Development of a novel technology for gene suppression based on formation of RNA structure

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Nucleic acid-based therapeutics, such as antisense and small interfering RNA (siRNA), are promising strategies against a large number of diseases. As many diseases are caused by abnormal gene expression, a temptation to remediate the aberrant expression of the cognate mRNA or protein has arisen to restore the proper function of relevant cellular machinery. An easy way to achieve this goal is to use siRNA or antisense nucleic acid to repress the expression of the specific gene. Although we need to use the nucleic acid analogues such as XNAs in these techniques to elongate their detention time in cell, it would result in the loss of repression activity since the translational machinery could not recognize the non-native structures in the duplexes containing XNAs because these techniques required cooperative reaction with enzymes.

Here, we introduce a simple method for target gene suppression by induction of a G-quadruplex structure in the relevant mRNA using single strand XNA (and native DNA or RNA) named staple oligomer (**Fig. 1**). RNA G-quadruplex structure is known to block protein synthesis. The role of the staple oligomer is just a trigger or inducer of the G-quadruplex structure in mRNA. We expected that this technology would be a "Next-Generation" Nucleic Acid Medicine. In this presentation, we show the results of the experiments representing the effective suppression of the target genes by the staple oligomers *in vitro* and *in vivo* (**Fig. 2**).

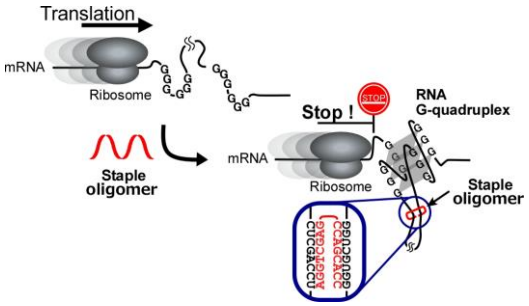

Fig. 1 Schematic illustration of translational inhibition caused by staple-induced G-quadruplex

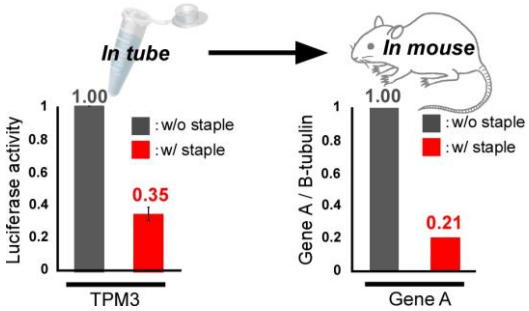

Fig. 2 Evaluation of translational suppression efficiency *in vitro* and *in vivo*.