BIOTRANS
LA ROCHELLE 2023

N°772 / PC
TOPIC(s) : Enzyme discovery and engineering / Biocatalytic cascade reactions

Exploring the substrate spectrum of two Adenosylcobalamine dependent thermostable ribonucleotide reductases

AUTHORS

Lobna ELTOUKHY / TU DRESDEN, ZELLESCHER WEG 20B, DRESDEN
Corresponding author : Christoph LODERER / christoph.loderer@tu-dresden.de

PURPOSE OF THE ABSTRACT

Deoxyribonucleotides are relevant molecules for medical and biotechnological applications. The synthesis of deoxyribonucleotides for biotechnological purposes requires an enzymatic cascade ending with reduction by ribonucleotide reductase enzymes. In vivo, ribonucleotide reductases are indispensable for all living cells as they provide the elementary segments for DNA biosynthesis and repair (1, 2). The project aims to investigate the substrate specificity of two Adenosylcobalamin-dependent ribonucleotide reductases to discover their potential for biotechnological applications.

T..maritima NrdJ (3) and TV74 NrdJm (4) were tested for their substrate specificity and capacity to reduce three categories of ribonucleotides: natural canonical, natural non-canonical, and non-natural non-canonical.

The capacity of Thermotoga maritima NrdJ for reducing nucleotides diphosphates and TV74 NrdJm for reducing nucleotides triphosphate was different and mainly dependent on the type of nucleotide and the effector.

The broad substrate specificity of both enzymes implies that we can incorporate them in further biological cascades to produce various deoxyribonucleotides di-and triphosphates relevant in medicine or other scientific fields.

FIGURES

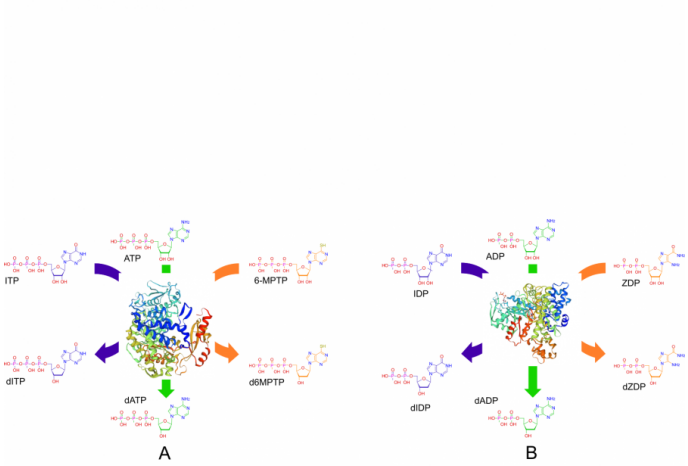

FIGURE 1

Structures of enzymes and used ribonucleotides di-and triphosphates

Figure 1: A. TV74 Nrdjm, B. T.maritima Nrdj reducing the three categories of the nucleotides natural canonical(ATP, ADP), natural non-canonical (ITP/IDP), non-natural non-canonical (6-MPTP, ZDP).

FIGURE 2

KEYWORDS

ribonucleotide reductases | non-canonical ribonucleotides | substrate specificity | deoxyribonucleotides

BIBLIOGRAPHY

1. Lundin, D.; Berggren, G.; Logan, D. T.; SjÖberg, B.-M. The origin and evolution of ribonucleotide reduction. Life (Basel, Switzerland) [Online] 2015, 5 (1), 604-636.

2. Nordlund, P.; Peter Reichard. Ribonucleotide Reductases [Online] 2006.

3. Larsson, K.-M.; Logan, D. T.; Nordlund, P. Structural basis for adenosylcobalamin activation in AdoCbl-dependent ribonucleotide reductases. ACS chemical biology [Online] 2010, 5 (10), 933-942.

4. Loderer, C.; Holmfeldt, K.; Lundin, D. Non-host class II ribonucleotide reductase in Thermus viruses: sequence adaptation and host interaction. PeerJ [Online] 2019, 7, e6700.