Poster Presentation

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Combating Multi-Herbicide resistance in Weeds with New GST Inhibitors

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Multiple herbicide resistance (MHR) in black grass (Alopecurus myosuroides) is a global problem which results in a loss of chemical control of black grass weeds in crops. MHR is associated with an enhanced ability to detoxify xenobiotics and has been linked to the expression of a phi class glutathione-s-transferase (GST), AmGSTF1 (1). When this GST is expressed in Arabidopsis thaliana the transgenic plants developed resistance to multiple herbicides (2).

A ligand fishing approach using AmGSTF1 immobilised on a streptactin column was used to identify potential ligands that bind to the protein. From this process a number of lead compounds were identified and variations produced on these using synthetic chemistry. Compounds were tested using a 1-Chloro-2,4-dinitrobenzene (CDNB) assay which measures the activity of the GST. Percentage inhibition was measured using this assay with compounds at 1, 10 and 100 μM to test efficiency of inhibitors.

Work has now focussed on using biophysical techniques, including thermal shift assays to confirm ligand binding to the AmGSTF1 as well as to identify and aid with conditions for crystallisation, in addition to surface plasmon resonance and microscale thermophoresis to further characterise ligand binding. The apo AmGSTF1 has successfully been crystallised and the crystals diffracted to a resolution of 2.0 Å. The structure was solved by Molecular Replacement from 1AXD Maize GSTF1. This structure has been used for initial computational docking studies of the ligands into the protein using GOLD. As two disordered loops regions exist in our structure we have created a chimeric structure in which the structure of the loops have been taken from the 1AXD maize GSTF1 to allow us to complete preliminary docking studies to assess feasibility of binding poses.

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