A CRISPR-based gene drive system to suppress populations of malarial mosquitoes

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Abstract

Synthetic gene drive systems using site-specific endonucleases to spread traits into a population, at rates much faster than simple Mendelian genetics, were first proposed more than a decade ago. Such gene drive systems have huge potential for transforming populations of insect pests and disease vectors in ways that are beneficial for human health and over meaningful timeframes. The advent of CRISPR-Cas9 has brought this possibility closer to fruition due to the adaptability and activity of this enzyme in being engineered to recognise virtually any sequence in a wide range of organisms. We have engineered a gene drive system designed to cause population suppression in the principle mosquito vector of malaria by using CRISPR-based driving constructs to target and disrupt genes with confirmed roles in female fertility. We see close to 100% transmission rates of the CRISPR drive alleles in each generation (instead of the 50% expected from Mendelian inheritance) and a rapid increase in frequency over subsequent mosquito generations in a caged experiment leading to a drastic decrease in the reproductive output. These results provide the basis for the development of a gene drive system that has the potential to substantially reduce mosquito populations to levels that would not support malaria transmission. Moreover, our approach is broadly applicable to a range of invasive pests and vectors of disease

Keywords: CRISPR

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