Gene Drives: Target Malaria is underestimating the risks

Plans for releases of transgenic mosquitoes are based on flawed data

17 March 2023 / The Target Malaria consortium has for several years been planning to conduct field trials using genetically engineered mosquitoes in Burkina Faso. The aim is to transfer artificial gene constructs, i. e. the so-called 'X-shredder', into wild populations of the mosquitoes. This gene construct is meant to reduce the number of female offspring, and thus bring about a decline in the overall population of mosquitoes (*Anopheles gambiae*) known to transmit malaria. However, as recent research shows, the planned releases are based on flawed data and incorrect assumptions.

After results from caged trials published in 2019 and 2020 seemed promising, the consortium announced plans for releases. However, in 2022, it became known that the plans were based on incorrect assumptions: after in-depth analysis, the Target Malaria experts had to conclude that the artificial genes were integrated into a different chromosome than the one they had previously assumed. The actual site of insertion may also need to be examined more closely, as this genomic region (near the centromeres) can have implications for the overall stability of the genome.

Target Malaria also made incorrect assumptions about the risk of gene flow to other species: although the strain of mosquitoes used in the trials has for decades been classified as *Anopheles gambiae*, it is now thought to be a hybrid between *Anopheles gambiae* and another species, *Anopheles coluzzii*. Again, this has major implications for risk assessment: Target Malaria had assumed that gene flow from the genetically engineered insects (*A. gambiae*) to another species (*A. coluzzii*) would be unlikely. However, if a hybrid strain was used for the trials, no such conclusions can be drawn on the likelihood of further gene flow.

In this context, it is also worrying that recently published results from 'X-shredder' experiments with the species A. coluzzii revealed unexpected genomic divergence within the offspring of the transgenic mosquitoes. This underlines the difficulty of correctly assessing the consequences of potential gene flow prior to any releases. Indeed, there are at least nine 'sibling species' of Anopheles mosquitoes that can cross with each other, six of them are also known to transmit Malaria.

The example of the 'X-shredder' shows that any predictions about the risks of releasing genetically engineered mosquitoes may be easily compromised by false assumptions, e. g. about the gene insertion site, the effects of gene flow or hybridisation. Consequently, what might start out as a small field trial, may end with the uncontrolled spread of an artificial genetic element within wild populations, causing long-term unexpected and potentially harmful effects. In this context, the expected benefits are also highly questionable.

The 'X-shredder' is intended to be a test case for the follow-up release of so-called 'gene drive' mosquitoes, which inherit gene constructs that can spread much faster in natural mosquito populations by overriding the natural mechanism of heredity. The 'X-shredder', which was developed in 2014, is not considered to be a gene drive. Nevertheless, the gene construct introduced into wild populations is meant to be passed on to several generations of mosquitoes.

Testbiotech has compiled the findings from recent publications in a backgrounder for the secretary of the Convention of Biological Diversity (CBD), who is currently preparing discussions on the risk assessment of gene drives to be held in the coming months. Testbiotech is, therefore, calling for planned releases of the 'X-shredder' and gene drives meant to spread within the mosquito populations to be stopped.

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Further information: Testbiotech backgrounder on risk assessment of gene drives [2]
Testbiotech backgrounder on horizon scanning of Synbio organisms [3]

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