Making lab and field progress towards the development of gene drive mosquitoes for malaria control in Africa

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- VCWG RBM Meeting
Target Malaria: who we are

• A not-for-profit research consortium, including:
  • Scientists from a wide range of disciplines i.e. molecular biologists, medical entomologists, population biologists, modellers and social scientists
  • Risk, regulatory, project management, communications, and stakeholder engagement experts
  • Teams from Africa, Europe, and North America
• A vision: To develop and share new, cost-effective and sustainable genetic technologies to modify mosquitoes and reduce malaria transmission
• Values: Excellence, co-development, evidence-driven, open & accountable
International support to innovation in vector control – AU and WHO

• Gene drive research is encouraged by the African Union (AUDA-NEPAD, 2018)

• Oct- 2020  WHO position statement encouraging research on innovative vector control tools including genetically modified mosquitoes
Recent Progress
Sterile Male (Non Gene Drive)  
Read more

Male Bias (Non Gene Drive)  
Read more

Male Bias & Female Fertility (Gene Drive)  
Read more
Small scale release of non gene drive genetically modified mosquitoes

- July 1, 2019 in the Village of Bana in Burkina Faso
- Permission from the National Biosafety Agency and from the Ministry of Environment
- Agreement from the community of Bana after several years of engagement
- The release had two main learning objectives:
  - to estimate the daily survival rate of male mosquitoes of the sterile male strain,
  - to understand the nature of their dispersal in and away from the release village.
- It also aimed at building a dialogue with the authorities and affected communities about genetic approaches to malaria control.
Results from the release of non gene drive genetically modified mosquitoes

- 20-day daily recapture and 7 months of monitoring
- Recaptured in swarms (important for reproduction)
- Recaptured inside homes for shelter
- Did not disperse beyond the release village boundaries and less mobile than wild-type
- Did not survive as long as their released non-modified siblings.
- Complete disappearance
- Scientific publications coming up (on entomology, laboratory and stakeholder engagement)

Next step: import of non gene drive genetically modified male bias mosquitoes by Burkina Faso and Uganda after regulatory approvals
Important progress in risk assessment

- Systematic identification of plausible pathways to potential harm
- Building on the results of a series of NEPAD workshops with African regulators and other workshops organized by FNIH
- Based on simulated release of the *doublesex* gene drive mosquito strain in West Africa
- Uses “problem formulation”, a rigorous scientific analysis
- Initial step in Environmental Risk Assessments
- Identified 46 potential pathways to harm to 4 “protection goals”: human health, animal health, biodiversity and water quality.
- Most common potential harms: increased human or animal disease transmission
- Will inform the next stages of an environmental risk assessment, a critical component of a regulatory dossier
Developing a first candidate gene drive mosquito QFS2 – *doublesex* gene

• Targets 2 locations in the *doublesex* gene with CRISPR-Cas9
• Homozygous females completely sterile and cannot bite
• Heterozygous females fertile and low fitness cost
• Successful population suppression in small cages at Imperial College London (Crisanti Lab)
• Testing in large cages at PoloGGB in Italy ongoing to verify population suppression in closer to nature conditions
• Based on previous *doublesex* strain with single target (Kyrou et al 2018)
• Potential candidate for the first Target Malaria gene drive
Capacity building in Africa

- Training
- Infrastructures

Insectary in Uganda
Lab and offices in Burkina Faso
Lab in Mali
Offices in Mali
For more information

- Website https://targetmalaria.org/
- Twitter @TargetMalaria
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