Considering the Risks and Rewards of Synthetic Biology

Student name: Rachel Polfer
Project advisor: Amy Camp

While *Plasmodium* parasites are ultimately the cause of malaria in humans, efforts to combat the spread of the disease often identify mosquito populations as effective targets for disruption of the pathogen's cycle of transmission. Female *Anopheles* mosquitos are central to the parasite's life cycle, functioning as vectors that carry the disease from one human to another. Progress has been made toward the development of *Plasmodium*-resistant mosquitoes with diminished potential to act as vectors, and in recent studies, transgenic *Plasmodium falciparum* resistant *Anopheles* mosquitoes carrying antipathogen effector genes have been successfully engineered[1]. In subsequent studies, a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-associated protein 9 (Cas9)-mediated gene drive system with the capacity to spread the relevant genes throughout a given mosquito population was developed[2]. This system has the potential to significantly and positively contribute to efforts aiming to disrupt the spread of malaria. However, there are risks involved in deploying such a system, and further research is necessary to understand the potential environmental, ethical, and social impact of gene-drives before their release into the environment may be considered.

CRISPR-based gene drive systems, such as the one described above, are one of many technologies being developed within the emerging field of Synthetic Biology. Many of the technologies being explored represent opportunities for substantial benefits, but there are still significant risks involved. In the case of CRISPR-based gene drive systems, daisy drive systems have been proposed in attempts to mitigate the systemic risks associated with the technology's deployment. In this presentation I will explore the biochemistry underlying both traditional gene drives and daisy drives, and investigate the potential for daisy drive systems to capture the benefits of traditional gene drive systems, while mitigating the associated risks.

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[1] Isaacs A.T., Li F., Jasinskiene N., Chen X., Nirmala X., Marinotti O., Vinetz J.M., James A.A. 2011. Engineered resistance to *Plasmodium falciparum* development in transgenic *Anopheles stephensi*. *PLoS Pathog*. 7(4): e1002017.

[2] Gantz V.M., Jasinskiene N., Tatarenkova O., Fazekas A., Macias V.M., Beir E., James A.A. 2015. Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito *Anopheles stephensi*. *PNAS.* 112(49): e6736-e6743.