Development of polyion complex (PIC) nanoparticles for biofilm infection control

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論 文 名　：Development of polyion complex (PIC) nanoparticles for biofilm infection control　（バイオフィルム感染対策に向けたポリイオンコンプレックス(PIC)ナノ粒子の開発）

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論　文　内　容　の　要　旨

Biofilm bacteria have been reported to be the main cause of bacterial infection worldwide. However, owing to its complex physicochemical characteristic, treating biofilm bacteria requires more effort than just using standard antibiotics. Nanotechnology offers an effective therapeutic alternative for biofilm bacteria as nanoparticles can be designed to overcome its physicochemical barrier. For this purpose, polyion complex (PIC) is an attractive technique for nanoparticle design, which has been widely used in biomedical settings such as drug delivery due to its facile preparation and versatile characteristics. In this thesis, the PIC nanoparticles were developed to understand the requirements of nanoparticles for the treatment of biofilm bacteria, and the diversification of PIC architecture into nanosheets was evaluated to widen its potential application in biofilm infections.

In Chapter 1, issues of biofilm and its infection in medical settings were highlighted, particularly in its resistance towards the conservative treatment using antibiotics and the weaknesses of available nanotechnology approaches against biofilm. PIC was then introduced as the potential research tool for understanding biofilm to develop better nanotechnology-based treatments. Finally, the research goals of the present thesis were described.

In Chapter 2, antibiotic-based PIC nanoparticles were fabricated using the pegylated cationic polypeptide, in which the side chain was further modified into several different modification rates. The side chain modification of polycation was found to be important in forming the antibiotic-based PIC and regulating the final nanoarchitecture of the formed PIC into micellar and vesicular via the enhancement of multimolecular interaction between the antibiotic and the polycation. Furthermore, upon exposure to biofilm bacteria, antibiotic-based PIC micelles showed better penetration into the biofilm than the vesicular PIC.

In Chapter 3, the diversification of PIC structures other than micelles and vesicles was evaluated via the regulation of the secondary structure of the similar pegylated cationic polypeptide using small polyphosphate–containing molecules. Interestingly, hexagonal nanosheets were obtained via complexation of the polycation and polyphosphate which bears 3 phosphates group. The polyphosphate molecules were found to induce the α-helix secondary structure in the polycations, which is crucial for forming nanosheets in the present PICs. Furthermore, proper tuning of the interaction strength between the polycations and the polyphosphate was important in obtaining regular hexagonal nanosheets.

In Chapter 4, the conclusion and perspective of the present thesis are described.