7th International Conference on Biochemistry and Molecular Biology

S3-K-02

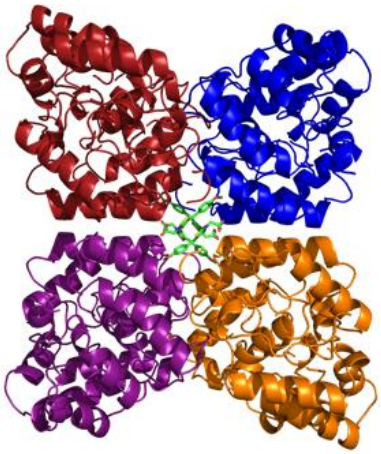
Towards Novel Herbicide Modes of Action by Inhibiting Lysine Biosynthesis in Plants

Cody J. Hall [1], Santosh Panjikar [2], Belinda M. Abbott [3], Anthony R. Gendall [4], Matthew A. Perugini [1] and Tatiana P. Soares da Costa [1,*]

[1] Department of Biochemistry and Genetics, La Trobe Institute for Molecular Science, La Trobe University, Bundoora, VIC 3086, Australia; 18608535@students.latrobe.edu.au, 17694478@students.latrobe.edu.au
[2] Australian Synchrotron, ANSTO, 800 Blackburn Road, Clayton, VIC 3168, Australia; santoshp@ansto.gov.au
[3] Department of Chemistry and Physics, La Trobe Institute for Molecular Science, La Trobe University, Bundoora, VIC 3086, Australia; B.Abbott@latrobe.edu.au
[4] Department of Animal, Plant and Soil Sciences, AgriBio, La Trobe University, Bundoora, VIC 3086, Australia; T.Gendall@latrobe.edu.au
* Correspondence: T.SoaresdaCosta@latrobe.edu.au; Tel.: +61 3 9479 2227.

Abstract: Weeds are becoming increasingly resistant to our current herbicides, posing a significant threat to agricultural production. Therefore, new herbicides are urgently needed. In this study, we exploited a novel herbicide target, dihydrodipicolinate synthase (DHDPS), which catalyses the first and rate-limiting step in lysine biosynthesis. Using a high throughput chemical screen, we identified the first class of plant DHDPS inhibitors that have micromolar potency against *Arabidopsis thaliana* DHDPS isoforms. Employing X-ray crystallography, we determined that this class of inhibitors binds to a novel and unexplored pocket within DHDPS, which is highly conserved across plant species. We also demonstrated that the inhibitors attenuated the germination and growth of *A. thaliana* seedlings and confirmed their pre-emergence herbicidal activity in soil-grown plants. These results provide proof-of-concept that lysine biosynthesis represents a promising target for the development of herbicides with a novel mode of action to tackle the global rise of herbicide resistant weeds.

Graphical abstract:



Keywords: lysine; herbicides; enzymes; weeds

Funding: This research was funded by the Australian Research Council (DE190100806, DP150103313 and IH180100006).