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Progress in the degradation relationship between macrophages and composite stent materials

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Abstract: *Bone tissue engineering is increasingly used in the repair of maxillofacial bone defects. The application of composite materials can make up for some of the shortcomings of single materials in the past, such as insufficient strength of single materials, poor biocompatibility, and degradation of biomaterials. Some problems, in which the degradation rate of composite materials in vivo does not match the rate of bone formation, is one of the main clinical problems faced by bone tissue engineering bone composite scaffold materials. The degradation of materials in vivo is mainly divided into two aspects: biological and chemical degradation. The participation of cells is an important part of biodegradation. Among them, the role of macrophages has attracted more and more attention. It can affect the degradation of materials through direct contact with the material itself or by secreting different factors. A good understanding of the mechanism of macrophages in material degradation helps us to better design and manufacture composite scaffold materials with a degradation rate that matches the bone formation in vivo.*

Keywords: *Bone tissueengineering, composite scaffold material, Biomaterial degradation, foreign body reaction; macrophage, inflammatory factors*

1. Introduction

The repair and treatment of jaw bone defects has always been a problem that clinicians are eager to solve, because the autologous bone in the repair of bone defects, so the application of artificial bone in the repair and treatment of jaw bone defects is more widely.

The evolution of artificial bone repair materials is generally from inert to bioactive materials to intelligent materials [2]. Generation 1st Bone Repair Materials [1] It refers to the physical and chemical characteristics of the material are mainly similar to the human bone tissue in strength and hardness. After implantation, the toxic effect of the material is small and the interaction with the body tissue, and the formation of the new bone is less, so it is called an inert material. The first generation of bone repair biomaterials can probably be divided into two categories: the first category: metals, such as titanium and titanium alloy also mainly used in oral repair, cobalt and chromium alloy, and the second category: synthetic category, such as we are known as ceramic materials. The 2nd generation biobone repair materials include synthetic or naturally derived biodegradable bioactive materials such as calcium phosphate, calcium carbonate, calcium sulfate and bioactive glass [2] These are composed of natural materials that are part of the body and thus have good repulsive and degradation, but also disadvantages, such as slow degradation rate and bone formation rate. Biomaterials that can be absorbed and degraded by the body based on this [3, 4] Emerging, such materials are mainly synthetic, and can be selected according to different diagnosis and treatment objectives, such as polyhexaglactone, polyhydroxybutyrate, which have been used in clinical practice. Hench scholars, defining materials that are both biodegradable and biologically active as 3rd generation bone repair [5, 6] It is to use some artificial means to change the original properties of the material, thus have the physical characteristics consistent with the purpose. For example, when we artificially increase the porosity of the material, we will increase the contact area between the material and the surrounding tissues and thus facilitate the

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growth of blood vessels and tissues. Common third-generation bioremediation materials [7] Include the familiar tissue engineering support materials. With the development of bone tissue engineering stent materials, a single material began to be replaced by composites due to the lack of certain properties. However, how the composite material reaches the appropriate material degradation rate matching the bone formation has become an important indicator of the material. Macrophages are immune cells [8] In recent years, studies have found that macrophages play an important role in foreign body reactions, and their different forms of expression can have different effects on the degradation of implant materials [9] Recent studies on the influence of macrophages on material degradation are collected and summarized below.

2. Advantages and application status of 1. Composite support materials

Application of Bone Tissue Engineering as Bone DefMaterial in Human Body [10] Today, has become a kind of mature and has a unique advantage of the bone defect repair materials. Among them, common clinical materials such as hydroxyapatite, three calcium phosphate, polyhydroxyacetic acid, different materials also have their own unique advantages [11] Like a strong material strength [12]; Good biocompatibility [13] The combination of them with widely used materials in the clinic to improve the function of existing materials to meet different clinical needs leads to the concept of composite materials. Some properties of the original materials can be improved by adding materials, 1) Material degradation rate: Diomede F [15] et al found that by increasing stent materials of PLA(polylactic acid (EV) or engineered EV (PEI-EV) with polyvinyl imines (PEI), it was found that the rate was significantly higher than in the unadded PLA material group. ; Shua C I [16] Through the preparation of PLLA/HAP, 3PLLA/1PGA/HAP, 1PLLA/1PGA/HAP, 1PLLA/3PGA/HAP and PGA/HAP groups and comparing the degradation of each group, 1PLLA/1PGA/HAP group found good performance in the aspect of material degradation, and the material degradation rate was also increased with the increase of PGA content. 2) biocompatibility aspects: Pan C1 [17] et al. In Zn-Mg(zinc-magnesium composite, we found that the biocompatibility of the material improves the material; 3) material strength: Bakhtiyari S S E [18] Analsimulated bone structure, design porous composite bracket with suitable mechanical properties, adding nano-titanium dioxide (nTiO2) to nano-biological glass-poly-3-hydroxybutylate (nBG / P3HB) composite bracket, and found that adding nTiO2 can increase the mechanical strength and modulus and compressive strength of the bracket [19] Equal also found that the mechanical properties increased significantly with HA content in sodium alginate (SA) / hydroxyl cellulose (HEC) / HA composite stents. These studies have demonstrated that material performance can be effectively improved in this respect by adding some superior properties in the composite. The degradation rate has always been a more severe problem for emerging stent materials in clinical applications, compared to material strength and biocompatibility. The effect of material degradation is two-directional; on the one hand, the appropriate material degradation rate facilitates the repair of the own bone defect; on the other hand, the too fast material degradation rate leads to the failure of the final repair [11], So how to regulate the degradation rate of materials to meet the clinical needs has been troubling many experts and scholars[14]And to regulate the degradation rate of materials in the body, we should first understand the degradation mechanism of materials in the body.

3. In-vivo degradation of biomaterials

The degradation of materials in the body can be largely divided into biological and chemical [20] Biodegradation is involved in enzymes, liposomes, microorganisms and macrophages, which is relatively controllable, and the degradation process is roughly [21]: The trauma, foreign body stimulation of the material and its degradation products are bound to cause an inflammatory response in the body [22] ", The cells secrete various types of cell media and enzymes, producing many free radicals and peroxide anions. The intervention of cells is an important link in biodegradation.

Studies also found that material into the body would stimulate foreign body reaction s closely related to material degradation (foreign body reaction) [23]. The implant surface is wrapped in a layer of protein to form a temporary matrix [24]. On the one hand, this temporary matrix of [25] It can play a role in stimulating macrophages aggregation and regulating macrophages function afterwards; while the transient matrix contains interleukin-1 (interleukin-1,IL-1), the transforming growth factor-β -, TGF-β) [26] They can raise macrophages in peripheral blood and other immune cells to converge around the plant. The acute and chronic inflammatory response of the body was then stimulated, and some enzymes and cytokines such as TNF-α, interferon- γ (IFN- γ), lipopolysaccharides promote polarized lower

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macrophages to type M1 macrophages, which can produce a series of inflammatory media including TNF-α, active oxygen intermediates (reactive oxygen intermediate,ROI), IL-1, interleukin-6, and IL-12. To sum up, the material can cause the host body to produce the foreign body reaction, With the participation of macrophages, lymphocytes, osteoplasts and other cells, the biological degradation of the material begins to become active, in which the role of macrophages in it deserves our attention.

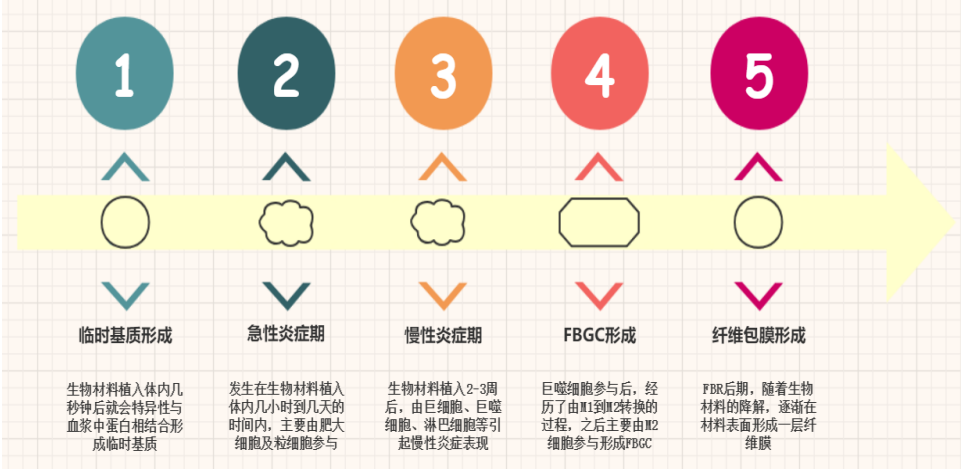

Figure 1: The FBR Process

Relationship between 3. Macrophages and the degradation of materials

3.1 Macrophages and their function

Macrophages play an important role in foreign body response, with macrophages acting as part of the body's immune system [27], It can both kill dead aging cells and antibodies through non-specific immunity [28] Specific immunity can also be activated by antigen presentation methods. Macrophages produce multiple subtypes after being activated [29]", The M1 /M2 phenotype is the two main forms of polarization in macrophages. Type M1, also known as classical activated macrophages, is mainly stimulated by factors such as lipoplysaccharides,LPS, interferon (interferon,IFN-[30] Type M1 macrophages have strong sterilization, kill tumor cells and can be identified by CD25, CD80, etc. For type M2 macrophages, it is mainly formed when encountering stimulation of factors such as IL-10, IL-13 or TGF-[31]. Mannitol receptors, CD163 and CD209 identify the cells to resist external infection and enhance regeneration [32]. Additional type M2 macrophages include three types of M2a, M2b, M2c [33] They play immune and restorative roles.

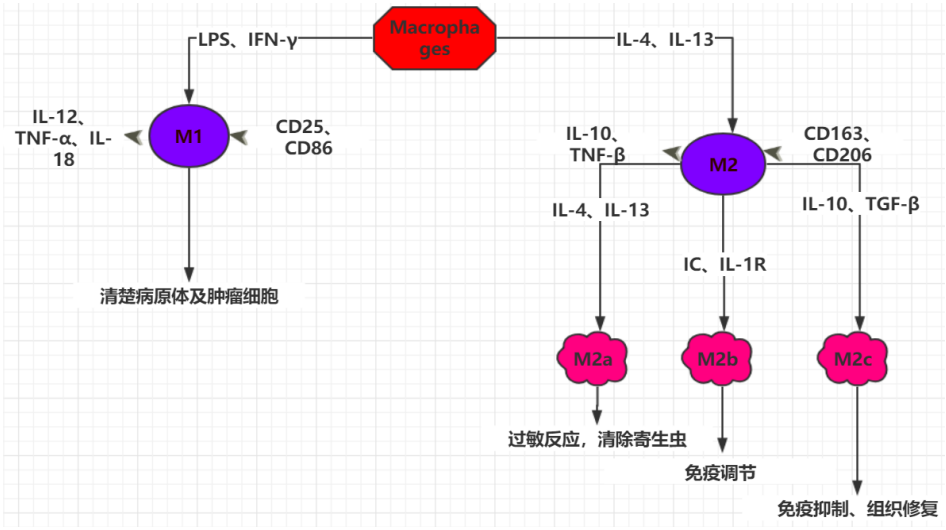

Figure 2: Macrophage polarization

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3.2 Research progress of the influence of macrophages on material degradation

Macrophages, as key cells in foreign body reactions, have also seen increasing studies on material degradation. Zhang [34] In studies of calcium silicate (mMCS) / GA) / polyhexantone (PCL) composite, others found a significant difference in the degradation rate of the material in vivo, suggesting promotes degradation by the involvement of cells. Macrophages, as important cells in foreign body reactions, also involve in vivo degradation of materials. Zhong [35] In the study of the degradation of calcium carbonate / hydroxyapatite, it was found that during the observation of the replanted body, a large number of macrophages around the phagocytic function of macrophages and the different substances secreted at different stages are closely related to the degradation of the material. Elgrabli Dan [36] The multi-wall carbon nanotubes found that macrophages participate in vivo degradation of the material through direct contact with the material; Sergin Ismail [37] The relationship between macrophages and atherosclerosis has been found that protein kinase C (PKC) has mediated mononuclear-derived macrophages (MDM) to accelerate the degradation of polycarbonate-based polyurethane (PCNUs) materials. These findings confirm that macrophages are directly or indirectly involved in the degradation of the material through either direct or indirect methods of secretion factors and their secretions.

4. Summary and Outlook

In conclusion, composite materials can be our future focus due to their flexible and regulatory characteristics. With the study of material degradation mechanism, the role of macrophages in material degradation should be valued, followed by the study of macrophages and material degradation. Macrophages affect material degradation is mainly divided into two aspects: one is to directly contact with the material or form foreign material through cytosis; and secondly, the specific secretion of macrophages has different effects on material degradation through chemical degradation channels. For example, the polarization secretion-related factors of M1 macrophages promote the development of inflammation and accelerate the degradation of materials. The foreign body reaction occurred later with the transformation of M1 to M2 macrophages, although the inflammatory response gradually weakened. Klopfleisch et al found that the increase of M1 macrophages is an important sign of increased material degradation rate, and type M2 often represents a material degradation rate. Therefore, whether the speed of material degradation can be regulated by regulating the different manifestations of macrophages, in order to achieve the clinical needs, can serve as a research direction in our future.

At present, the effects of macrophages on the degradation of macrophages on the material degradation, the mechanism of macrophages, respectively, the influence of macrophages on material degradation should be further studied. These will help us better understand the mechanism of macrophages in material degradation, and help us design and make more suitable materials.

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