Preliminary X-ray Analysis of RNA Oligomers Containing CUG Repeats

Sato Yoshiteru, Kousei Kimura, Akio Takénaka, *Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama, Japan.* E-mail: yoshsato@bio.titech.ac.jp

Human genome contains so many different types of repetitive sequences. Some of them are tandem repeats of trinucleotides, and their unusual expansions cause genetic diseases including type 1 myotonic dystrophy (DM1) and Huntington's disease (HD). The unit sequence for DM1 is CTG in the 3'-untranslated region of the myotonic dystrophy protein kinase (DMPK) gene, and that for HD is CAG in the ORF of exon-1 of the HD gene.

The two complementary sequences may induce increase or decrease of the repeats during DNA replication or repair of DNA. The direct origin of DM1 is, however, the transcribed RNA fragments with CUG repeats, which forms a specific structure and inhibits other protein syntheses. In the present study, structural versatility of such DNA and RNA fragments has been examined.

In the case of $(CUG)_n$, native PAGEs show that the even repeat (n=even number) is more stable than the odd repeat. This may be ascribed to the structural difference at the hairpin head. The PAGEs also suggest that duplex formation is dependent on coexisting cationic species and their concentration. Crystal data of $(CUG)_6$ are a=b=39.6 and c=141.0Å, space group $R32$ and one oligomer in the asymmetric unit. An approximate crystal structure has been solved by molecular replacement techniques at 1.9 Å resolution and shows that the fragment forms a duplex similar to an A-form RNA.

Keywords: RNA structure, x-ray alalysis, genetic disease