Nucleic Acids Chemistry beyond the Watson-Crick Double Helix (65): Microscopic analyses for elucidating molecular mechanisms at the interaction between berberine and bulged RNA

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Phytochemicals (PCs) show a broad spectrum of biological activities such as antioxidant, antibacterial, and antitumor properties. The biological activities of PCs are thought to be provided by affecting protein functions in cells. In contrast, by considering the chemical structural properties of PCs, which contain multiple heterocycles with nitrogen atoms, it corresponds to those of chemicals that tend to interact with RNAs rather than proteins.[1] Thus, some of the biological activities of PCs are likely to be resulted from their interaction with RNAs. However, the biological importance of PCs is still not evident in the context of their influence on the functions of RNAs.

In this study, to verify the biological activities of PCs mediated by direct interaction with particular RNA unit, an integrated investigation based on physicochemical and structural analyses was demonstrated using a berberine (BRB) as a model PC. BRB is one of the biologically active chemicals in medicinally important plants. An approach to identify RNA motifs interacting with BRB was performed using RNA-capturing microsphere particles (R-CAMPs), which we have originally established to optimize functional RNA aptamers.[2] A minimal RNA motif consisting of a cytosine bulge with UA and GU neighbouring base pairs was found for the interaction with BRB. Detailed analyses of the interaction were performed by NMR-based structure determination followed by molecular dynamics simulation and physicochemical analyses, such as UV melting and ITC, highlighting importance of electrostatic and stacking interactions for the stabilization of the RNA upon BRB interaction (Figure). The results suggest the potential biological activities of PCs mediated by their interaction with RNAs. In addition, the basic knowledge of the chemical properties for the RNA recognition by PCs would be useful for the development of therapeutic drugs that target functional RNAs.

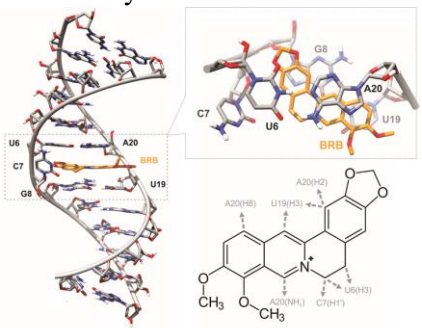

Figure. Tertiary structure and interactions between BRB and RNA.

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