Photoreactive Molecular Glue for Immobilizing DNA Aptamer onto Targeted Proteins

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Because of high target-selectivity and synthetic accessibility, DNA aptamers are promising as an alternative to antibodies. However, many of the DNA aptamers so far developed do not have sufficient binding affinity to the target and therefore have not been applied for practical use. Previously, we developed water-soluble molecular glues bearing multiple guanidinium (Gu+) ion units that can strongly adhere to biomacromolecules through multiple salt-bridge interactions with oxyanions.1

In the present study, we developed “photoreactive molecular glue” that can immobilize a DNA aptamer onto the target protein by light. The molecular glue tightly adheres to a DNA aptamer/protein complex and covalently crosslinks it upon photoirradiation. By means of this molecular glue-mediated photo-crosslinking, we successfully enhanced the inhibitory effect of a DNA aptamer, which binds to receptor protein c-Met,2 against its interaction with hepatocyte growth factor (HGF; Figure 1). Without the UV exposure, molecular glue readily comes off the aptamer, resulting in the negligibly weak inhibition of the HGF/c-Met interaction.


Fig. 1 Schematic illustration of immobilization of a DNA aptamer onto the target protein (c-Met) via photoreactive molecular glue by light, resulting in the enhanced inhibition of HGF/c-Met interaction.