S19-3 Optimization of gene therapy effect by spaciotemporal control of expressed proteins

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Therapeutic effects of in vivo gene therapy, which tries to treat diseases by administering therapeutic genes to patients, are obtained via proteins expressed from the genes administered. Therefore, to optimize the therapeutic effects of gene therapy, it is important to control not only the distribution of gene vectors but also that of expressed proteins. Studies using protein pharmaceuticals have clearly demonstrated that the therapeutic effect depends largely on the spatio-temporal distribution of proteins, such as retention time and tissue disposition. These results strongly suggest that precise control of the spatio-temporal distribution of proteins increases the efficacy of in vivo gene therapy. Based on these considerations, we tried to increase the therapeutic effect of plasmid DNA-based gene therapy by controlling the profile of proteins expressed form vectors. To increase the residence time of proteins, we developed plasmids with few CpG motifs and achieved sustained expression of proteins at therapeutic levels for as long as several months. Separately, we designed fusion proteins that have different tissue distribution characteristics. Delivering plasmids expressing the designed fusion proteins resulted in sustained retention of proteins in the systemic circulation or tumor tissues. In this presentation, our experimental results of gene delivery of murine interferons will be reviewed to discuss the importance of the control of spatio-temporal distribution of proteins for gene therapy. In addition, the use of cells, not vectors, as ‘carriers’ for proteins will be briefly discussed.