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DNASe I and STRUCTURE CATALYTIC SITE

Nurul Sulviani[1] dan Zulham Yamamoto[2*]

[1]Master Program in Biomedical Sciences, Faculty of Medicine, Universitas Sumatera Utara, Indonesia
[2] Departement of Histology, Faculty of Medicine, Universitas Sumatera Utara, Indonesia
* Corresponding author : zulham@usu.ac.id

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ABSTRACT

This Article describes 3Dimention studies carried out of catalytic site over the past year which have advanced of understanding the substrate to recognizition and how the catalytic mechanism of the several key DNAse I. The hydrolysis reaction that occurs in DNASe I is influenced by Mg 2+ and Ca 2+ but let the Binding of DNASe I ions is still unclear, the active side is found, the amount and mechanism of Ca2+ and Mg2+ . The results of the review in this article indicate that DNASe I is needed externally from experimental animals and simulations improve the binding reaction of Ca 2+ and Mg 2+ which is supported by some literature that uses crystallographic studies where Ca 2+ ions can stabilize DNASe I and also in the presence of Mg 2+ ions that can accelerate the hydrolytic failure of the cation. The results of the review explain the role of cations collectively electrostatic matching between DNASe I and DNA.

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Introduction

Deoxyribonucleic acid (DNA) is a polymer molecule consisting of small subuni DNASe I is a part of the pancreatic endon-ucleus that has an important role in the catalysis and hydrolysis of double-stranded DNA1. Several previous studies used in the trea-tment of pulmonary complica- tions have shown catalytic activity and hydrolysis of DNASe I2.Overall, DNASe I has an important role in DNA hydrolysis, providing nutrients at certain times in DNA, can perform protection and intervention in the process of DNA degradation, cleaning DNA from extracellular media and also the reaction of polymerized actin3. DNASe especially bpDNASe I has been studied exte-nsively where DNASe i has high physiological pH activity due to the presence of Mg 2+ and Ca 2+.

DNASe I activity is 100-fold lower in buffered States and conditions containing only one type of Cation5. This is due to the presence of factors that can cause enzymatic reactions. Hence the importance of the divalent carbon bonds Ca 2+ and mg 2 + for the structural integrity of DNASe I6, where the CA 2 + oxidation protecting bpDNASe I from proteolytic/degradation obtains two disulfide reduction bonds. Equilibrium dialysis with the support of spectroscopic studies concluded that bpDNASe I there are two strong bonds, and some weak cations catalytic binding site.

Some previous studies suggest that the disulfide and calcium bonds bind the Active Side (Side 1 and side 2) so that it becomes a functional part of DNASe I. Based on the study of X-ray structure and biochemical studies of DNASe I is Ca 2+. In a previous study with molecular dynamics simulation (md) in an explicit solvent conducted on DNASe I found that the presence of four CA 2+ and Mg 2+ cations has an important role in optimizing the electro-static match between the enzyme and negatively charged DNA14,15. Mg 2 + binds to the catalytic side of DNASe I which has a role in hydrolysis with the help of cations, so that this event can provide an understanding of the direct relationship between cations from the biological function of DNASe

Both active sides of DNASe I bind Ca2+ as a single unit to bind active sites I and II20. Divalent mg 2+ Cation is also in the catalytic pocket of DNASe I which has a role in hydrolysis. In catalytic site DNASe I obtained from ln1dk structure of chemically modified bpdnase I Complex. The active side of Mg 2 + involves two histidines His 134 and His 252 that coordinate scissile phosphates that often require Mg2+ in catalytic activity. Important role divalent cations participate in DNA hydrolysis or to stabilize DNA groups near DNA

Content

Deoxyribonuclease (DNAse I)

DNAse I is a class of enzy-mes that catalyze the hydrolysis of DNA with mechanism and by clea-ving the phosphodiester bonds of DNA and Ca2+ and Mg2+ reaction.24 Encoded complecs by multiple genes and express with controlled by tissues, DNAse is capable to mechanism of hydrolyzing DNA in both of intracellular and other mechanism extracellular spaces. This enzyme belongs to endonuclease pancreatic and can plays a key role to determining and concentration of extracellular DNA (ecDNA).

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There are nine high resolution X-Ray apoptotic endonucleases-,containing bpDNASe I and listed on text (IANTN, 2A40, 2A42, 2A41, 2D1K, 3DNI and IATN) five of which belong to the DNAse I group site I, namely DNAse I site I, DNAse I-like 1 (DNase X), DNAse I-like 2, and DNAse I-like 3 (DNAse γ). Furthermore, there are three other endonucleases from the DNAse I 3DNI and IATN from site catalytic stie II group including the all site III contains with Ca2+ but not Mg2+ . DNASe I activity is 100-fold lower in buffered States and conditions containing only one type of Cation. This is due to the presence of factors that can cause enzymatic reactions. Hence the importance of the divalent carbon bonds Ca 2+ and mg 2 + for the structural integrity of DNASe I, where the CA 2 + oxidation protecting bpDNASe I from proteolytic/degradation obtains two disulfide reduction bonds. Equilibrium dialysis with the support of spectroscopic studies concluded that bpDNASe I there are two strong bonds, and some weak cations catalytic binding site.

Some previous studies suggest that the disulfide and calcium bonds bind the Active Side (Side 1 and side 2) so that it becomes a functional part of DNASe I. Based on the study of X-ray structure and biochemical studies of DNASe I is Ca 2+. In a previous study with molecular dynamics simulation (md) in an explicit solvent conducted on DNASe I found that the presence of four CA 2+ and Mg 2+ cations has an important role in optimizing the electro-static match between the enzyme and negatively charged DNA. Mg 2 + binds to the catalytic side of DNASe I which has a role in hydrolysis with the help of cations, so that this event can provide an understanding of the direct relationship between cations from the biological function of DNASe I.

All of the observation supported and was analyzed with analysis of bound Crysthallographic of water molecules. And therefor with bound water molecules observed with site I and site II.

DNAse I Catalytic site.

DNAse I (Figure 1) is a DNA-specific site I, II,II and IV

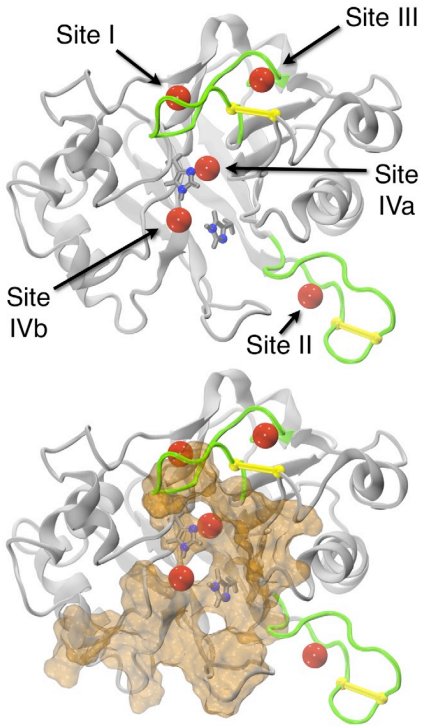

Figure 1. DNASe I ion binding site

enzyme and is often used to study DNA and protein interactions with preservation crysthallography. DNAse I is the most active endonuclease in DNA of mammalian cells, accounting for almost 100% of the total pancreatic endonuclease and activity in relevance and important organs, blood, and urine. Renal tubular epithelial cells and salivary glands express the highest amount of DNAse I enzyme. Overall, these results demonstrate that bpDNase I has at least three possible

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binding sites for divalent cations. The discovery of site III, in addition to the well-known sites I and II with strong affinity for Ca2+, is particularly intriguing because it appears to preferentially bind Mg2+. Verification of this site's ability to stabilize Mg2+ is still pending. In bpDNase I without actin. The presence of bound water molecules in three structures is the only evidence for the existence of a fourth putative site close to the bpDNase I catalytic pocket, which may be occupied by Mg2+ and must therefore be investigated from scratch. structural drift in simulations of bp DNase I The bp DNase I molecular dynamics simulations performed in the were used to further study the confirmed or potential cation-binding sites identified above.

Different kinds of metal ions are present in the solution. The initial placements of Na+ surrounding the enzyme in all seven simulations were established using a Coulombic potential grid and, crucially, were not situated in cation-binding sites. 2 provides a summary of the characteristics of the seven scenarios. According to the computed Ca-RMSD values between the free 3DNI bpDNase I and the simulated structures, which varied from 1.0 (Sim3) to 1.7 (Sim1) 60.1 A ° (2), no significant structural reorganizations took place over the trajectories. The stability of these simulations is attested to by the small standard deviations (0.1 A°).

All generated structures, on the whole, stayed fairly close to the 3DNI crystal11,25 . structure. Number, area and coordination of cations in bpDNase I reenactments Locales I and II in bpDNase I, indistinguishable to their X-ray partners, were exceptionally solid cation-binding pockets, continuously possessed by particles all through the directions . Na+ Suddenly possessed these locales within the nonappearance of Ca2+ (Sim1). Particle coordination was ideal for both Na + and Ca2+. Locales I and II were encourage fortified by authoritative Ca2+ (Figure 2), given its maximal coordination number (CNmax) of , higher than for Na + (CNmax of). In expansion, compared to Na+, the participation of Cys101 within the Cys101-Cys104 bridge fortified the amino corrosive side-chain coordination of Ca2+ at location II Both the amino-acid structure and the tricapped trigonal kaleidoscopic geometry of locales I and II are indistinguishable to those of crystallographic structures. Location III, close to location I (Figure 1), favored Mg2+ within the X-ray structures of bpDNase I in complex with actin

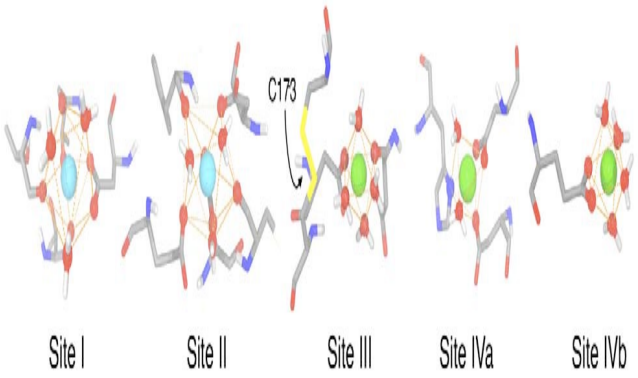

Figure 2. Coordination Sphares of Ca2+ and Mg2+ bound to DNASe I

Basic impacts of particles at desti-nations I, II and III

Sites I and II are found in circles L1 (Leu195 to Tyr211) and L2 (Tyr97 to Pro113) individually (Figure 1). The auxiliary solidness of L1, reflected by the moo temperature variables in 3DNI and the low root cruel square vacillation (RMSF) values (0.760.1 A ° on average) in our

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reenactments, was not influenced by the nature of the bound particle (Figure 3). Then again, the nearness of particles influenced L2, which was more adap than L1 (Figure 3). Na + in location II driven to higher L2-RMSF values (1.360.1 A° on normal) than Ca2+ (0.960.1 A ° on normal). The reenactments encourage highlight that when Na + was bound at location II, the Gly100-Cys104 region significantly veered off from the setup watched with Ca2+ bound at this location (Figure 3). This proposes that Ca2+ at location II restricts L2 adaptability and stabilizes one of at slightest two possible conformations of L2. Mg2+ at location III was facilitated to Asp172, securing the Cys173-Cys209 bridge from diminishment. Appropriately, one water molecule included within the Mg2+ coordination circle was also interacting with Cys173 (Figure 2). This water atom, firmly bound by both Mg2+ and Cys173, did not trade with the solvent and in part protected the Cys173 sulfur iota, reducing its openness. This circumstance was particular to Mg2+ , since the coordination circle of Na + at location III was shaped by exchangeable water particles that seem not secure Cys173. Cation official at the already obscure location III gives a comprehensive interpretation of the resistance of the Cys173-Cys209 disulfide bridge to b-mercaptoethanol assault in a location I-defective bpDNase I variant [26]. Individually, cations stabilized the enzyme's structure, either directly (Ca2+ at location II) or in a roundabout way (Mg2+ at destinations III and IV).

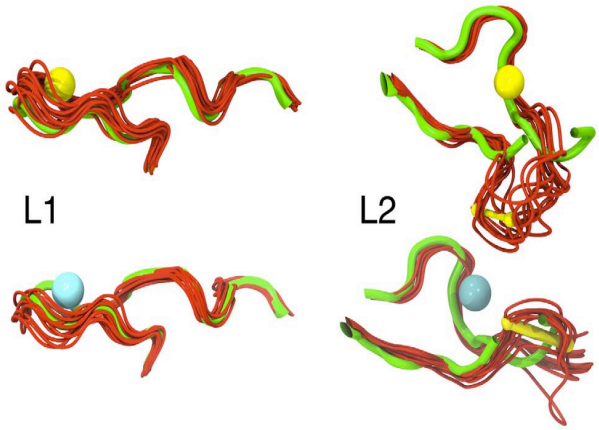

Figure 3. L1 dan L2 dynamics

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