

## MEETING ABSTRACTS

# EXPLORING THE EVOLUTIONARY POTENTIAL OF THE $\alpha$ E7 CARBOXYLESTERASE

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The evolution of insecticide resistance is a model system for studying enzyme evolution. Three insect species have independently evolved catalytic organophosphate (OP) detoxification through a single active-site mutation in the  $\alpha$ E7 carboxylesterase. To explore the evolutionary potential of  $\alpha$ E7, we subjected  $\alpha$ E7 from the sheep blowfly to nine rounds of mutation and screening. The final variant contained 11 mutations which increased the rate of OP-hydrolysis more than 1000-fold. Atomic resolution X-ray crystal structures of the evolutionary intermediates reveal the changes in structure and dynamics at each step in the evolutionary trajectory, and hint at the molecular basis for the increased rate of OP hydrolysis. This work explores the potential for the development of  $\alpha$ E7 as an enzyme therapeutic for OP poisoning, and worryingly for insecticide resistance, this work suggests that more efficient OP detoxification could be readily acquired by insect pests.