The binding motif of naphthyridine-azaquinolone dimer (**NAD**) in CAG-repeat RNA

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The expansion of CAG repeats in the human genome causes serious neurological diseases, represented by Huntington's disease. Previously, we reported a small-molecule naphthyridine-azaquinolone (**NA**), which showed strong and specific binding towards CAG repeat DNA while a weak binding towards CAG-repeat RNA. In the last CSJ meeting, we reported the synthesis of an RNA-binding small molecule: naphthyridine-azaquinolone dimer (**NAD**). **NAD** is one of the **NA** derivatives where two **NA** moieties are connected by an aliphatic linker (**Fig** (**A**)). **NAD** showed a much higher affinity to CAG repeated RNA than **NA**, while it was not clarified how **NAD** bound to CAG repeated RNAs ~~at that time~~.
In this paper, we would report the SPR experiments performed to clarify the binding of **NAD**. For this purpose, we prepared three different biotinylated-RNAs that contain one of three potential binding sites (1) $(CAG)_3$ in the single strand region; (2) $(CAG)_3/(CAG)_3$ internal loop and (3) $(CAG)_3$ in the loop region. (**Fig** (**B**)) These RNAs were immobilized on SA chips, the responses of **NAD** were investigated. Only the RNAs with two or three CAG repeats in single strand region showed strong response against **NAD** (**Fig** (**C**, **D** and **E**)). These studies strongly suggest that a $(CAG)_3$ in the RNA single strand region would be the binding site of **NAD.**