Towards the Development of Herbicides Targeting Lysine Biosynthesis

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Summary Herbicide resistance is one of the biggest threats to our natural environment and agricultural industry. The rapid emergence of herbicide-resistant weeds has been driven by repeated application of the same herbicides, combined with a lack of new herbicides entering the market in the past 30 years. Therefore, we urgently require herbicides with new modes of action to tackle the herbicide resistance crisis we are facing. Although many commercial herbicides inhibit the biosynthesis of amino acids in plants, the lysine biosynthesis pathway is yet to be exploited as a herbicide target. Our goal is therefore to validate lysine biosynthesis enzymes as herbicide targets and develop inhibitors of these enzymes as novel herbicide leads. To achieve this, we are characterising the structure and function of plant lysine biosynthesis enzymes using enzyme kinetic assays, circular dichroism spectroscopy, analytical ultracentrifugation and X-ray crystallography. We are developing small molecule inhibitors of several of these enzymes, with screening being conducted in vitro using biochemical assays, as well as in planta against *Arabidopsis thaliana*. The herbicidal efficacy of lead inhibitors against weeds is being validated against the most problematic weed in Australia, *Lolium rigidum*. The relationship between lead inhibitor mechanisms and physiological outcomes is being probed using X ray crystallography, toxicity assays, and systems biology. This work has the potential to provide novel herbicide modes of action to help combat the global herbicide resistance crisis.

Keywords Herbicide-resistance, lysine, amino acid biosynthesis, herbicide, enzyme, ryegrass