Re-engineering amino acid metabolism in wheat grain using CRISPR/Cas9

Supervisory team:
Rothamsted supervisor: Prof Nigel Halford (Rothamsted Research)
Academic supervisor: Dr Gary Barker (University of Bristol)
Dr Andy Bailey (University of Bristol), Dr Vladimir Nekrasov (Rothamsted Research), Dr Caroline Sparks (Rothamsted Research), Dr David Withall (Rothamsted Research)

Host institution: Rothamsted Research (Harpenden)
Submit applications for this project to the University of Bristol

Project description:

Lysine is an amino acid that most animals, including humans, cannot make and so must acquire through their diet. Unfortunately, cereal grains contain low concentrations of lysine, resulting in nutrient deficiency in humans and farm animals, such as pigs and chickens, that are dependent on cereal grain for their nutrition. This has resulted in imported soybeans taking much of the market for pig and chicken feed manufacture in the UK and EU, while in developing countries, lysine deficiency is a major cause of malnutrition in people who are reliant on cereal grains for their protein intake. Lysine deficiency does not occur in people in developed countries because they can acquire lysine from meat, but current levels of meat consumption are unsustainable. Reducing our dependence on meat will require the development of a sustainable and readily-available global supply of plant-sourced lysine, which will be unachievable without major changes to global agri-food systems, unless cereals can be re-engineered to accumulate higher concentrations of lysine in their grains. Lysine is synthesised from another amino acid, aspartate, via a multistep biochemical pathway. The key control point is a reaction catalysed by the enzyme DHDPS, which is feedback-inhibited by lysine.

The student will perform genome editing, using CRISPR/Cas9 and a DNA-repair template, via homology-directed repair to edit a wheat DHDPS gene so that the enzyme it encodes no longer binds lysine. The student will do this in wheat that has already been edited and has high concentrations of aspartate in the grain, using selection agents to identify plants containing a lysine-insensitive DHDPS. These agents include a lysine analogue that competes with lysine for incorporation into proteins, and compounds that inhibit DHDPS itself. These compounds will have to be synthesised and the student will have the support of a synthetic chemist as well as plant molecular biologists and Rothamsted's Cereal Transformation Team, making the project genuinely multidisciplinary. Crucially, the inhibitors bind DHDPS over the lysine binding site and changes that render DHDPS lysine-insensitive will also make it resistant to the inhibitors.

The student will grow the edited wheat to maturity, characterise the editing events that have occurred and measure the concentration of lysine and other amino acids in the grain. The student will also investigate the effects of deregulating DHDPS on other aspects of amino acid metabolism, in particular the synthesis of other amino acids derived from aspartate.