Investigation on methods of surface modification of tissue engineering materials *○

Polymer surface group transformation and bioactive molecule immobilization

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Abstract: This paper aimed to present the surface modification of tissue engineering materials and its correlation with cell compatibility from the aspects of cell-compatibility polymer surface group transformation and bioactive molecule immobilization.

INTRODUCTION

Surface modification of tissue engineering materials provides material surface histocompatibility while retaining the physio-mechanical properties. Surface modification of materials plays an increasingly important role in the development of tissue engineering. The surface physicochemical properties of tissue engineering materials greatly affect material histocompatibility. For this reason, surface modification of material is performed. Groups or bioactive molecules that can promote cell adhesion and growth are introduced while retaining the physio-mechanical properties, which can markedly improve the cell compatibility of materials. The presently used methods of surface modification of cell compatibility polymers include surface group transformation and bioactive molecule immobilization, in addition to previously published plasma surface modification and surface grafting modification[1-11].

DATA AND METHODS

Retrieval strategy

Using the terms “tissue engineering, tissue engineering materials, cell-compatibility, cell-compatibility materials, surfaces modify”, pertinent literature published between January 1963 and January 2009 in the English language was computer-retrieved from Pubmed database. At the same time, literature published between January 1963 and January 2009 in the Chinese language was also retrieved from Wanfang database. A total of 144 manuscripts were obtained and primarily screened, and the cited previously published studies were read, to exclude the repetitive studies.

Inclusion and exclusion criteria

Inclusion criteria: manuscripts pertaining to biocompatibility of tissue engineering materials.
Exclusion criteria: Repetitive contents or Meta analysis studies.

Data synthesis

A total of 144 manuscripts were primarily screened and 30 that completely correspond to criteria were included for further analysis. Of them, 11 manuscripts addressed cell compatibility of tissue engineering materials[1-11], and 19 focused on surface modification of cell compatibility materials[12-30].

RESULTS

Polymer surface group transformation

The reaction of groups existing in polymer or the reaction of groups or atoms with high reactive activity existing in groups of main chain produces small molecular functional groups on polymer surface. Polyolefine materials with saturated main chain, such as polyethylene and polypropylene, provide stable main chain. Functional groups can be introduced into oxidized surface, and hydroxy group can be introduced by oxidizing polypropylene hollow fiber membrane using persulfate[12].

Polymers containing easy-to-hydrolyze esterfunction, such as polymethyl methacrylate and polyethylene terephthalate, produce carboxyl group[13] on the surface through partial hydrolysis in alkaline solution. Then the carboxyl group reacts with ethylenediamine to enable the introduction of amino group[14] and with acetic anhydride to allow the introduction of hydroxy group[15].

Fluoropolymer surface can be modified through photochemical method. For example, under the ultraviolet light, hydroxy group or sulfonic group[16] can be introduced into polytetrafiuoroethylene through reaction with alkaline solution, thioester, or pentaerythritol tetranitrate.

Bimolecular nucleoplilic-substitution of nitrogen and lactone takes place during polyurethane surface treatment using 1, 3-propane sulton, which causes the formation of sulfonic and carboxyl groups and then enhances polyurethane hydrophilicity. Therefore, cell compatibility of materials can be enhanced by controlling the amount of sulfonic group or carboxyl group[17].

Immobilization of bioactive molecules

Bioactive molecules introduced into material surface can promote cell adhesion and growth. Therefore,

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immobilization of bioactive molecules onto material surface is an effective method to enhance cell compatibility. Protein, as an important bioactive molecule, has been much reported regarding its immobilization onto material surface. The methods of immobilizing proteins onto polymer surface primarily include physical adsorption and chemical immobilization.

Physical absorption is an easy method to immobilize bioactive molecules. Static electricity absorption can immobilize bioactive molecules with many negative charges, such as heparin, into the regions with positive charges. Interaction of protein and polymer molecule can enable protein absorption on polymer surface[18]. The protein crosslinking is accomplished through photoradiation or crosslinking agent.

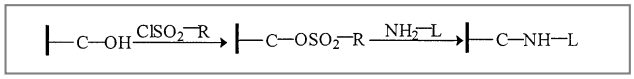
An effective method to obtain long-term histocompatibility is to firmly immobilize bioactive molecules onto material surface through chemical bonding between some groups of bioactive molecules and reactive groups of matrix surface. This method overcomes the drawbacks that bioactive molecules physically absorbed can not be immobilized onto material surface for long time and easily detach from material surface. Immobilization of bioactive molecules require some reactive groups on matrix surface, such as -OH, -COOH, and -NH_2. Therefore, the precondition of immobilization is to modify the material surface and produce above-mentioned groups.

For the chemical bonding of bioactive molecules, scholars pay more attention to material surface design, that is to say, the surface groups that can react with bioactive substance are designed according to the characteristics of bioactive substance. To enable cells to effectively recognize protein immobilized on material surface, some considerations should be taken in the process of chemical immobilization: ① Stereo-hindrance effect limits the reaction of protein molecule reactive site and surface functional group, which weakens protein immobilization. ②Protein reactive sites are embedded due to limitation of physical structure of material surface. Immobilization causes protein denaturation, and the best interaction can not be established between cell receptor and protein. Pre-introducing spacer arm into polymer surface helps overcome aforementioned drawbacks. Generally, the chemical immobilization of protein is divided into two steps[19]: polymer surface activation and reaction between activated material surface and protein.

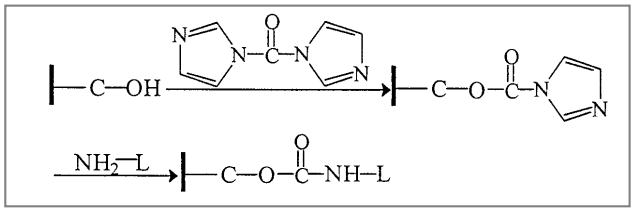
Immobilization of protein on hydroxyl polymer surface

Hydroxyl group-containing polymer surface can be activated using sulfonyl halide, carbodiimide, epoxy resin, diisocyanate, haloalkane in organic solvents including propionitrile, dichloromethane, acetone, and benzene[20].

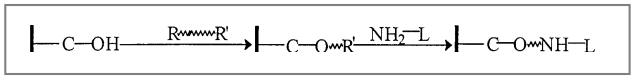
Hydroxyl groups are activated by sulfonyl chloride to produce reactive sulfonate, which further reacts with amino groups or sulfonic groups in protein to form C-N or C-S chemical bond to immobilize protein.



Hydroxyl groups can be also activated by imide and produce imide-N-methyl ester. Because the resulting ester contains detached groups, which react with amino groups in protein to produce amino-ester bond to immobilize protein[21].



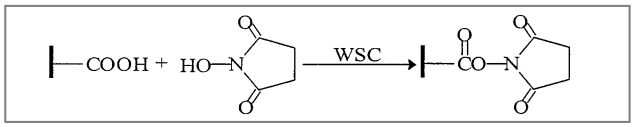
When bifunctional coupling agent, such as hexamethylene diisocyanate, reacts with hydroxyl groups in polymer, hydroxyl groups react with one end of coupling agent and form an intermediate product with a spacer arm, and the other end of coupling agent react with protein to immobilize the protein[22].



Immobilization of protein on carboxyl polymer surface

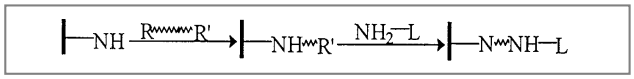
To immobilize protein on carboxyl polymer surface, carboxyl groups must be activated using commonly used agents N-hydroxysuccinimide and 1-2-methyl-amine propyl-3-ethyl-carbodiimide. Activation takes place in either water solution or organic solvent[23].

N-hydroxysuccinimide-activated surface reacts with protein in water/organic solvent system. 1-ethyl-3- 2-methyl-amine propyl-carbodiimide activated surface couples with protein in protein-water solution[24].



Immobilization of protein on amino polymer surface

Amino polymer surface can be activated by bifunctional group-containing coupling agents[25]. The commonly used coupling agents include diisocyanate, binary aldehyde, and epoxy resin. Diisocyanate activation is often accomplished in organic solvent, while diisocyanate coupling with protein is performed in buffer[26]. Glutaral is frequently used to protein immobilization on amino polymer surface due to its rapid reaction with polymer surface and protein. Binary aldehyde activation and binary aldehyde coupling with protein are often accomplished in water solution[27].



Photochemical immobilization

Photochemical immobilization is accomplished under the presence of bifunctional coupling agent. Photochemical immobilization includes three ways[28]: ① Bifunctional compound is first immobilized to polymer surface, and then couples with protein under the light radiation; ② Bifunctional coupling agent is first immobilized to polymer surface under the light radiation, and then couples with protein; ③ Protein is coupled first to bifunctional compound and then to polymer surface under the light radiation. The used photoactivating agents include light sensitive azo, benzophenone, and acrylic ester.

Other surface modification methods

Besides above mentioned methods of modification of tissue engineering materials, much attention has been also paid to recently developed ion infusion and self-assembled monomolecular layer biological material surface. Infusion of Si

ions into polyurethane, polypropylene, and polystyrene enhances the hydrophilicity of material surface and greatly improves endothelial cell adhesion[29]. Functional groups introduced into silicon rubber surface react with biological medium through exposure on the material surface and form highly ordered monomolecular layer[30], which exhibits important significance for studying interaction of living body and polymer materials and developing surface modification methods.

CONCLUSION AND PROSPECTS

The surface physiochemical properties of tissue engineering materials greatly affect the histocompatibility of materials. Therefore, it is necessary to modify material surface, and under the precondition of retaining physiomechanical properties of materials, introducing the groups or bioactive molecules that promote cell adhesion and growth can markedly improve the cell compatibility of materials.

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组织工程材料表面改性方法研究：聚合物表面基团转变和生物活性分子的固定*○

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内蒙古自治区高等学校科学研究项目(NJ06026)*

摘要：文章从细胞相容性聚合物表面基团的转变、表面生物活性分子的固定等几个方面论述了组织工程材料的表面改性及其与细胞相容性的关系。

关键词：表面改性；表面基团的转变；表面生物活性分子的固定；组织工程材料；组织相容性材料
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