Exploration of charge-neutralized PEGylated polyion materials to overcome transmucosal barriers

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（経粘膜バリアを克服するための電荷中和 PEG 化ポリイオン材料の探索）

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論 文 内 容 の 要 旨
Thesis Summary

Polyion materials have been widely applied in the biomedical field due to their unique physicochemical properties and convenient design. Particularly, polyion complexes (PICs) allow electrostatic-interaction-based complexation with opposite charges in completely aqueous conditions. In addition, neutral polymer segments, such as poly(ethylene glycol) (PEG), could be introduced to provide biocompatibility. The current thesis discussed the utilization of polyion materials with a charge-neutralised state to overcome biological barriers. Particularly, the issues of the mucus layer and cellular entry (phospholipid membrane barrier) were focused on for overcoming transmucosal barriers. Two types of polyion materials, namely zwitterionic polymers and polyion complexes (PICs) were investigated for this purpose. The first material is sulfobetaine-type zwitterionic polymers (SBs), which was obtained as a random copolymer of 3-dimethyl (methacryloyloxyethyl) ammonium propane sulfonate (DMAPS) monomer and PEGylated methacrylate monomer. The second material is polyion complex (PIC) nanomaterials, which are promising drug carriers and submicrometer-scaled charge-neutralised self-assembles of oppositely charged PEGylated polypeptides. In Chapter 1, the research background and current situation of polyion materials were overviewed, and the scope of the present thesis was clarified. In Chapter 2, Both SB and PIC materials were evaluated to examine their potential to conquer cellular entry barriers through some cell experiments. In Chapter 3, SB polymers were evaluated as an epithelial layer-penetrating material by varying several parameters, such as the presence/absence of PEG chains, polyion concentrations, and the presence/absence of mucin. In Chapter 4, several kinds of PIC nanomaterials were compared as a platform to clarify PIC-cell surface interaction to obtain insights into overcoming the phospholipid membrane barrier. Specifically, polyion chain length, chemical modification of ionic residues, the degree of crosslinking of PIC domains, and the impact of PIC morphology on cellular internalization behaviour were carefully examined. Finally, in Chapter 5, some concluding remarks and future perspectives were given.