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TOPIC(s) : Enzyme discovery and engineering

## Expanding the portfolio of native Amine Dehydrogenases by extensive biodiversity screening

### AUTHORS

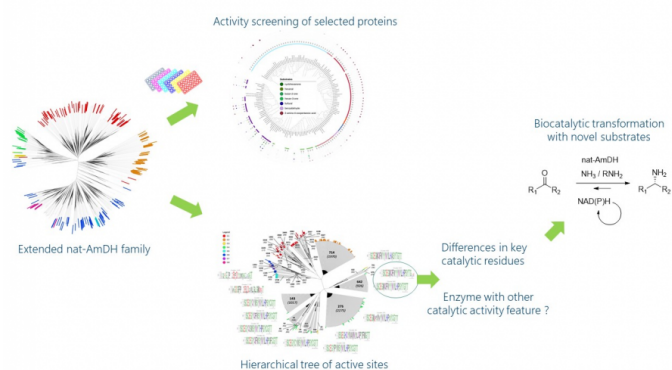
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### PURPOSE OF THE ABSTRACT

In the course of the discovery of biocatalysts for amine production, interest in oxidoreductases has grown, particularly for enzymes catalyzing the NAD(P)H-reductive amination of ketones with ammonia to primary chiral amines. Previously restricted to engineered  $\alpha$ -aminoacid dehydrogenases, this enzymatic toolbox has been recently extended by the discovery of genes coding for native AmDHs (nat-AmDHs) by our group[1] [2], in addition to reductive aminases and engineered  $\alpha$ -deaminating L-lysine dehydrogenase.

Following the preliminary success of identification of other nat-AmDHs among metagenomic databases[3], a deep exploration of available sequenced biodiversity has been conducted. This gave rise to an extended nat-AmDH family of 17k sequences for which representative enzyme products were experimentally tested for reductive amination activity. The exploration of their active site diversity based on an Active Site Modelling and Clustering analysis[4], supported by crystallographic structures[2] [5] and 3D-models, led to the discovery of homologs with key structural variations that will be highlighted. Biocatalytic transformations with novel ketone and amine substrates will also be detailed (Figure 1). Furthermore, we will briefly present the in silico strategy carried out to isolate new distant homologs among a generated pool of  $\sim 20M$  NAD(P)-binding protein sequences, using HMM-HMM profile comparison. This work is supported by the Agence Nationale de la Recherche through the MODAMDH (ANR-19-CE07-0007) and ALADIN (ANR-21-ESRE-0021) projects.

## FIGURES



**FIGURE 1**

Identification of key enzymes among the extended nat-AmDH-family  
no legend

**FIGURE 2**

## KEYWORDS

amine dehydrogenases | biodiversity screening | metagenomic data | in silico analysis

## BIBLIOGRAPHY

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