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Metagenomic opine dehydrogenases – expanding the enzymatic toolbox for reductive aminations

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PURPOSE OF THE ABSTRACT

Opine dehydrogenases (EC 1.5.1.X) are metabolic enzymes found in various species across the tree of life that perform the reductive coupling of pyruvate and amino acids yielding opine products[1]. These chiral secondary amine dicarboxylic acid derivatives represent a valuable class of compounds for the synthesis of bioactive molecules such as peptidomimetics[2]. However, the use of these enzymes as industrial biocatalysts for reductive amination is often restricted by their narrow substrate scope. The only reported example CENDH (N-(1-D-carboxyethyl)-L-norvaline dehydrogenase) was therefore extensively engineered to meet industrial needs [3]. Our study aimed at expanding this underexplored enzyme class by metagenome mining. Metagenomes from extreme environments are often able to provide enzymes with superior properties and altered substrate specificities[4]. Here we report the discovery of 6 novel metagenomic opine dehydrogenases (mODHs). These enzymes exhibit unique substrate specificity and higher thermostability compared to known examples (Figure 1). The feature that they preferably utilize negatively charged polar amino acids is so far unprecedented for opine dehydrogenases. While they still suffer from a relatively narrow substrate scope, their enhanced thermostability and the orthogonality of their substrate preference makes them a valuable addition to the toolbox of enzymes for reductive aminations. In addition, enzymatic reductive aminations with highly polar amines are very rare in the literature, our work contributes to filling that gap.

FIGURES

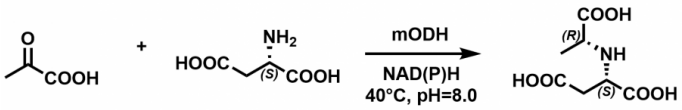

FIGURE 1

FIGURE 2

Figure 1

Representative reaction catalysed by the novel metagenomic opine dehydrogenases

KEYWORDS

biocatalysis | opine dehydrogenases | metagenome mining | reductive amination

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