Elongation of Hydrocarbon Chain Modified to GAVIL Peptide Promotes More Stable Micelle Formation

Shomu Fujimoto,*[a] Taufik F.N. Hakim,[b] Takashi Ohtsuki,[b] Mizuki Kitamatsu[a]

[a] *Department of Applied Chemistry, Kindai University, 3-4-1 Kowakae, Higashi-Osaka, Osaka 577-8502, Japan* [b] *Department of Interdisciplinary Science and Engineering in Health Systems, Okayama University, 3-1-1 Tsushimanaka, Okayama 700-8530, Japan.*
E-mail: kitamatu@apch.kindai.ac.jp

In recent years, intracellular delivery of therapeutic nucleic acids have attracted attention as one of treatments for hereditary diseases such as cancer. Of the intracellular delivery, we interested in the delivery for an assembly by micelle peptide. Therefore, we devised an intracellular delivery method of therapeutic genes using micelle peptide, "**GAVIL**" that forms spherical aggregates in aqueous solution. The GAVIL peptide that we designed so far has two Args at its N-terminus, and we expected an electrostatic interaction between the Args and siRNA. On the other hand, it is also expected that a stability of the GAVIL peptide assembly is reduced due to the interaction. Therefore, we expected more stable micelle formation by extending the chain length of the hydrophilic and hydrophobic moieties of the **GAVIL** peptide. In this study, we synthesized several types of peptide with different lengths of hydrophilic and hydrophobic portions of **GAVIL** peptide, and compared the stability of micelles using several measuring devices. We confirmed the completion of the synthesis of all peptides using MALDI-Tof-MASS and HPLC. We also compared the stability of micelles using critical micelle concentration (CMC) measurements and DLS measurements. As a result of the comparative experiment, it was confirmed that the stability of the micelle improved with the extension of the hydrocarbon chain of the peptide. Furthermore, we observed that the shape of the micelles varies depending on the concentration of the peptide. In our poster presentation, we will discuss the shape change and stability of micelle due to changes in hydrophobic chain length of **GAVIL** peptide.

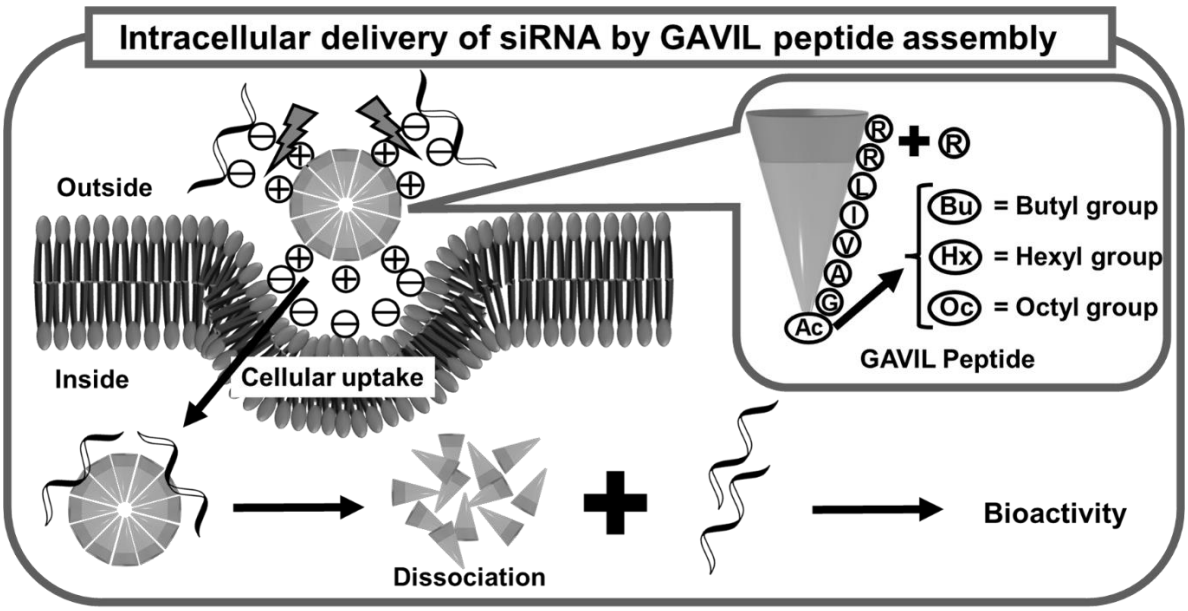

Figure 1. Schematic diagram of intracellular delivery of therapeutic nucleic acids using **GAVIL** peptide. First, positively charged Args and negatively charged siRNA are attracted by electrostatic interaction. Then, after penetrating into the cell, the micelle dissociates in a concentration-dependent manner, and the siRNA exerts its effect.

References

[1] U. Khoe, Y. Yang, S. Zhang. *Langmuir.* **2009**, 25(7), 4111-4114 (2009).