Development of Biocompatible Polymers and Their Potential Applications in Surface Coatings, Proteins Stabilization, and Cells Cryopreservation

ルバイヤ, アンジュム

（様式２）

氏　　名　：Rubaiya Anjum　ルバイヤ　アンジュム

論 文 名　：Development of Biocompatible Polymers and Their Potential Applications in Surface Coatings, Proteins Stabilization, and Cells Cryopreservation
（生体適合性高分子の創製と表面コート剤、タンパク質安定化剤、細胞冷凍保存剤への応用）

区　　分　：甲

論　文　内　容　の　要　旨

Cell-protein-biomaterial interactions are widely reported to be critical in tissue engineering and regenerative medicine. The biomaterials used in these applications must be biocompatible and have tenable physical and mechanical properties. Cells interact with the materials via adsorbed proteins on their surfaces. Understanding the effect of interfacial water in modulating the amount and conformational change of adsorbed proteins—which determine cell adhesion behavior including spreading and cellular function, is important for improving the biocompatibility of polymers. Based on the intermediate water (IW) concept, presence of IW, which is proposed as one of the interfacial water, in biomaterials is a key factor in modulating the interaction of proteins with biomaterials, because the first event of biomaterial implantation is hydration of material surfaces. The present study was designed to investigate whether changes in water content of polymer coatings affect fibroblast adhesion, proliferation and migration to promote wound repair. Furthermore, to clarify part of the role of hydrated water, we examined the hydration sate of osmolytes which have been demonstrated to stabilize proteins and influence biological functions by regulating hydration structure of proteins. Based on the results, efficient and biocompatible synthetic stabilizers have been developed for the preservation of cells and proteins. We focused on the use of biocompatible polymers in our thesis studies, and the whole thesis work was separated into five parts.

In **Chapter 1**, biocompatible biomaterials have been described briefly.

In **Chapter 2**, we reported on poly(ω-methoxyalkyl acrylate)s (PMCxAs) (x, number of methylene carbons between the ester and ethyl oxygen, x = two to six) as coating materials for controlling fibroblast cells (NHDFs) behavior, including adhesion, migration, differentiation, and collagen secretion. The biocompatible PMCxAs have different amount of IW. Among the analogous, PMC4A coating was found to be increased cells spreading, protein adsorption, focal adhesion formation, migration, NDHFs differentiation, and collagen production, whereas PMC2A coating was found to be decreased cellular activity (Figure 1 (a)). Our findings suggested that there was an optimal value of polymer parameters to activate the cells, and that cell adhesion was influenced by the balance of polymer hydrophilicity and hydrophobicity, as well as the hydration water content of polymers, which modulated fibronectin adsorption. Therefore, we may speculate that PMCxAs might be used as coating materials for biomaterials for skin regeneration and wound healing treatment.

In **Chapter 3**, we discussed the effect of trimethylamine oxide (TMAO) side chains containing poly *N*-[3-(dimethylamino)propyl]acrylamide *N*-oxide (PDMAO) on protein stabilization. This study was designed by getting inspiration from the results of the relationship between the protein stabilization capability and the hydration structure of *N*-oxide derivatives, where TMAO exhibited higher protein stabilizing ability due to its higher hydration number. Thermal denaturation and enzyme activity results suggested that PDMAO had a stronger protein preservation impact than other commonly used additives. The stabilizing capacity of PDMAO is linked to its hydration structure, and another mechanism might be the polymeric influence of the TMAO side chains of the polymer, which is also thought to enhance the local concentration of TMAO. As a result of our findings, the TMAO-containing polymer might be used as a possible stabilizer in biochemical and medical applications, and the schematic representation of this study is shown in Figure 1 (b).

In **Chapter 4**, we discussed the effect of PDMAO on cells cryopreservation using alone or in combination with the low concentrations of DMSO (2.5%, w/v) to reduce the quantity of DMSO in cryoprotective solution. In vitro cytotoxicity studies using A549 cells demonstrated no or less toxicity of PDMAO. A considerable cryoprotection effect on A549 cells was observed using PDMAO alone, while the combination of 7% (w/v) PDMAO and 2.5% (w/v) DMSO resulting in significantly higher post-thaw cell survival (≈ 80%) than 2.5% DMSO alone. The differential scanning calorimetry results suggested that PDMAO had a predominant amount of non-freezing water (NFW), and also had a higher ability to inhibit ice formation due to strong interaction with water. Furthermore, the presence of IW in hydrated PDMAO indicate the biocompatibility of PDMAO. Therefore, replacing a toxic cryoprotectant (DMSO) with a non-toxic and biocompatible TMAO-bearing polymer might be a feasible alternative for a variety of cell-based therapeutic applications.

In **Chapter 5**, the summary and perspective of this study were described.

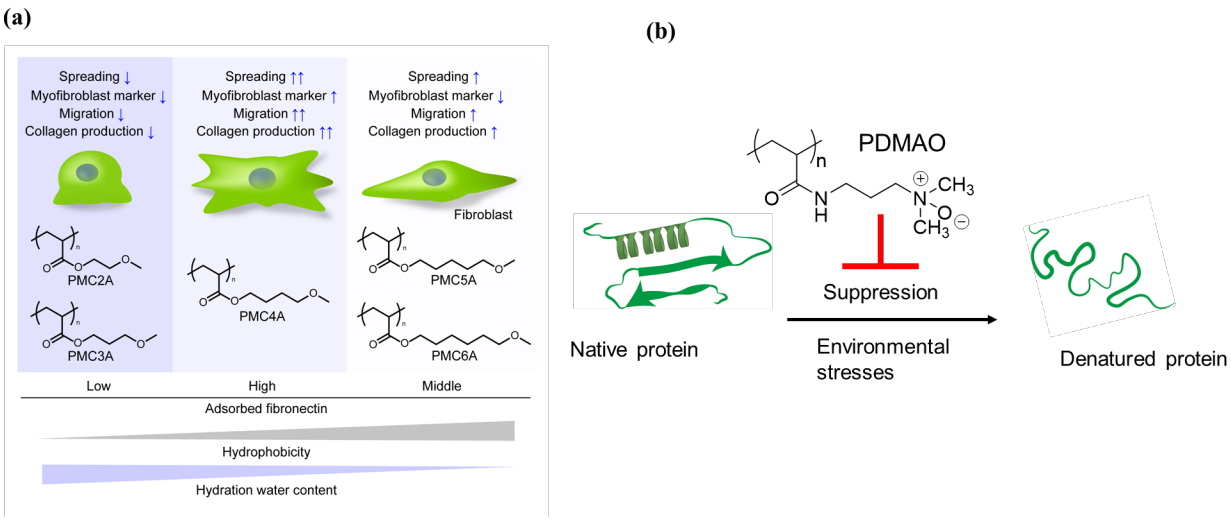

Figure 1 (a) Schematic representation of fibroblast cells behavior on PMCxA-coated substrates (Chapter 2).
(b) Schematic illustration of hypothesized protein stabilizing action of PDMAO (Chapter 3).