# NMR study on the binding of naphthyridine dimer to d(CGG) triad

([1]*SANKEN, Osaka University,* [2]*Institute for Protein Research, Osaka University,* [3]*Yokohama National University)* ○Shuhei Sakurabayashi,[1,2] Kyoko Furuita,[2] Takeshi Yamada,[1] Toshimichi Fujiwara,[2] Kazuhiko Nakatani,[1] Chojiro Kojima[2,3]

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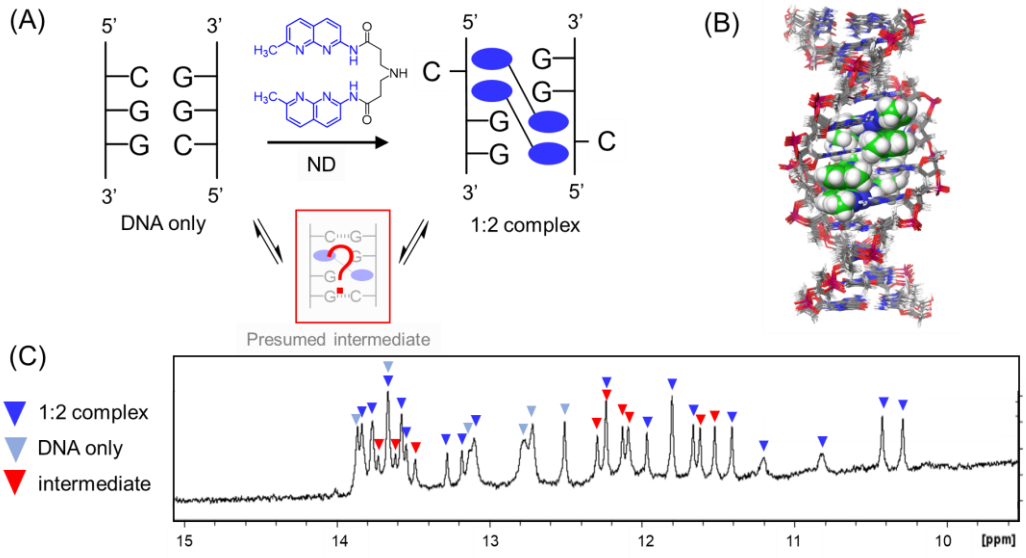
More than 40 neurodegenerative disorders are caused by expansions of simple sequence repeats in the human genome. Fragile X syndrome is a repeat expansion disease caused by the aberrant CGG repeat expansions in an *FMR1* gene. Naphthyridine dimer (**ND**, Fig. 1B) is a synthetic small molecule, which binds to d(CGG) triad, a structural motif found in the hairpin structure found in CGG repeat.[1] Our previous studies have shown that two molecules of **ND** bind to the CGG sequence, but we did not obtain presice structural information of the complex of **ND** and d(CGG) triad.

In this study, the binding of **ND** to a dsDNA oligonucleotide containing a d(CGG) triad was investigated by NMR spectroscopy. The complex structure of the 1:2 (= dsDNA : **ND**) complex was determined using $^{1}$H-$^{1}$H NOESY spectra. Also, to obtain the information on binding dynamics of **ND** toward DNA, we optimized the NMR measurement conditions such as temperature, the concentration of **ND**, and magnetic field to observe the intermediate. As a result, we revealed that approximately 30% of the intermediate corresponding to 1:1 (= dsDNA : **ND**) could be observed under the optimized conditions, and constructed the binding model of the intermediate. These obtained structural insights allow to improve the molecular properties of **ND**, and understand dynamic binding profiles.




(A) The binding mode of **ND** to d(CGG) triad. (B) the 1:2 complex structure of d(CGG) triad and **ND** determined by NMR. (C) 1D $^{1}$H-NMR spectrum of the binding intermediate of imino proton region.