

## Crystal structures of DNA duplexes containing two consecutive T-T mispairs obtained both in the presence and absence of mercury ion

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### 1 Introduction

DNA molecule is an attractive material in nanotechnology due to its chemical stability, ease of chemical synthesis and sequence design, and relatively simple structure due to base complementarity. Recent discoveries and extensive studies of metal-mediated pairs of natural and artificial bases expand considerably the design possibility of functional DNA molecules. The mercury-mediated T-T base pair (T-Hg(II)-T) has been investigated for more than fifty years. Recently, we observed that Hg(II) ion significantly stabilizes a DNA duplex by binding selectively to a T-T mispair. Based on this phenomenon, a DNA-based Hg(II) sensing system was developed. However, structural information of a metallo-DNA duplex containing a T-Hg(II)-T base pair has been missing for long time. In order to obtain the structural information, we have performed X-ray analyses of a DNA duplex containing two consecutive T-T mispairs both in the presence and absence of Hg(II) [1, 2].

### 2 Experiment

The DNA dodecamer d(CGCGATTTTCGCG) was designed to fold as a self-complementary duplex containing tandem T-T mispairs at the center. For phase determination by the multiple anomalous diffraction (MAD) method, the DNA dodecamer containing 5-bromocytosine at the third position was also synthesized. Crystal structures of the DNA were determined both in the presence and absence of Hg(II) ion.

### 3 Results and Discussion

In the presence of Hg(II), two DNA strands form an anti-parallel right-handed double helix, which is known as the B-form helix. At both ends of the double helix, canonical Watson-Crick G=C and A-T base pairs are formed. In the central part of the double helix, two Hg(II) ions bridge the T bases of the T-T mispairs, thereby forming consecutive T-Hg(II)-T base pairs. The distance between the N3 atom of T and the Hg(II) ion is 2.0 Å. It suggests that the N3 nitrogen releases an imino-proton even at neutral pH and directly bonds to Hg(II). The N3-Hg(II)-N3 bond is linear and the N-N distance is 4.0 Å. The propeller twist angles of the T-Hg(II)-T base pairs ( $-22^\circ$  and  $-20^\circ$ ) are remarkably larger than that of the canonical Watson-Crick base pairs in the B-form DNA ( $-1^\circ$ ), probably because there is no extra bond except the N3-Hg(II)-N3 bonds between two T residues and owing

to the repulsion of carbonyl groups. Although the C1'-C1' distances of the T-Hg(II)-T base pairs (9.5-9.6 Å) are 1 Å shorter than those in the canonical Watson-Crick base pairs ( $\sim 10.7$  Å), the B-form conformation of the metallo-DNA duplex is not distorted. In the B-form DNA, the helical axis runs through the center of base pairs, and the Hg(II) ions in the mercury-mediated base pairs are therefore aligned along the helical axis. The distance between the two Hg(II) is 3.3 Å. The relatively short distance between the two Hg(II) cations indicates that metallophilic attraction may exist between them.

In the absence of Hg(II), the DNA duplex adopts an unusual non-helical conformation, which is totally different from the B-form double helix observed in the presence of Hg(II). At both ends of the non-helical DNA duplex, four canonical Watson-Crick G=C base pairs are formed and take a left-handed twist, which is well known as Z-form. The central part of the duplex adopts right-handed helical form. Therefore, the whole DNA molecule can be characterized as an unusual non-helical structure.

In conclusion, the first crystal structure of a metallo-DNA duplex containing consecutive Watson-Crick-like T-Hg(II)-T base pairs has been solved. The structure itself and the Hg(II)-induced structural switching from a non-helical form to the B-form provide the basis for structure-based design of metal-conjugated nucleic acid nanomaterials and devices.

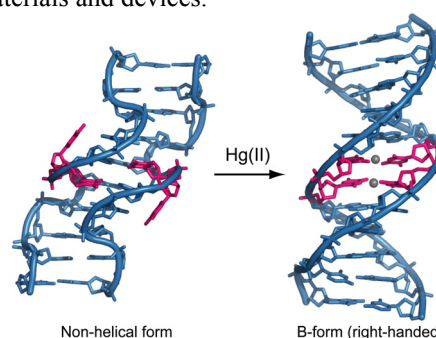


Fig. 1: Hg(II)-dependent structural switching of DNA

### References

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- [2] H. Yamaguchi, J. Kondo *et al.*, *Nucleic Acids Res.*, **42**, 4094-4099 (2014).

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