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CRISPR vs. Malaria: How Gene drives are rewriting the rules of disease control

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Malaria persists as a continuous health threat in many countries especially in sub-Saharan Africa, where vaccines and insecticides are not effected due to resistance and limited coverage. CRISPR based gene drives offer a new method that can either reduce mosquito population or stop them from spreading the disease. Technological improvements like split derive and recorded rescue genes have enhanced safety and control. However, there are concerns that it might affect the ecosystem in some way. With careful planning and more research transitions can be made from laboratory to field use

Keywords: CRISPR-Cas9, Malaria control, Gene derive, *Plasmodium* Transmission

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INTRODUCTION

The Unrelenting Burden of Malaria: Why New Solutions Are Urgently Needed

Malaria is the deadliest infectious illness to public health, particularly in sub-Saharan Africa, where it affects children under the age of five. Despite decades of vector control and medicinal therapies, mosquito-borne illness continues to claim 600,000 lives per year [8]. Because of pesticide resistance in mosquito populations, growing prices, and implementation difficulties, the efficacy of conventional treatments is declining, implying an urgent need for alternative ways. CRISPR gene drive technology is a new method for modifying mosquito genomes and reducing malaria transmission at its roots [1].

How CRISPR Gene Drives Work

Through CRISPR-Case9 technology, the natural ways of traits inheritance are manipulated, and this is the basic principle behind CRISPR gene derive. Typically, each parent gets 50% chance to inherent particular gene to offspring. But in a gene derive system, it is ensured by the scientist that targeted gene not only copied onto the homologous chromosome but also inherited across generations so that trait spread through population [6]. To control malaria, this technique can reduce mosquito population or modify them in such a way that their capacity to transmit *Plasmodium* is lost.

The two strategies that are used for these purposes are named as: population suppression and population modification. In population suppression mosquito population is drastically reduce population by disrupting reproductive genes such as doublesex (dsx), responsible for female development and fertility. After altering this gene, the ability of female mosquitoes to bite or lay eggs is diminished which causes population to shrink overtime [7]. On the other hand, in population modification, mosquitos reproduce normally but they cannot spread malaria. They carry modified genes that are involved in the expression of anti-*Plasmodium* peptides and prevent the parasite from completing life cycle in vector. The malaria resistant trait becomes more widespread by mating of these modified mosquitoes with wild population and there is no risk of species extinction [2].

From Theory to Reality: Laboratory Successes

The concept of gene derive has moved from theory to reality through several groundbreaking experiments. In 2015, Gantz and collogues created a genetically modified *Anopheles stephensi* that included antimalarial antibodies and a fluorescent marker gene. These genes stopped the parasite *Plasmodium* falciparum to transmit under lab conditions [3]. But unfortunately, resistance developed in the mosquitoes, Carballar-Lejarazu *et al*. (2020) tackle this by inserting a vital gene along the antimalarial elements. This help the mosquito to stay healthy along with successful inheritance of gene.

Split design system has been designed to address the concerns related to uncontrolled spread of modified gene in wild population. In this system, Cas9 (cutting enzyme) and guide RNA (guide Cas9 to the target gene), the two main components of CRISPR are divided so that they inherited independently. By this self-propagating nature of the drive becomes limited and it gives better control during experiment. It is tested and proved by scientist that split drives could work in semi field environment and reduce the mosquito population by more than 90% without harming the environment [1].

Preparing for Real-World Deployment

To real world use, scientist have started mathematical modeling to assess that how gene drive work outside the lab. A modal suggested that a gene drive targeting *Anopheles gambiae* could reduce 95% population across West Africa within four years assuming the climate and atmosphere constant and ideal [7]. But in real ecosystem, which is dynamic, there are many factors that could affect the outcome. To investigate the model, researchers conducted large scale trials in 2023 and the results suggest that the models may hold in practice [4].

Important ethical questions arise over deliberate eradication or alternation of species because every creature play role in ecosystem. Though, the mosquitoes are not considered as keystone species but their removal could effect food web. Cartagena Protocol on Biosafety have been established for the safe and responsible use of gene drives [7; 9].

The Future of Malaria Control

To fight malaria effectively, CRISPR gene drives could be integrated with existing public health tools. Immunity against *Plasmodium* is generated by vaccines such as RTS,S/AS01 and the more recent R21. Moreover, gene drive (which target the mosquito vector itself) offer a complementary solution. The combination of vaccine and gene derives can tackle the parasite and its vector at the same time [5]. Similar genetic tools are investigated to fight with other diseases like Zika, Dengue and Lyme disease by researchers and broadening the horizon for genetic interventions in global health [9].

CONCLUSION

To sum up, CRISPR-based gene drives are an innovative development in the fight against vector-borne diseases. The technology's aptitude to severely reduce or even eradicate malaria programs makes it one of the most significant tools ever found for public health, even though it is still undergoing rigorous evaluation and improvement. The next era will be life-threatening.

In order to get closer to a world free of malaria, we must determine whether these artificial genetic invasions can spread from controlled environments into the wild.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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