Development of PET technology for the pharmacokinetic study of siRNA medicine

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Small interfering RNA (siRNA) is a short double-stranded nucleic acid molecule which induces sequence-dependent gene silencing, and gene therapy using siRNA is expected to be a novel treatment strategy.[1] A delivery system of siRNA molecules to the targeted tissue is indispensable to establish siRNA therapy. Many studies on *in vivo* application of siRNA using DDS carriers such as liposomes and micelles have been reported.

To obtain the pharmacokinetic information of siRNAs or their carriers *in vivo*, non-invasive real-time imaging with positron emission tomography (PET) is one of the ideal techniques. PET enables to determine the biodistribution and topical accumulation of positron-labeled compound. This technique can be applied in pre-clinical studies, in which drug candidates labeled with positron is injected into animals. The circulation profile, biodistribution in various tissues, and eventual elimination of drug candidates from the body can be monitored non-invasively in the same animals.

For the purpose of pharmacokinetic study of DDS carriers, we previously developed a novel [^{18}F]-labeled prove to label the carriers and PET imaging technology.[2] However, since siRNA is possible to dissociate from these carriers after injection into bloodstream in some formulations, *in vivo* behavior of siRNA is quite important for the development of siRNA medicines. Pharmacokinetic information of siRNA molecules, like as the carriers, is considered to be necessary and indispensable for the development of siRNA delivery.

In the present study, we synthesized [^{18}F]-labeled siRNA for examining the pharmacokinetics of liposome/siRNA complex with PET imaging. We also applied *in vivo* fluorescence imaging system for the investigation of *in vivo* behavior of siRNA medicine. PET imaging technology with positron-labeled siRNA would be useful for development of siRNA delivery system.