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The aminoacyl-tRNA decoding site (A site) is a molecular switch in the ribosome guaranteeing high translation fidelity. The secondary structure of the A site is conserved except at a few nucleotides between bacteria, mitochondria and eukaryotic cytoplasm. X-Ray analyses have revealed that tertiary structures of the three types of A sites are surprisingly different [1,2]. Therefore, on the basis of the many crystal structures obtained, it is suggested that these three main cell types possess different dynamical states and barriers in the molecular switches controlling translational fidelity, underlying the different evolutionary pressure on decoding. Aminoglycosides are highly effective antibacterial drugs that decrease translation accuracy by binding to the "on" state of the bacterial A-site molecular switch. On the other hand, toxicity to human resulting from the clinical use of aminoglycoside has been considered to originate from the binding of these drugs to the mitochondrial and cytoplasmic A site. Our X-ray analyses have revealed that the binding modes of aminoglycosides to the mitochondrial and cytoplasmic A sites, in which aminoglycosides bind to the "off" states of the A sites, are surprisingly different from those found in the bacterial A site [3].

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Keywords: ribosomes, RNA structure, antibiotic binding

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Crystal structure of Z-DNA d(CGCGCG) complexed with Ca^{2+} ion , and Mg^{2+} ion

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In solution, negatively charged DNA was neutralized by positively charged metal ions such as monovalent Na^+, K^+ and divalent Ca^{2+}, Mg^{2+}. These cations are essential for DNA folding and sometimes decide the helical conformation of DNA by hydrogen bonding networks. We determined crystal structures of DNA hexamer d(CGCGCG) with very high concentration of Mg^{2+} and Ca^{2+} ions by new temperature control technique we developed. Two kinds of DNA crystal were obtained from crystallization solution containing 500mM $MgCl_2$ and 500mM $CaCl_2$ by annealing from 338K to 293K, respectively. X-ray experiment was carried out using synchrotron radiation at BL38B1 in SPring-8. X-ray diffraction data were collected at high resolution (1.2 Å for $MgCl_2$ and 1.1 Å for $CaCl_2$). These crystals belong to new crystal form $P3_2$ (a=b=18.5 Å, c=72.7 Å) and left-handed DNA helixes were stacked along a long c-axis in $MgCl_2$ crystal. That's entirely different from a usual crystal ($P2_12_12_1$, a=17.9 Å, b=30.8 Å, c=43.7 Å) obtained from 20mM, 50mM and 250mM Na^+ solution. Initial phases of $MgCl_2$ crystal were determined by molecular replacement with the program of AMoRe, and structural refinement and model building were carried out with the program of Refmac 5.0 and Coot 0.2, respectively. 68 H_2O molecules and 8 Mg^{2+} binding sites were determined with R=23.3 % and R_{free}=26.9%. Phosphate groups of Z-DNA were connected with the other phosphate group of neighboring Z-DNA via two Mg^{2+} ions. This structural motif would be utilized in storing DNA in compact room with high salt condition.

Keywords: metal ions in biology, DNA crystallography, DNA structure

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X-Ray analyses of DNA duplexes stabilized by bicyclic-C residues

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Base-modified nucleic acids are being evaluated for applications in biotechnology and as therapeutic agents. We found that a nucleotide carrying 7,8-dihydropyrido[2,3-*d*]pyrimidin-2(3H)-one, which is a cytosine derivative with a propene attached at the N4 and C5 atoms (hereafter bicyclic-C or X), increases the stability of DNA duplexes [1]. To establish the conformational effects of X on DNA and to obtain insight into the correlation between the structure and stability of X-containing DNA duplexes, the crystal structures of $[d(CGCGAATT\text{-}X\text{-}GCG)]_2$ (GX9) and $[d(CGCGAAT\text{-}X\text{-}CGCG)]_2$ (AX8) have been determined at 2.9 Å resolutions, respectively. The global and local conformations of the X-containing duplexes and the unmodified duplex are very similar. The X and the counter G bases form a pair in the canonical Watson-Crick geometry, similar to the previously reported GX9* [2]. On the other hand, the final omit map of AX8 suggests that X forms two types of pairs with the counter A residue, one is a wobble type and the other is a Watson-Crick like as the first example. In the former pairing, the adenine base must be protonated, while in the latter, X or A might adopt an imino form through tautomerization. Another interesting finding is that the base stacking interactions at the base pair steps containing the X residues are significantly changed. These changes in stacking areas, however, explain the increased stability of X-containing DNA duplexes.

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Keywords: DNA structure, base modification, DNA stability

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X-ray structure of A and B-DNA under high hydrostatic pressure (up to 2 GPa)

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