Development of a Method to Control the Function of G4-based DNA Aptamer; IRDAptamer

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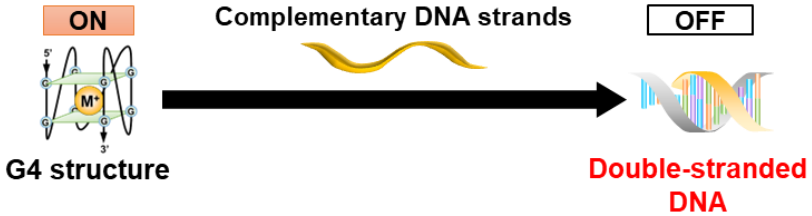
In recent years, there has been much activity in the development of molecular-targeted drugs that can bind specifically to disease-related proteins. However, some of these drugs are associated with potential side effects, when their targeted disease-related proteins are also expressed in normal cells.[1] Therefore, it has been desired to design and develop the drugs which work only in the site of the disease in order to reduce their side effects. We previously designed ion-responsive DNA aptamer (designated as IRDAptamer) libraries and identified IRDAptamers targeting each disease-related molecule.[2] IRDAptamers are Guanine-rich DNA oligonucleotides and they form a G-quadruplex (G4) structure through binding with cations. It was confirmed that the formations of G4 structure enhanced the binding affinity of IRDAptamers to their individual target proteins. In addition, IRDAptamers forming G4 structure have been shown to be highly stable in serum medium and to be capable of intracellular uptake into cancer cells without any reagents. Therefore, IRDAptamers can serve as promising drugs for molecularly targeted therapy in the cells. In this study, we carried out to develop the method for the regulation of G4 structure to control the functions of IRDAptamers.

We focused on complementary DNA strands to control G4 structure of IRDAptamer targeting Ser/Thr protein phosphatase Scp1, which is known to promote gastric cancer cell migration. First, we designed a variety of complementary DNA strands which bind different sites of Scp1-targeted IRDAptamer and it was revealed that the binding ability of Scp1-specific IRDAptamer was controllable by the incubation of the complementary DNA strands. CD spectrum analyses and ethidium bromide (EtBr) staining assays indicated that G-quadruplex structure of IRDAptamers were destroyed after the addition of the complementary DNA strands. In addition, the cellular uptake of IRDAptamer was also substantially reduced by the incubation of the complementary DNA strands. These results suggested that complementary DNA strands are suitable for the regulation of the biological effects of IRDAptamers.



1) K. Chan, et al., *BMJ.* **2020**, *369*,736. 2) Kaneko A., Chuman Y., et al., *Catalysts,* **2020**, *10*, 1153.