Non-Toxic Delivery, Controlled Intracellular Localization and Enhanced Gene Silencing of siRNA by Small Peptides

Masayuki Fujii[1)]*, Ryosuke Fujita[1)], Maika Sonokawa[1)], Masaaki Hisano[1)], Yojiro Kotake[1)], Gengo Kashiwazaki[2)] and Takashi Kitayama[2)]*

1) Department of Biological and Environmental Chemistry, Kindai University, 11-6 Kayanomori, IIzuka, Fukuoka 820-8555, Japan (mfujii@fuk.kindai.ac.jp)
2) Department of Advanced Bioscience, Faculty of Agriculture, Kindai University, Nara 631-8505, Japan

Recently, small interfering RNA (siRNA), one kind of RNA interference (RNAi) technology represent the most common and, to date, the most effective method to inhibit target gene expression in human cells. It is also a common recognition that non-toxic delivery of siRNA is an urgent problem for the therapeutic application of siRNA [1]. For the efficient gene silencing in vivo, prolonged circulation of siRNA with take efficient and non-toxic cellular uptake and resistance against enzymatic degradation are indispensably required.

In the present study, we investigated the intracellular delivery using some hybrid peptides as transfection reagents and the silencing effect of siRNA targeting human telomerase reverse transcriptase (*hTERT*) mRNA in 3 human cancer cell lines, Jurkat and HeLa [2]. The complex of siRNA and a specific amphiphilic peptide (Pfectβ7) or its hybrid with an intracellular transport signal peptide could be effectively taken up into cells. The complex also showed a high silencing effect against *hTERT* mRNA (FIG1).

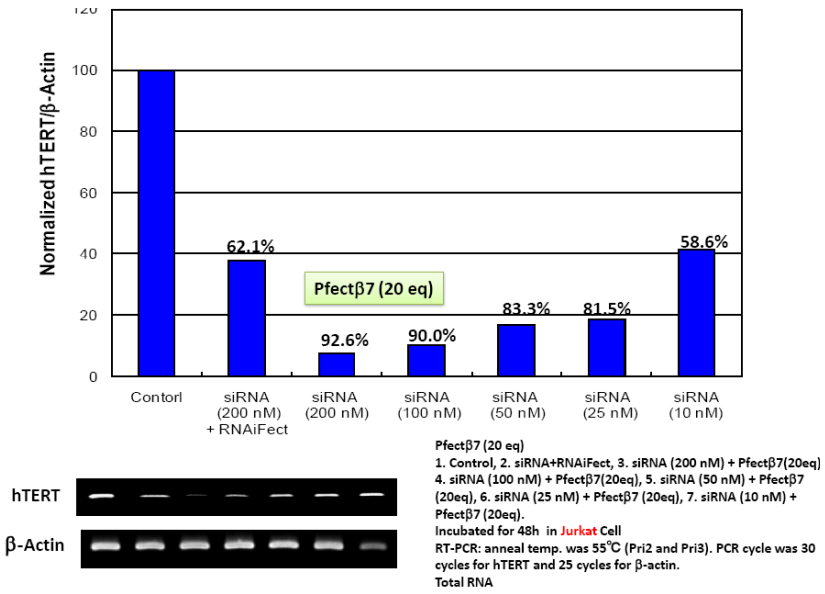

FIG 1. Silencing of hTERT by siRNA-Pfectβ7 Complex

Moreover, the combination of siRNA-nuclear export signal (NES) peptide conjugates and the amphiphilic peptides suppressed the expression of *BCR/ABL* chimeric gene in chronic myelogenous leukemia (CML) cell line K562 up to 95.2 % [3]. The amphiphilic peptides and their hybrids showed almost no cyto-toxicity and protected siRNA against intracellular nuclease digestion in 10% FBS (half life time was over 48h).

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References

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