

MEETING ABSTRACTS

THE SEARCH FOR RESISTANCE-BREAKING AND SPECIES-SELECTIVE MOSQUITOCIDAL INHIBITORS OF *Anopheles gambiae* AChE

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The widespread deployment of insecticide-treated bednets (ITNs) in sub-Saharan Africa has led to a dramatic decline in malaria mortality. However, wide-spread and growing resistance of *Anopheles gambiae* mosquitoes to the pyrethroid class of voltage-gated Na⁺ channel modulators used on these nets jeopardizes this achievement, and has prompted the search for suitable insecticidal AChE inhibitors to replace pyrethroids. Such compounds would have three favorable characteristics: excellent contact toxicity towards susceptible adult *An. gambiae*, good contact toxicity to those that bear the G119S resistance mutation of AChE, and very weak inhibition of human AChE.¹ We will review our work on the development of aromatic and heterocyclic core methyl and dimethylcarbamate AChE inhibitors,² and including both enzymatic inhibition potencies and mosquito contact toxicities. Finally, the inhibition selectivities of particular compounds will be rationalized in the context of our recently obtained high resolution X-ray structures of G119S *An. gambiae* AChE.³

Keywords: mosquito; malaria; carbamate; resistance; G119S

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References

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