論文の内容の要旨

論文題目　Design of Novel Polymer Vesicles Self-Assembled via Polyion Complex Formation from Oppositely Charged Block Copolymers and Their Application for Bioreactor

(荷電性ブロック共重合体間の静電相互作用を形成駆動力とする新規超分子中空構造体の設計とその機能性リアクターとしての応用)

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Vesicles and biomembranes have existed since the first cells and play critical role is compartmentalization functions as varied as nutrient transport and DNA protection. Whereas phospholipids are the natural amphiphiles of cell membranes, vesicle-forming materials used in products ranging from cosmetics to anticancer agents can be synthetic as well as biological. Amphiphilic block copolymers approach to vesicle formation, which have the same basic architecture as lipids, were self-assembled in selective solvents. Especially, poly(ethylene glycol) (PEG) is a biologically inert polymer, which has been extensively used in drug delivery system and is declared to be safe for *in vivo* use by the Food and Drug Administration in USA. It was proposed that PEG conjugation creates a steric hydrophilic barrier surrounding liposome, protecting PEG-liposome from opsonizing plasma proteins, and increasing their intravascular persistence. The steric barrier created by PEG conjugation also prevents PEG-liposome aggregation and fusion and thus stabilizes PEG-liposome dispersions. However, the shielding effect imparted by PEGylated lipids is limited by the maximum amount of PEGylated lipids that can be incorporated into the liposome bilayer before phase separation occurs and separate PEG-lipid micelles are formed. The most optimum PEG surface coverage on liposome was reported to be 10 mol% of 5 kDa PEG. There is a physical limit when optimizing the steric shielding and biocompatibility of PEG-liposome.

Considering the general interest for polymer vesicle systems with biocompatible

composition of PEG and biologically-relevant characteristics, self-assembly from the oppositely charged block copolymer composed PEG and poly(amino acid) provide a new idea for carriers of therapeutic and compartments of diagnostic enzymes in aqueous medium.

In the present study, the molecular design of functional materials to synthesis of novel polymer vesicles with polyion complex (PIC) membrane for carriers or containers of various water-soluble compounds such as smart bio-reactor system are described, mainly based on the strategy as shown in **Figure**. **Chapter 2** describes well-defined synthesis of oppositely charged block copolymer with the same block compositions. **Chapter 3** describes preparation and characterization of PICsomes with semipermeable membrane to penetrate only small solute. **Chapter 4** describes new utilities for the PICsome encapsulating functional biomolecules, myoglobin, was investigated. The PICsome encapsulating protein was an ideal formulation structure not only for protein-carriers but also for a suitable functional biomacromolecules of bio-reactor.

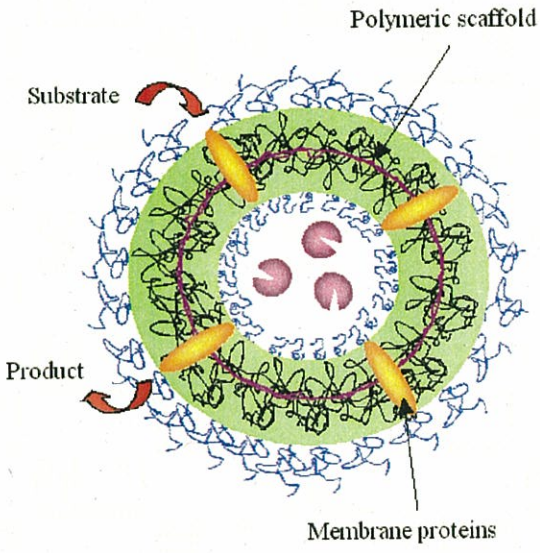

Figure. Schematic representation of a polymer-stabilized bioreactor with encapsulated enzyme.