

Accepted Manuscript

The role of disulfide-bridge on the activities of H-shape gemini-like cationic lipid based siRNA delivery

Xiao-Fei Ma, Jing Sun, Chong Qiu, Yi-Fan Wu, Yi Zheng, Min-Zhi Yu, Xi-Wei Pei, Lin Wei, Yu-Jie Niu, Wen-Hao Pang, Zhen-Jun Yang, Jian-Cheng Wang, Qiang Zhang

PII: S0168-3659(16)30330-3
DOI: doi: [10.1016/j.jconrel.2016.05.051](https://doi.org/10.1016/j.jconrel.2016.05.051)
Reference: COREL 8294

To appear in: *Journal of Controlled Release*

Received date: 8 September 2015
Revised date: 17 May 2016
Accepted date: 23 May 2016



Please cite this article as: Xiao-Fei Ma, Jing Sun, Chong Qiu, Yi-Fan Wu, Yi Zheng, Min-Zhi Yu, Xi-Wei Pei, Lin Wei, Yu-Jie Niu, Wen-Hao Pang, Zhen-Jun Yang, Jian-Cheng Wang, Qiang Zhang, The role of disulfide-bridge on the activities of H-shape gemini-like cationic lipid based siRNA delivery, *Journal of Controlled Release* (2016), doi: [10.1016/j.jconrel.2016.05.051](https://doi.org/10.1016/j.jconrel.2016.05.051)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

The role of disulfide-bridge on the activities of H-shape gemini-like cationic lipid based siRNA delivery

Xiao-Fei Ma¹, Jing Sun¹, Chong Qiu¹, Yi-Fan Wu, Yi Zheng, Min-Zhi Yu, Xi-Wei Pei, Lin Wei, Yu-Jie Niu, Wen-Hao Pang, Zhen-Jun Yang*, Jian-Cheng Wang**, Qiang Zhang

State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing, 38 xueyuan Road, 100191, China.

*Corresponding Author:

Jian-Cheng Wang, Ph.D, Tel/Fax: 86-10-82805932, Email: wang-jc@bjmu.edu.cn; & Zhen-Jun Yang, Ph.D, Tel/Fax: 86-10-82802503, Email: yangzj@bjmu.edu.cn;

¹These authors equally contributed to this work.

Abstract

In our previous study, a H-shape gemini-like cationic lipid (ssGLCL, formerly named as CLD), composed of two hydrophilic lysine heads and two hydrophobic oleyl alcohol tails with a bridge of the redox-active disulfide-bond, had been synthesized and used as a nanocarrier for delivering small interfering RNAs (siRNAs) into cells. In order to further elucidate the role of disulfide (-S-S-) bridge on the activity of ssGLCL based siRNA delivery, a comparable ccGLCL bridged with a non-reducible carbon-carbon bond was synthesized and used as control in this study. Both two H-shape GLCL molecules could individually self-assemble into cationic nanoparticles in water phase and complex with negatively-charged siRNA into nanoplexes with particle size of ~ 200 nm and zeta potential of ~ +30 mV, and exhibit effective siRNA delivery both *in vitro* and *in vivo*. Investigation of internalization pathway displayed that both ssGLCL/siRNA and ccGLCL/siRNA nanoplexes were predominantly internalized into MCF-7 cells by the clathrin-mediated endocytosis pattern. Although a lower cellular uptake of siRNA was found in the human breast cancer MCF-7 cells, the ssGLCL/siRNA nanoplexes could exhibit similar or even stronger down-regulation effects on the targeted EGFR mRNA and protein in MCF-7 cells when compared to the ccGLCL/siRNA nanoplexes. Furthermore, mechanistic study showed that the enhanced down-regulation effects of ssGLCL/siRNA nanoplexes on targeted mRNA and protein were probably attributed to the increased release of siRNA from lysosomes to cytoplasm following the cleavage of redox-active disulfide-bridge in ssGLCL. Therefore, we believed that the redox-active H-shape ssGLCL could be a potential nanocarrier towards improving siRNA delivery.

Keywords: siRNA delivery, gemini-like lipid, disulfide bond, biodegradation, nanocarrier.

1. Introduction.

Nowadays small interference RNA (siRNA) is regarded as a significant potential therapeutic agent for diverse diseases, especially tumors [1-4]. However, its inherent defects

Download English Version:

<https://daneshyari.com/en/article/7861561>

Download Persian Version:

<https://daneshyari.com/article/7861561>

[Daneshyari.com](https://daneshyari.com)