Large-scale analysis of RNA alkylation using OFF-ON type alkylators

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RNAs perform versatile functions in cells ranging from carrying genetic information to regulating and catalysis. The functional role of RNAs related intimately to their diverse structures. These structural elements provide unlimited potential for small molecule targeting. Among those types of ligands which can perform chemical modifications on structured RNA can help to understand and regulate the RNA biology. However, it is difficult to develop small molecules that specifically react with RNA due to the similarity of RNA secondary and tertiary structures. Therefore, evaluating the alkylation reactivity and selectivity of alkylators at a large scale enables the rapid and efficient interrogation of RNA alkylation.

In this study, we developed a new system to analyze RNA alkylation on a large scale (Fig. A). We used the reactive OFF-ON type vinyl-quinazolinone (VQ) alkylator as a reactive moiety, which was activated through protonation-accelerated pathway from its precursors ($VQ\text{-}NMe_2$). The N_3-modified $VQ\text{-}NMe_2$ conjugated with berberine was synthesized and applied to a large-scale analysis using RNA structure libraries.[2)] As a result, the reactivity profile was successfully created and validated. We would reveal the detailed analytical procedure and ranking data in the poster.

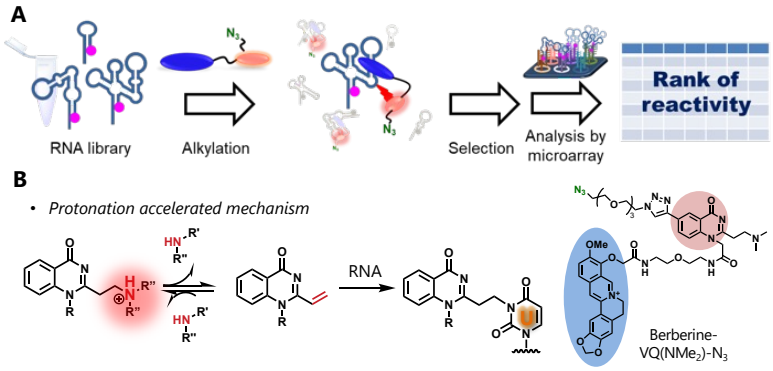

Fig. (A) The overview of large-scale analysis of RNA alkylation. (B) The structure and reaction mechanism of $VQ\text{-}NMe_2$.

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