# Anticipating and Combating the Challenge of Insecticide Resistance

**Dr Peter Mabbitt, Australian National University, 2017**

Insect pests spread disease and destroy crops. The ability to control the populations of pest insects through the use of insecticides has improved the lives of people around the world. The agricultural sector is important to Australia's economy; the sector creates employment for over 1.6 million Australians. Insecticide use is essential to protect Australia's crops and livestock. Worryingly, there are over 500 reported instances of insects gaining resistance to insecticides. In order to combat this resistance we need to understand, at the molecular level, how insects detoxify insecticides.

We have investigated the molecular basis of insecticide resistance in the sheep blowfly. An enzyme in the sheep blowfly, known as alpha-esterase 7 (E7), has changed function so that it detoxifies organophosphate-insecticides. The function changing mutation results in insecticide resistance and has spread to over 90 % of the blowfly population. We have used x-ray crystallography to look at the three-dimensional structure of E7 and to understand the mechanism by which OP-insecticides are detoxified. We discovered that parts of the enzyme move in order for it to efficiently break down insecticides and that by fine-tuning these movements there is potential for E7 to become better at detoxifying insecticides. To predict the mutations that could lead to increased insecticide resistance we used laboratory directed evolution. We found that only a few mutations are required for E7 to become more efficient at breaking down insecticides, suggesting that it is plausible that increased resistance will evolve in wild blowfly populations. Given the possibility that E7 will become a more efficient insecticide-detoxifying enzyme, we have begun to design and test new insecticides that prevent E7 function and will therefore restore the sheep blowfly's sensitivity to existing insecticides.