Photoreactive Molecular Glue for Enhancing the Efficacy of DNA Aptamers

([1]*Graduate School of Engineering, The University of Tokyo*, [2]*Faculty of Science, The University of Hong Kong*) ○Ai Kohata,[1] Kou Okuro,[2] Takuzo Aida[1]
Keywords: Molecular Glue; Photo-Immobilization; DNA Aptamer; Protein

DNA aptamers are attractive synthetic analogues of antibodies because of their high target selectivity and physicochemical stability. However, for practical utilization under physiological conditions, their binding affinities to target proteins are not sufficiently high. To overcome this problem, DNA aptamers with photoreactive motifs have been developed for covalent conjugation with target proteins. However, chemically modified aptamers are not guaranteed to maintain their intrinsic affinities to target proteins.

In the present study, we developed "photoreactive molecular glue (^{BP}Glue-N_3)" that can provide a universal strategy for enhancing the efficacy of DNA aptamers.[1] ^{BP}Glue-N_3 noncovalently adheres to a DNA aptamer/target protein conjugate, and then covalently stabilizes it upon UV exposure. By means of ^{BP}Glue-N_3-mediated photocrosslinking, we successfully enhanced the inhibitory effect of DNA aptamer SL1, which selectively binds to a receptor protein c-Met,[2] against its interaction with hepatocyte growth factor (HGF; Figure 1). Without the UV exposure, ^{BP}Glue-N_3 readily comes off the aptamer, resulting in the negligibly weak inhibition of the HGF/c-Met interaction.

1) A. Kohata, *et al.*, *J. Am. Chem. Soc.* **2021**, *143*, 13937. 2) R. Ueki, *et al.*, *Chem. Commun.* **2014**, *50*, 13131.

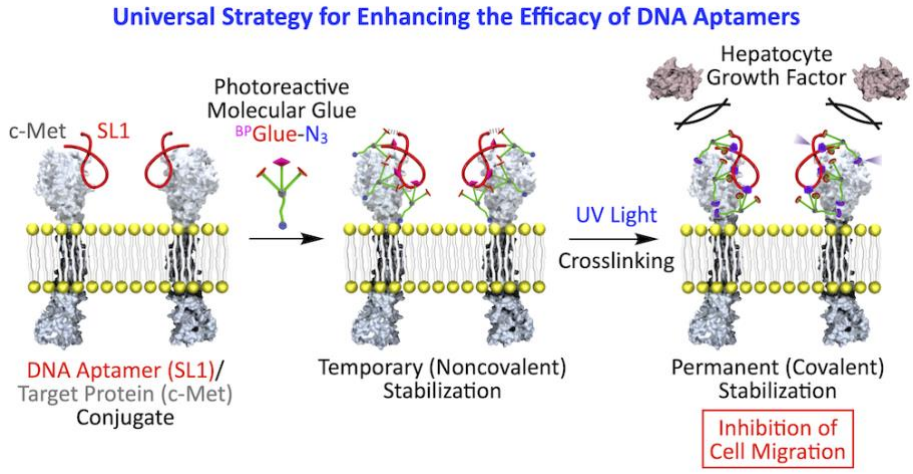

Fig. 1 Schematic illustration of how the efficacy of DNA aptamer (SL1) can be enhanced by photoreactive molecular glue (^{BP}Glue-N_3).