Synthesis of D-3-Phenyllactic Acid by D-2-Hydroxy Acid Dehydrogenases

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D-2-hydroxy acid dehydrogenases (D-2-HADHs), including D-lactate dehydrogenases (D-LDHs), reduce 2-oxo acids into corresponding D-2-hydroxy acids, yet they have presented lower activities toward 2-oxo acids with bulky C_3 functional groups. Four putative D-2-HADHs from lactic acid bacteria have been selected based on their amino acid sequences and investigated for catalytic activities on the reduction of phenylpyruvate (PPA) to D-3-phenyllactic acid (PLA). The enzyme from *Pediococcus claussenii* has shown the highest catalytic efficiency and substrate selectivity for the PPA over pyruvate. Structural and mutational studies of the enzyme have revealed that it belongs to the D-LDH family, and phenylalanine at the position 51 stabilized PPA binding. The structural information obtained has also been applied to mutate the D-LDH from *Pediococcus acidilactici*, whose wild-type has a tyrosine at the same position. The resulting *P. acidilactici* D-LDH Y51F mutant, as well as Y51L and Y51M, had over 138-fold increase in catalytic efficiency than the wild-type. Activities for other substrates such as 2-oxobutyrate and 3-methyl-2-oxobutyrate, have also increased in the Y51F mutant.