Structural insight into the exonuclease activity of Apurinic/Apyrimidinic Endonuclease 1 (Ape1) in DNA processing

Tung-Chang Liu(劉東璋)[2] ,Chung-Ting Lin(林俊廷)[1], Ruei-Yue Liang(梁瑞岳)[2]
and Yu-Yuan Hsiao(蕭育源)[1,2*]

[1]Department of Biological Science and Technology, National Chiao-Tung University, Hsinchu, Taiwan

[2]Institute of Molecular Medicine and Bioengineering, National Chiao-Tung University, Hsinchu, Taiwan

Abstract

Multifunctional protein Ape1 is composed of N-terminal redox domain and C-terminal nuclease domain. The N-terminal redox domain with redox activity is responsible for regulation of cell proliferation, growth and apoptosis. The C-terminal nuclease domain with both endo- and exo-nuclease activity is participated in Base excision repair (BER), Nucleotide incision repair (NIR), DNA proofreading, and apoptosis. The catalytic properties and working mechanisms of the endonuclease activity of Ape1 have been already well-studied; however, the molecular mechanisms and related cellular functions of Ape1 exonuclease activity are remain unclear. Here, we determined two crystal structures, including Ape1-dsDNA-1nt-5'-overhang complex and Ape1-dsDNA-2nt-5'-overhang complex. Our crystal structures and biochemical assays were shown mApe1 is an exonuclease and prefer to digest dsDNA. In addition, we also identified the potential working partner of Ape1. Ape1 and TREX1 both are members of SET complex on ER membrane. Through co-immunoprecipitation experiments and nuclease activity assays, we demonstrated that Ape1 interacts with TREX1 directly and works cooperatively in damaged base contained dsDNA processing. In conclusion, we not only provide the structural insight into the exonuclease activity of Ape1 but also identify the working partners of Ape1 to clarify the roles of Ape1 in DNA processing.

Keyword : Ape1, exonuclease, TREX1, DNA repair, apoptosis