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Data Article

Data on PAGE analysis and MD simulation for the interaction of endonuclease Apn1 from *Saccharomyces cerevisiae* with DNA substrates containing 5,6-dihydrouracil and 2-aminopurine

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**Abstract**

This article presents new data on nucleotide incision repair (NIR) activity of apurinic/apyrimidinic endonuclease Apn1 of *Saccharomyces cerevisiae*, which is known as a key player of the base excision DNA repair (BER) pathway, see “Yeast structural gene (APN1) for the major apurinic endonuclease: homology to *Escherichia coli* endonuclease IV” [1], “Abasic sites in DNA: repair and biological consequences in *Saccharomyces cerevisiae*” [2] and “Characterisation of new substrate specificities of *Escherichia coli* and *Saccharomyces cerevisiae* AP endonucleases” [3]. The characterization of NIR activity of wild type Apn1 and mutant form Ape1 H83A were made by denaturing PAGE analysis, and MD simulations of Apn1 complexed with DNA containing 5,6-dihydro-2'-deoxyuridine (DHU) and 2-aminopurine (2-aPu) residues. This data article is associated to the manuscript titled “Apurinic/
apyrimidinic endonuclease Apn1 from *Saccharomyces cerevisiae* is recruited to the nucleotide incision repair pathway: kinetic and structural features" [4].

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### Specifications table

| Subject area                        | Biochemistry                                      |
|-------------------------------------|---------------------------------------------------|
| More specific subject area          | Structural enzymology, enzymatic catalysis        |
| Type of data                        | Text file, graph, autoradiograph, figure, movie   |
| How data was acquired               | Data was obtained using PAGE assay, stopped-flow technique, non-linear regression fitting and MD simulation |
| Data format                         | Analyzed data                                     |
| Experimental factors                | Used DNA is 12mer duplex containing damaged nucleotide DHU or abasic site and fluorescent 2-aminopurine residue located upstream/downstream of damaged site |
| Experimental features               | Interaction of WT or H83A Apn1 with substrate DNA was analyzed by denaturing 20% PAGE MD simulation was performed in the AMBER 14 MD modeling software with GPU accelerated code |
| Data source location                | Institute of Chemical Biology and Fundamental Medicine of Siberian Branch of the Russian Academy of Sciences, 8 Lavrentyev Ave., Novosibirsk, 630090, Russian Federation |
| Data accessibility                  | Data are available with this article              |
| Related research article            | [4] E.S. Dyakonova, V.V. Koval, A.A. Lomzov, A.A. Ishchenko, O.S. Fedorova, The role of His-83 of yeast apurinic/apyrimidinic endonuclease Apn1 in catalytic incision of abasic sites in DNA, Biochim. Biophys. Acta 1850 (2015) 1297–1309, [https://doi.org/10.1016/j.bba_gen.2015.03.001](https://doi.org/10.1016/j.bba_gen.2015.03.001) |

### Value of the data

- The data of MD simulation provide information for the structures of WT Apn1 complexed with NIR substrates, containing 5,6-dihydouracil and 2-aminopurine residues.
- The data illustrates that efficiency of NIR catalysis driven by Apn1 depends strongly on the spatial structure of DNA-substrates.
- The data could be useful guidelines for further design of new anti-fungal and anti-malarial agents as much as yeast Apn1 belongs to Endo IV family, which members are not found in mammalian cells, but are present in many microorganisms.

### 1. Data

Data reported here describe the features of nucleotide incision repair (NIR) of DNA catalyzed AP-endonuclease by Apn1 from *Saccharomyces cerevisiae* as revealed from kinetic studies and MD simulation analysis.
1.1. How is optimization of obtained data (kinetic traces) using stopped-flow technique executed?

To optimize the kinetic scheme, which would describe the kinetic traces obtained by stopped-flow technique [4], the proposed mechanisms should be examined by adding a gradual stage of the enzyme–substrate complex transformation, with replot and analysis of residuals being carried out. Global nonlinear least-squares fitting of the data obtained was performed in the DynaFit software (BioKin Ltd., USA) [5]. The scree test was conducted for validation of the proposed kinetic scheme (Fig. 1). Two- or three-step binding mechanisms describing Apn1’s interaction with substrate DHU(2-aPu) in BER buffer are represented as Schemes 1 and 2, respectively.

1.2. The influence of Mg2+ concentration

Dependence of AP endonuclease activities of WT or H83A Apn1 on Mg2+ ion concentration was tested using 12mer DNA duplexes containing tetrahydrofuran analog of AP site (F), and downstream mispaired 2-aPu residue. The main difference of NIR and BER buffers is 5 mM Mg2+ ions presence or absence, respectively (Fig. 2).

1.3. The assay of NIR activity of Apn1 wt AND and H73A in the case of DNA substrate containing 2-aminopurine upstream to DHU

PAGE assay of NIR activities of WT Apn1 or H83A Apn1 during the interaction with DNA duplex containing upstream 2-aminopurine residue of DHU (Fig. 3). Experiments were carried out in BER or NIR buffer. ODN duplex (2-aPu)DHU is 5’-d(CTCT(2-aPu)(DHU)CCTTCC)-3’ complemented with 5’-d(GGAAGGCCGAG)-3’.

Fig. 1. The scree test for the scheme describing WT Apn1 interaction with substrate DHU(2-aPu) in BER buffer. Oligodeoxyribonucleotide (ODN) duplex DHU(2-aPu) is 5’-d(CTCT(DHU)(2-aPu)CCTTCC)-3’ complemented with 5’-d(GGAAGCCGAG)-3’. Concentrations of WT Apn1 and ODNs were 2.0 and 1.5 μM, respectively. Root mean standard deviations (R.M.S.D.) of the residuals after fitting to an n-step binding model are plotted versus n. The number of steps corresponding to the beginning of the shallow-slope (scree) region appears to be the minimal number for adequately describing the binding.

Scheme 1. Kinetic scheme of the interaction of Apn1 with substrate DHU(2-aPu), containing two binding steps.
1.4. The influence of Zn$^{2+}$ ion concentrations on interaction of Apn1 WT and H83A with (2-aPu)DHU

Experiments on reactivation of Apn1 forms during the interaction with substrate (2-aPu)DHU were conducted under different Zn$^{2+}$ ion concentrations in the reaction solution (Fig. 4.).
1.5. Study of NIR activity of WT Apn1

NIR activity of WT Apn1 was recorded by stopped-flow technique [4] (2-aPu fluorescence intensity detection) or monitored using denaturing PAGE (Fig. 5).

1.6. Molecular dynamics simulations of WT Apn1 complexed with DNA containing DHU

In this MD simulation, a WT Apn1 molecule contained three Zn$^{2+}$ ions and was complexed with duplex DHU. Oligodeoxyribonucleotide duplex DHU is 5'-d(CTCTC(DHU)CCTTCC)-3' complemented with 5'-d(GGAAGGGGAGAG)-3'. Fig. 6 demonstrates MD movie for WT Apn1 complexed with substrate DHU. In Fig. 7 distance changes between the N3 atom of the DHU residue and the side chain oxygen of Asn-279 in molecular complex Apn1–DHU during 45 ns MD simulation are presented. General characteristics of MD simulations of Apn1 complexed with the DHU, DHU(2-aPu) or (2-aPu)DHU duplex are illustrated in Figs. 8 and 9.

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.dib.2018.09.007.

MD movies for WT Apn1 complexed with substrates DHU(2-aPu) (5'-d(CTCTC(DHU)(2-aPu)CTTCC)-3' complemented with 5'-d(GGAAGGGGAGAG)-3') or (2-aPu)DHU (5'-d(CTC(2-aPu)(DHU)CCTTCC)-3' complemented with 5'-d(GGAAGGGCAGAG)-3') are presented in Figs. 10 and 11, respectively.
2. Experimental design, materials and methods

2.1. S. cerevisiae WT and H83A Apn1 and DNA-substrates

Expression and purification of wild type (WT) Apn1 and mutant form H83A Apn1 were carried out as previously described [6–8].
Oligodeoxyribonucleotide (ODN) duplexes used as DNA-substrates were synthesized and purified according to [6,7].

2.2. Kinetic data analysis

Global nonlinear least-squares kinetic analysis was performed in the DynaFit software (BioKin Ltd., USA) [5] as described in [9,10].

2.3. An incision assay

The DNA cleavage kinetics in vitro conditions was studied using electrophoresis in polyacrylamide gel (PAGE) as described previously [6,7]. The measurements were conducted at 25 °C in BER or NIR.
reaction buffer (BER buffer: 100 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES)-KOH (pH 7.6), 100 mM KCl; NIR buffer: 20 mM HEPES-KOH (pH 7.6), 50 mM KCl, 0.1 mg/mL BSA, 1 mM DTT, 5 mM MgCl₂).

2.4. MD simulations

The initial structure of a DNA duplex (PDB ID: 2NQJ [11]) was manually truncated to a 12mer and edited according to a nucleotide sequence being studied containing 2-aPu and/or DHU residues. Zn²⁺ ions were placed in the PDB file according to refs. [12,13] and the data obtained on the CheckMyMetal server and RaptorX-Binding server [14]. Parameterization of Zn²⁺ ions in a protein for MD simulations remains a challenge with classical mechanics. In this work, we tested different approaches to
Zn$^{2+}$ parameterization: the cationic dummy atom (CaDA) approach [15] that involves virtual atoms to impose an orientational requirement for zinc ligands; the polarizable atomic multipole-based electrostatic model [16]; and the classic nonbonded atom method [17]. Finally, we found that the nonbonded atom method is more suitable for our purposes; accordingly, in this work, we chose this approach. Parameterization of Zn$^{2+}$ ions was carried out as in ref. [17]. Structure refinement and molecular dynamic simulation were performed as in [7] using AMBER 14 molecular modeling suite [18,19]. The force field parameters for the 2-aminopurine-5'-phosphate residue were retrieved from ref. [20]. The partial atomic charges and force fields for the DHU residue were custom-parameterized calculated by the RESP method [21] based on the quantum mechanical calculation in the HF/6–31G* using Gaussian'09 software [22]. A 45 ns MD simulation was conducted using the AMBER 14 GPU-accelerated code [18,23] by means of the ff99SB force field [24,25]. Molecular graphics, MD movie generation, and trajectory analysis were carried out in the UCSF Chimera software [26].

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Transparency document. Supporting information

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