Boston University

OpenBU | **http://open.bu.edu**

BU Open Access Articles | BU Open Access Articles

2019-02-28

Discovery of macrocyclic inhibitors of apurinic/apyrimidinic endonuclease 1

Richard Trilles, Dmitri Beglov, Qiujia Chen, Hongzhen He, Randall Wireman, April Reed, Spandan Chennamadhavuni, James S Panek, Lauren E Brown, Sandor Vajda, John A Porco, Mark R Kelley, Millie M Georgiadis. 2019. "Discovery of Macrocyclic Inhibitors of Apurinic/Apyrimidinic Endonuclease 1." JOURNAL OF MEDICINAL CHEMISTRY, Volume 62, Issue 4, pp. 1971 - 1988 (18). https://doi.org/10.1021/acs.jmedchem.8b01529

https://hdl.handle.net/2144/39199

"Downloaded from OpenBU. Boston University's institutional repository."

Supporting Information

Discovery of macrocyclic inhibitors of Apurinic/apyrimidinic endonuclease I

Richard Trilles[†], Dmitri Beglov[‡], Qiujia Chen[§], Hongzhen He[§], Randall Wireman[‖], April Reed[‖], Spandan Chennamadhavuni[†], James S. Panek[†], Lauren E. Brown[†], Sandor Vajda[‡], John A. Porco, Jr. [†], Mark R. Kelley*[‖], and Millie M. Georgiadis*[§⊥]

[†]Department of Chemistry and Center for Molecular Discovery (BU-CMD), Boston University, Boston, Massachusetts 02215, 7 United States

[‡]Department of Biomedical Engineering, Boston University, Boston, Massachusetts 02215, United States

[§]Department of Biochemistry and Molecular Biology, and [‖]Department of Pediatrics and Herman B. Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, Indiana 46202, United States

[⊥]Department of Chemistry and Chemical Biology, Purdue School of Science, Indiana University-Purdue University Indianapolis, Indianapolis, Indiana 46202, United States

* *Corresponding authors*

Supporting information includes Figure S1.

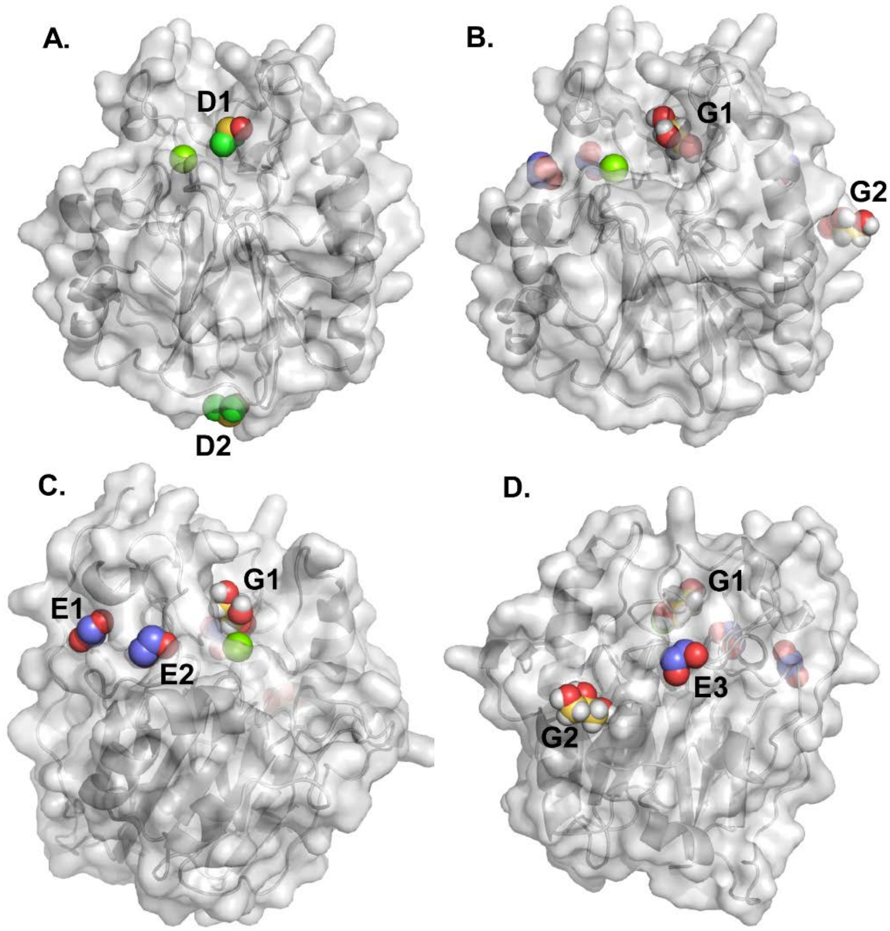

Figure S1. Crystallographic solvent mapping analysis. (A) DMSO binding sites, D1 and D2, (DMSO structure, 6MK3) are shown as van der Waals models with C, green, S, yellow, O, red. D1 is located within the active site of APE1 (gray semi-transparent surface with gray cartoon rendering); Mg^{2+} is shown for reference as a green sphere. D1 is bound to the AP site shown in Figure 1. (B) Two glycerol binding sites G1 and G2 are shown with C, yellow, H, white, O red (Glycerol structure, 6MKO) bound to APE1. G1 overlaps with D1 from (A). Ethylene glycol binding sites are shown for the DMSO structure (6MKO) with C, blue, O, red with G1 shown for reference in (C) and (D). Ethylene glycol was used as a cryoprotectant in this case. E1 and E2 are shown with G1 and Mg^{2+} (green sphere) for reference on one face of APE1. E3 is shown on the opposite face of the molecule with G2 for reference. The solvent binding sites are found in the active site as well as in a number of small distant pockets on the surface of the molecule.