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FIGHTING MALARIA USING PARATRANSGENIC VECTORS USING ENGINEERED ENTEROBACTER CLOACAE EXPRESSING DEFENSIN

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Enterobacter cloacae bacterium is a known symbiont of most *Anopheles* gut microflora and nominated as a proper candidate for paratransgenic control of malaria. Here, we describe a strategy that uses symbiotic bacteria to deliver anti-malaria effector molecule to the midgut lumen, thus rendering host mosquitoes refractory to malaria infection. *Enterobacter cloacae* was engineered to secrete defensin, a natural plant anti-*Plasmodium* effector protein. The engineered *E. cloacae* inhibited oocyst

formation of the rodent malaria parasite *Plasmodium berghei* by up to 92.8% in *Anopheles stephensi*. Significantly, the proportion of mosquitoes carrying parasites (prevalence) decreased by up to 75%. Interestingly, the wild strain of *E. cloacae* could inhibit oocyst formation by up to 72%. These findings provide the foundation for the use of either wild or genetically modified *E. cloacae* bacteria as a powerful tool to combat malaria.

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