Poster Presentation

MS29.P57

An unusual metal ion configuration in a viral DNA-packaging nuclease active site

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Nucleic acid metabolism is fundamental to many biological processes. A large class of enzymes such as RNase H, reverse transcriptase, retroviral integrase, topoisomerase, DNA and RNA polymerase, transposase, Holliday-junction resolvase, RNAi slicer Argonaute, and viral DNA-packaging terminase, utilize a common two-metal-ion catalytic mechanism for cleavage or synthesis of nucleic acid chains. Here we report an unusual metal-ion cluster in the active site of the nuclease domain of a viral DNA-packaging terminase unveiled by X-ray structures up to 1.38 Angstrom resolution. Two Mg2+ ions are situated in a coupled octahedral coordination system with liganding oxygen atoms from aspartic acid residues as well as water molecules. The two Mg2+ ions are located within a strikingly short distance of ~2.5 Å, which is unusual given the 1.6 Å atomic radius of Mg2+ and is shorter than previously observed metal-metal distances in metallocluster-containing enzymes or other biological systems. This provides the structural basis for distinguishing Mg2+ from other metal ions such as Ca2+ which are well known to support binding of the nucleic acid substrate but not support catalysis. Such an ultra-short distance between two metal-ions may be essential for generation of a highly positive niche, leading to nucleophilic attack at the phosphodiester bond of DNA. These results have defined the precise chemical configuration of the active site in nucleases using two-metal-ion catalytic mechanism. Moreover, assembly of this two-metal-ion cluster in the viral DNA-packaging terminase is mediated by an adjacent Lys residue, likely serving as a regulatory mechanism for activation of the nuclease activity of the terminase during packaging of viral genome.

Keywords: nuclease, two-metal-ion mechanism, DNA packaging