Development of cell-targeting bubble liposome for effective gene delivery with ultrasound

Mutsumi Sugiia a,*, Ryo Suzuki a, Yusuke Oda a, Johan Unga a, Daiki Omata a, Hitoshi Uruga a, Yoichi Negishi b, Kazuo Maruyama a

a Faculty of Pharma-Sciences, Teikyo University, Tokyo, Japan
b School of Pharmacy, Tokyo University of Pharmacy and Life Science, Tokyo, Japan

ARTICLE INFO

Article history:
Available online 25 November 2015

Keywords:
Cell-targeting bubble liposome
Gene delivery
Ultrasound

Previously, we developed a gene delivery system using Bubble liposomes (perfluoropropane gas-entrapping liposomes; BLs) and ultrasound (US) [1]. The combination of BLs and US can deliver plasmid DNA into the cytoplasm via the formation of transient membrane pores by cavitation. To enhance the efficiency of gene delivery, it is important to induce the cavitation of BLs at the vicinity of cells. In brief, cell-binding BLs would be useful for gene delivery to induce the cavitation on the cell membrane. In this study, we prepared the BL conjugated cyclic RGD (cRGD) peptides which could bind to tumor neovessel [2], and we investigated gene transfection efficiency for Human Umbilical Vein Endothelial Cells (HUVECs) with cRGD conjugated BLs (cRGD-BLs) and US.

Binding assay: Fluorescence labeled cRGD-BLs were incubated with HUVECs at 4 °C. After 1 hr, the cells were washed and the fluorescence intensity was measured with flow-cytometer. Gene delivery: Luciferase coded plasmid DNA (pCMV-Luc) and either cRGD-BLs or BLs (60 μg/mL) were added to HUVECs. Then, US (2 MHz, 2.5 W/cm², 10 sec.) was exposed. After that, HUVECs were washed with PBS and incubated for 24 hr. Finally, luciferase expression was measured. cRGD-BLs effectively bound to HUVECs compared to non-targeted BLs. Luciferase expression in the group of treatment with cRGD-BLs and US was higher than that with BLs and US (Fig. 1). This result suggested that cRGD-BLs effectively delivered pCMV-Luc into HUVECs. Although the mechanism of enhancement for gene delivery efficiency is not clear, it is thought that many transient pores as a route of gene delivery might be opened by the cavitation of cRGD-BLs after binding on cell membrane. We found out that cRGD-BLs could enhance the gene delivery efficiency with US. Therefore, the combination of cell-targeting BLs and US would be an effective gene delivery system.

Acknowledgements

This study was supported by MEXT-supported Program for the Strategic Research Foundation at Private Universities, 2013–2017.
Fig. 1 - Luciferase activity in HUVECs transfected with pCMV-Luc.

REFERENCES