An. amharicus* and *An. bwambae*) do not overlap in their distributions, so will never meet and mate.
- *An. gambiae* and *An. coluzzii* do hybridise in the wild. Genetic evidence shows that first generation hybrids (F1 hybrids) are usually found at a frequency of ~1%, although in Guinea Bissau, in the far west of the species distributions, it can be higher. The low frequency of hybrids in most locations is due to assortative mating i.e. both species prefer to mate with their own species.
- Genes that confer a fitness advantage will spread between *An. gambiae* and *An. coluzzii*. For instance, *kdr*, an insecticide resistance mutation, has passed from *An. gambiae* into *An. coluzzii*. It is possible that a gene drive construct will move between the two species, even if it does not confer any fitness advantage. Both of these species are important malaria vectors, so in this context gene flow would be desirable. If it does not occur naturally, we may transfer the construct by hybridisation in the lab.
- *An. gambiae* and *An. coluzzii* also hybridise with *An. arabiensis* in the wild. First generation (F1) hybrids have been found at very low frequencies (0.02-0.76%) in both East and West Africa. It is unclear whether these hybrids lead to gene flow or are a genetic 'dead end', but one study found evidence of gene flow between *An. gambiae* and *An. arabiensis* in Uganda. Further work is being done as part of the Ag1000G project to look at the extent of hybridisation and gene flow in other countries. At the moment there is no convincing evidence that insecticide resistance genes have moved between these species.
- F1 hybrids of other *An. gambiae s.l.* species have been identified in the wild (such as *An. gambiae* x *An. melas* and *An. gambiae* x *An. bwambae*). These hybrids occur at extremely low frequencies. Again, it is unclear to what extent hybridisation results in gene flow between the species, and there is no evidence of insecticide resistance genes passing between the species.
- Mosquitoes outside the *An. gambiae* complex are too distantly related to mate with species within the complex and transfer genes. The most closely related species outside the *An. gambiae* complex is *An. christyi*, which is separated from *An. gambiae s.l.* by ~9 million years of evolution. This species exists in highland areas of East Africa. It is morphologically and genetically distinct from *An. gambiae s.l.* species. Genetic analysis has shown that gene flow does not occur between *An. gambiae s.l.* species and *An. christyi* (unpublished data from Fontaine et al. 2015).

Summary:

1. Gene flow is possible between any species of the *An. gambiae* species complex.
2. Despite this, most of the *An. gambiae* s.l. species rarely hybridise, and some species never meet, so gene flow is generally very low or zero in the wild.
3. The exception to this is *An. gambiae* and *An. coluzzii*; there is gene flow between these species when they occur at the same location.
4. There is no detectable gene flow between species of the *An. gambiae* complex and any other mosquito species, including other species that are found in Africa.

Selected references:

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