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Regulation, functional significance and potential manipulation of lysine metabolism in plants

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Lysine is an important essential amino acid for humans and non-ruminant livestock. Lysine amounts are limited in most major crop plants, particularly because one of the lysine biosynthesis enzymes, dihydrodipicolinate synthase, is feedback inhibited by lysine. Successful overproduction of lysine in plant seeds has been possible by seed-specific expression of bacterial genes encoding a lysine-insensitive bacterial dihydrodipicolinate synthase. However, lysine overproduction was also associated with increased levels of saccharopine and α-amino adipic acid, two metabolites of lysine catabolism (Fig. 1). In order to explore possibilities to reduce lysine catabolism in plant seeds, we have studied the molecular and biochemical regulation of this pathway. Our results suggest that lysine catabolism is a super-regulated metabolic pathway, which may serve multiple functions in plants. To test the functional significance of lysine catabolism in plants we have isolated a knockout mutant within the gene encoding the bifunctional enzyme lysine-ketoglutarate reductase/saccharopine dehydrogenase, which comprises the first two enzymes in the lysine catabolism pathway (Fig. 1). The morphology of the knockout mutant is indistinguishable from the wild-type plant under normal growth conditions, but it possesses significantly higher lysine levels in the seeds. We are currently testing the potential biotechnological significance of this knockout mutant, as well as of other mutants in which lysine catabolism is reduced specifically in the seeds by a RNAi co-suppression approach.

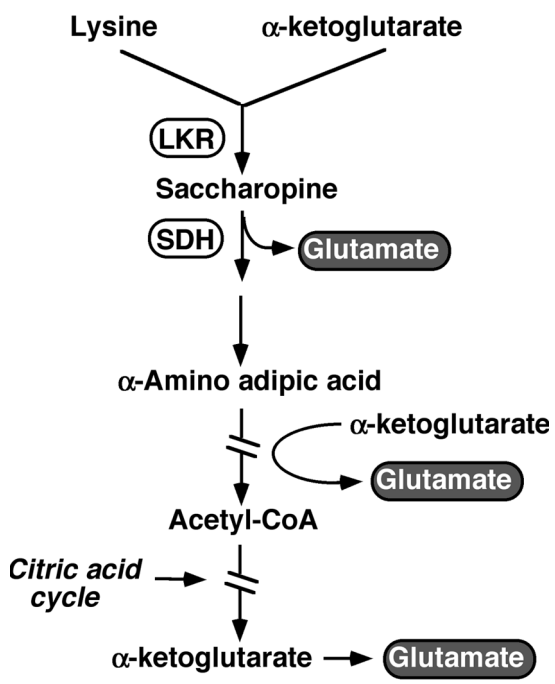

Fig. 1 *The lysine catabolism pathway and metabolites derived from it. Abbreviations: LKR, lysine ketoglutarate reductase; SDH, saccharopine dehydrogenase. Not all enzymes are indicated. Broken arrows represent several non-specified enzymatic reactions. The three glutamate residues that can be produced form a single lysine molecule are illustrated in shaded boxes.*

The lysine catabolism pathway is not only used to control lysine homeostasis in plant cells. In some plant tissues, as well as under some stress conditions, This pathway is also being used to generate glutamate, an important signaling molecule in plant development and response to stress. This process is regulated by novel transcriptional, post-transcriptional and post-translational controls of the expression of the LKR/SDH gene. Lysine catabolism into glutamate is important for mammalian brain function via glutamate receptors. Plants also possess homologues of animal glutamate receptors whose function is just beginning to emerge.

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