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O6-carboxymethyl-G forms a sequence context dependent wobble base pair with T

F. Zhang¹, M. Tsunoda², K. Suzuki², Y. Kikuchi^{1,2}, O. Wilkinson^{3,6}, C. Millington^{3,7}, G. Margison⁴, D. Williams³, A. Takénaka^{2,5}

¹Iwaki-Meisei University, Graduate School of Science and Engineering, Iwaki, Japan, ²Iwaki-Meisei University, Faculty of Pharmacy, Iwaki, Japan, ³University of Sheffield, Centre for Chemical Biology, Department of Chemistry, Krebs Institute, Sheffield, UK, ⁴University of Manchester, Centre for Occupational and Environmental Health, Faculty of Medical & Human Sciences, Manchester, UK, ⁵Chiba Institute of Technology, Research Institute, Narashino, Japan, ⁶University of Sussex, Genome Damage and Stability Centre (GDSC), Brighton, UK, ⁷Université de Rennes, Institut de Génétique et Développement de Rennes, Rennes, France

Previously, we reported the crystal structure of DNA d(CGCGXATTCGCG), which revealed that X (O6-carboxymethyl-G) at the 5th position forms a Watson-Crick (WC) type pair with T (Fig. 1a) similar to the canonical A:T pair [1]. In order to investigate the versatility of X in the base-pair formation, another DNA d(CGCXAATTTGCG) containing X at the 4th position has been X-ray analyzed using four different crystals. In the four crystals, the T bases are always largely wobbled into the major groove side to form a hydrogen bond between N3 of T and the carboxyl group of X. In addition, a water molecule bridges between the two bases through two hydrogen bonds to stabilize the pair formation (Fig.1b). This high-wobble (hW) pair is quite different from the previously reported one [1]. Now we succeeded to reveal the two types of pairing modes of X:T pair, WC type and hW type. Since the four crystals were obtained in different conditions, the large displacement of T cannot be ascribed to the interactions with solvent cations. Another possibility is Hoechst33258 used for crystallization. But, as the crystals were obtained in both the presence and the absence of Hoechst33258, this is not the case. The remaining possibility would be the location of the modified base, because the sequence of the used DNA contains an AATT tract at the center and two CGCG tracts at the both ends. The AATT tract is well known to be more flexible ($\omega^* \approx -16^\circ$) than CGCG tract ($\omega^* \approx -8.7^\circ$). We found that the WC type X:T pairing requires a large ω angle (-18°) between the bases. When X is located at the 5th position (in the AATT tract), the WC type is allowed to occur, while at the 4th position (in the CGCG tract) the WC type is difficult to occur. Here it could be concluded that X form a pair with T in the mode of WC if it is in the flexible tract, while in the mode of hW if it is in the rigid tract, because T base is out of the base stacking. * propeller twist angle between the two bases.

[1] Zhang, F., Suzuki, K., Tsunoda, et al. (2013). *Nucleic Acids Res.*, 41, 5524-5532.

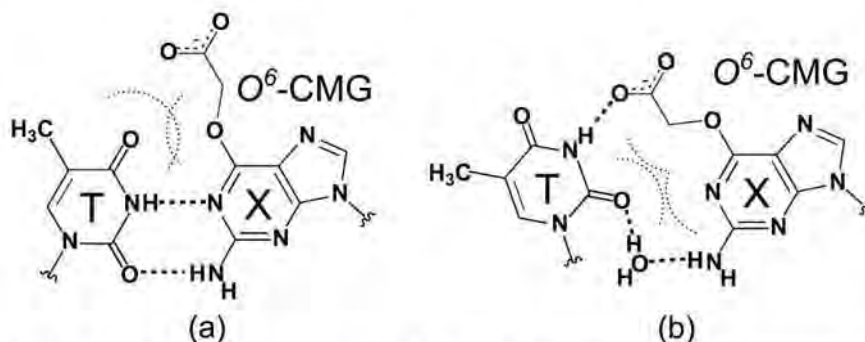


Fig.1. Two pairing modes of X with T; WC mode (a) and hW mode (b).

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