Effect of changing charge ratio in a polyion complex vesicle system and its application

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(ポリイオンコンプレックスベシクル系における荷電比変更の効果とその応用)

論　文　の　要　約

Fabrication of block copolymer-based nanostructures, especially vesicles, has drawn great attentions in biological applications in past 20 years, because of the structural property of vesicles, which made them to be good carriers and containers for biomedical applications, such as drug delivery and diagnostics. Among them, polyion complex vesicle (PICsome) is a block-polypeptide-based vesicle with semipermeable hydrophilic membrane, which is suitable for loading large biomolecules and useful as a container of enzymes. However, conventional PICsomes are prepared at the neutral charge ratio of component polyions, which have limited the scope of preparation conditions and applications, and encapsulation efficiency of payloads. In this thesis, effect of charge ratio of the component polyions on the PICsome formation was investigated to modulate PICsome properties and expand the scope of their applications.

In Chapter 1, the structure control with block-copolymers, particularly for vesicle structures, and their applications were introduced. Also, the advantages of PICsomes was highlighted, and remaining issues of PICsomes were raised. Then, the scope of the present thesis was described.

In Chapter 2, PICsome formation at a catiomer-rich condition was evaluated. The PICsome(2.0) was successfully formed at cationic/anionic residue ratio (C/A) of 2.0, which possessed unilamellar vesicle structure and catiomer-rich PIC membrane. Compared with a conventional PICsome prepared at C/A = 1.0, PICsome(2.0) showed an unusual increase in the PICsome size via an Ostwald ripening, which resulted from higher dynamic nature of the PIC membrane formed at unbalanced charge ratio.

In Chapter 3, vesicle induction from protein-PIC assemblies was examined to improve protein encapsulation efficiency of PICsomes via a two-step process. First, protein-PIC assemblies were prepared from polyions and anionic protein, and, then, vesicle induction was tested by addition of homo-catiomer. Structural transformation to vesicle was succeeded, and, unexpectedly, a yolk-shell PIC structure, in which a protein-condensed PIC core was encapsulated by a unilamellar PIC vesicle, was found under the catiomer-rich condition with a high protein encapsulation efficiency.

In Chapter 4, detailed investigation of the yolk-shell PIC structure was performed, particularly focusing on the formation mechanism. Structural and kinetic analyses of the yolk-shell structure revealed that the formation of yolk and shell structure was coupled by phase separation of protein-based assembly and polymer-based PIC from protein-PIC assemblies, which can be achieved at catiomer-rich condition. The formation of yolk-shell PIC provides a worthful approach for fabrication of complicated structures based on a simple self-assembly process of PIC formation.

In Chapter 5, conclusion and perspective of the present thesis was described.