Development of SARS-CoV-2 Spike Protein-Binding Molecules Using G4-Based DNA Aptamer: IRDAptamer

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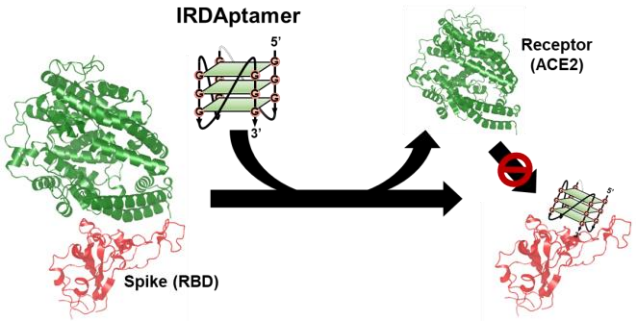
COVID-19, which reached pandemic levels, is caused by Sever Acute Respiratory Syndrome coronavirus2 (SARS-CoV-2). The SARS-CoV-2 binds via its spike protein, which protrudes from viral surface, to the cell receptor initiating the entry process into target cells. [1] These facts indicate the importance of developing novel spike-binding molecules as therapeutic agents for COVID-19. Recently, RNA/DNA aptamer that can bind to their targets with high specificity and affinity have been widely noticed as novel molecular targeted drug, which can replace antibody drugs.[2] In addition, Guanine-rich sequence forms a G-quadruplex structure based on Hoogsteen base paring through the binding with cation and shows high structural stability. These facts indicate that G-quadruplex DNA aptamer may be used for therapeutic agents.

In this study, we carried out the identification and sequential optimization of binding molecules for spike protein using IRDAptamer library, a G4-based DNA aptamer originally developed in our laboratory.[3] CD spectrum analysis and ELISA binding assay showed the identified and optimized aptamer was induced the parallel type G-quadruplex structure in the response to K^+, and the binding to spike protein was strongly dependent on K^+. Kinetic analysis by Biolayer interferometry (BLItz) system revealed high affinity binding to spike protein. Furthermore, the aptamer showed high serum-resistance under the physiological condition in the response to K^+. These results suggested that the optimized spike-specific IRDAptamer for SARS-CoV-2 may be used as a diagnostic and therapeutic agent for COVID-19.



1) S. Jian, et al., *Nature* **2020**, *581*, 221. 2) Y. Haixiang, et al., *Angew. Chem. Int. Ed.* **2021**, *60*, 16800. 3) A. Kaneko, M. Mizunuma, Y. Chuman, et al., *Catalysts* **2020**, *10*, 1153.