

## MEETING ABSTRACTS

# STRUCTURAL STUDIES OF *Anopheles gambiae* ACETYLCHOLINESTERASE PROVIDE INSIGHT TOWARDS IMPROVED INSECTICIDES FOR MALARIA VECTOR CONTROL

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Malaria is transmitted by the *Anopheles gambiae* mosquito in sub-Saharan Africa and tropical regions where the disease is prevalent. Indoor spraying with anticholinesterase insecticides is a proven method to control populations of the mosquito and to reduce spread of the disease; however, widespread use of insecticides has led to the rise of an insecticide-resistant G119S mutant acetylcholinesterase in the mosquito which threatens ongoing disease-control efforts. We have solved high resolution X-ray structures of the G119S mutant acetylcholinesterase of *An. gambiae* (G119S AgAChE), in the ligand-free state and in complex with a potent difluoromethyl ketone inhibitor, revealing the structural basis of insecticide resistance<sup>2</sup>. Although resistance-breaking inhibitors of G119S AgAChE exist, they also inhibit human acetylcholinesterase and thus lack the necessary species selectivity to be safely used as insecticides. In our structures, we see specific features within the active site gorge, including an open “back door”, that are distinct from human acetylcholinesterase. These differences provide a means for improving species-selectivity in the rational design of improved insecticides for malaria vector control.

**Keywords:** *acetylcholinesterase; structure; malaria; insecticide*

## References

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