Fluorinated Polyimide as Biomedical Polymer

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1. Polyimides as Biomaterials

Aromatic polyimides are a class of high-performance polymers that are highly thermally stable and have a high glass transition temperature and relatively low dielectric constant. Various polyimides have become increasingly important in a variety of technological applications, such as semiconductor devices, high-temperature adhesives, and high-performance composite materials. However, we have clarified that polyimides containing a fluorinated group are promising materials for medical devices [1-10]. We have already reported the gas exchange and blood compatibility of the polyimide hollow fibers fabricated from soluble fluorinated polyimides synthesized with a chemical imidization at ambient temperature. The polyimide fibers show not only a high gas exchange (O_2 transfer and CO_2 removal) but also suppression of platelet adhesion, suggesting the possibility of a novel membrane oxygenator with the advantage of both increased gas exchange and excellent biocompatility. In addition, we demonstrated that the fluorinated polyimide suppresses neutrophil adhesion and complement activation. It is well-known that neutrophils are a predominant subpopulation of leukocytes and that their stimulation with an inflammatory mediator activates the release of reactive oxygen species (ROS), resulting in cell and tissue damage. Activation of the complement system also appears as a key event eliciting secondary production and inflammatory mediators. The *in vivo* lecukocyte and complement activation are often observed during cardiopulmonary bypass and hemodialysis. Interestingly, neutrophil adhesion and complement activation for the polyimide films significantly depended on the curing temperature in preparing the films and decreased with an increase in the temperature.

A series of fluorinated polyimides cured at different temperatures was prepared, and plasma protein adsorption on the polyimide films was evaluated *in vitro* using a micro-bicinchoninic acid protein assay and a gold-colloid labeled immunoassay. Interestingly, the amounts of plasma protein adsorbed on the polyimide surface strongly depended on the curing temperature. The amounts of BSA, Fbg, and IgG adsorbed on the surface determined using the BCA assay decreased with an increase in the temperature. On the other hand, the amounts of IgG adsorption determined using the immunoassay in human plasma increased with the temperature, while those of HSA and Fbg decreased. These results indicated that the competitive plasma protein adsorption on the polyimide films undoubtedly occurred and that the specific plasma adsorption surface for IgG was formed by the curing process. The contact angle of water and the z-potential value on the polyimide surface also strongly depended

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On the curing temperature, indicating that the hydrophobicity and the electrical repulsive force formed on the surface had a significant influence on the competitive plasma protein adsorption.

We have already reported that a polyimide hollow fiber has not only a high gas exchange (O_2 transfer and CO_2 removal) but also biocompatibility. We consider that the competitive plasma protein adsorption on the polyimide surface obtained in this study is one of the important factors in elucidating the mechanism of *in vivo* biocompatibility of the fluorinated polyimide.

2. Polyimides for Tissue Engineering

Controlling the cell morphologies of a material is of interest with regard to tissue cultures, because the morphologies are closely related to cell functions. The cell spheroids, which are a spherical mass composed of many cells and extracellular matrices, have been used in the research areas of tissue engineering or cell chips, because they appear to mimic not only the morphology but also the physiological functions of cells in living tissue and organs, unlike the conventional two-dimensional monolayer culture of cells. The spheroid is well-known to sustain viability for extended culture periods and maintain high levels of cell functions when compared with those of cells as monolayers.

Recently, we succeeded in fabricating a micropattern on a fluorinated polyimide surface using a rubbing method by high pressure and reported a specific interaction between the cells and the fluorinated polyimide surface modified by the rubbing [10-13]. We demonstrated that the morphologies of rat skin fibroblast cells attached to a rubbed fluorinated polyimide film were three-dimensional multicellular spheroids. However, the influence of rubbed surface on the spheroid formation was not elucidated yet. In addition, we have to control the size of the spheroid, because the spheroid of more than 200-300 μm diameters undergoes the necrosis.

We prepare a novel fluorinated polyimide surface using both a rubbing machine with a rubbing cloth and an ion-beam irradiation apparatus for cell culture. We succeeded in preparing a micropatterning on a fluorinated polyimide surface using a rubbing machine, indicating that cell aggregates or spheroids are easily formed on the patterned surface. The rubbing method without any chemical modification is a simple process and can easily prepare large surface areas, suggesting that the rubbing may become a novel cell culture method and that the rubbed film may be a novel micropatterned biomaterial to facilitate cell-cell communication or biochemical cross-talk. In addition, the cells were selectively adhered on the ion-irradiated surface, suggesting that the polyimide surface may become a novel cell culture method. We believe that the modulation of the cell function by a rubbed and ion-irradiated surface is one of the most important considerations during the design and manufacture of novel biochips or tissue engineered materials.

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