From the structure analysis of RNA to the identification of novel drug targets

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It is well known that local structures in long RNAs, such as mRNAs, viral genomic RNAs and long non-coding RNAs, are required for their functions. We are analyzing interactions between small molecules and RNAs by the NMR spectroscopy to confirm that RNA local structures can be the target of small molecule drug. For example, a small molecule BzDANP having a three-ring benzo[c][1,8]naphthyridine system can bind to an RNA stem having C-bulge and inhibit the pre-miRNA-136 processing (Bioorg Med Chem. 27, 2140-2148, 2019). NMR is quite useful for the interaction analysis between small molecules and RNAs. Imino proton resonances can be observed selectively typically in 15-12 ppm where no other signals are observed. Some examples for the interaction analysis as well as the structure determination by NMR will be shown.

To identify the structured region in long RNAs, we improved the RNA secondary structure prediction method (http://www.rna.it-chiba.ac.jp/vsfold5/) and developed a system to visualize the possible structured regions in long RNAs (http://www.rna.it-chiba.ac.jp/～vswindow/). These systems can be used to find the drug target in long RNAs. Now, it is time to start the long RNA target small molecule drug discovery.