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Biosynthesis of Bioadaptive Materials: A Review on Developing Materials Available for Tissue Adaptation

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Biomaterials are increasingly being evolved to actively adapt to the desired microenvironments so as to introduce tissue integration, reconstruct stability, promote regeneration, and avoid immune rejection. The complexity of its mechanisms poses great challenge to current biomimetic synthetic materials. Although still at initial stage, harnessing cells, tissues, or even entire body to synthesize bioadaptive materials is introducing a promising future.

1. Introduction

Implantable devices and scaffolds can replace damaged tissues, restore function, and alleviate pain. Creating materials that instigate a specific and desired biological response is the driving force behind current biomaterial design[1]. Traditionally, biocompatibility means to create simple, inert materials that do not produce toxic effects. These ideas are being achieved by a new generation of bioadaptive materials that actively interact with local organisms to allow directed tissue integration and regeneration[1,2].

To achieve this, scaffold surfaces should encourage optimized cell adhesion and development as would normally occur in vivo[3]. In recent years, it has become increasingly apparent that the cells' response to microenvironmental signaling goes far beyond the ability of the cells to chemically sense specific extracellular matrix (ECM) ligands, and encompasses a wide range of physical cues that are generated at, or act on, the adhesive interface between cells and the surrounding matrix (Fig. 1)[4–6]. This review will discuss methods being developed to mimic the natural structure that would adapt to the microenvironmental needs of biomaterials.

2. Traditionally Synthetic Materials

2.1. Physical cues promoting tissue integration by cell adhesion

Cell-biomaterial interactions are primarily governed by cell adhesion, which arises from the binding of cellular integrin receptors to biomacromolecules adsorbed, tethered, or deposited onto a surface or the extracellular matrix[7]. Studies have shown enormous sensitivity of cells to various features of their environment[6].

Implant integration is affected by surface texturing. In vitro study showed without osteogenic supplements, topographically treated human mesenchymal stem cells (hMSCs) produced similar bone mineral compared with cells cultured with osteogenic media, but their gene profiles of cell differentiation are distinct[8]. Osteoblasts exhibit roughness-dependent phenotypic characteristics that they appear to be more differentiated with reduced proliferation on rougher surfaces[9,10]. Various nanostructures of scaffolds can be realized by many techniques. Production methods of hydroxyapatite (HA) are classified according to the used reagents (solutions, slurries, pastes, and powders), dispersion media (gas, liquid, solid),

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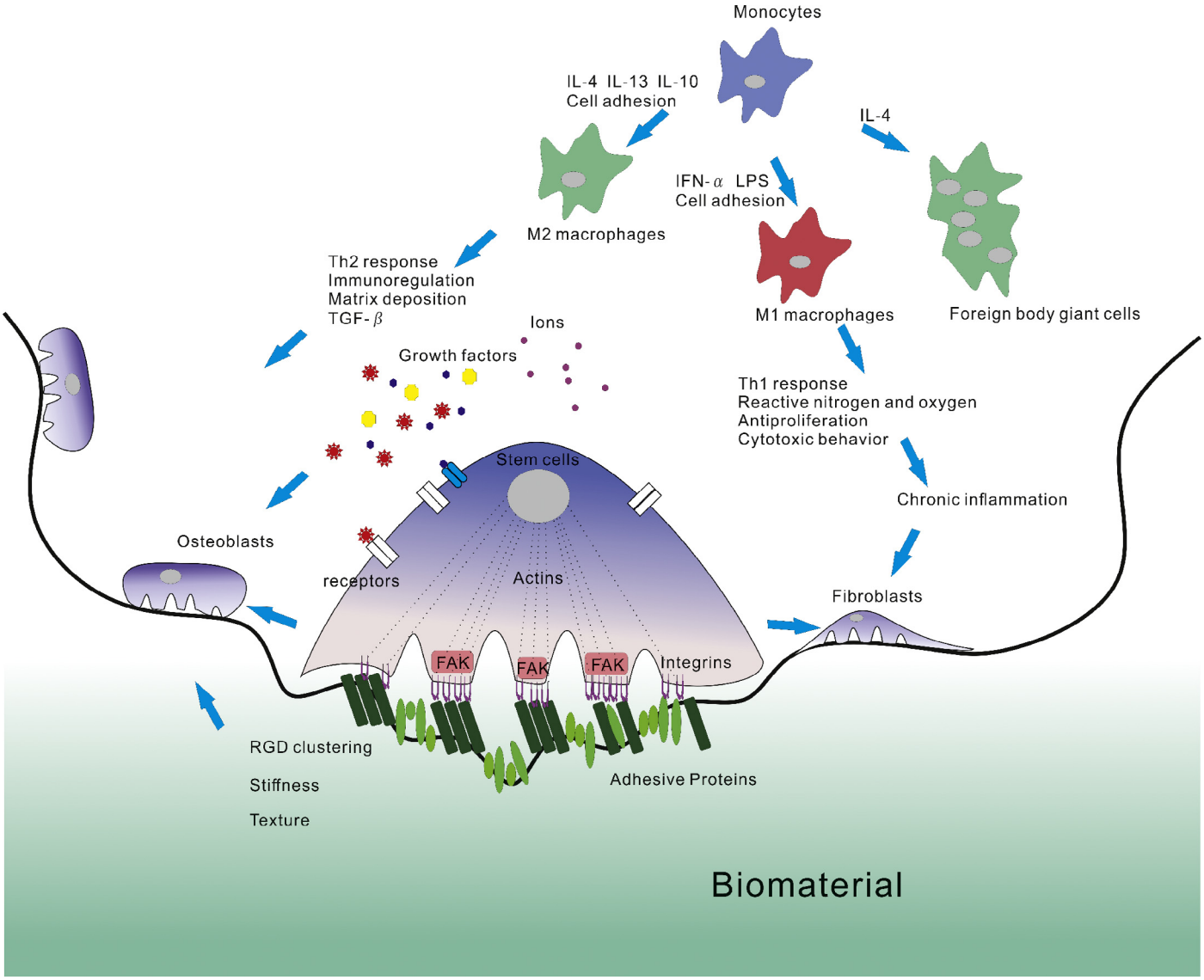

Fig. 1. Organism response of biomaterial involves crosstalk of stem cells and macrophages. The regulation is determined by material stiffness, texture, adhesive proteins, and molecules (ions, drugs or growth factors) released from the biomaterial, etc. The great complexity comes not only from the enormous mechanisms but also from the precise spatiotemporal control of these regulation mechanisms.

dispersion tools (nozzle, propeller, sieve, mold). By using different methods, diameters of HA particles vary from 10 nm to 10 mm[11]. Crystallite size of HA can also be manipulated by changing pressure synthetic conditions[12]. Benefiting from computer-aided design and manufacturing (Cad/Cam), novel fabrication methods including prototyping, electrospinning and lithography are being developed[13,14].

Cells also respond differentially to various surface chemistry. Cells bind to adhesion associated proteins with the help of integrin receptors, which play a critical role in the mechanic-transduction process by connecting the cytoskeleton to the ECM, and converting mechanical stimuli into biochemical signals[15–17]. ECM proteins in bone include collagen and non-collagenous glycoproteins[17]. Salasznyk et al. showed that the cells contacting with type I collagen or vitronectin alone may be sufficient to induce differentiation of these cells[18]. Moursi et al. have demonstrated a role for fibronectin during calvarial osteoblastic differentiation in vitro[19,20]. Klees et al. reported the signaling pathway regulating osteogenic differentiation of hMSCs on laminin-5, in the absence of any soluble osteogenic supplements, was via focal adhesion kinase (FAK) activation[21].

Bioadhesive ligand clustering is a key parameter for the rational engineering of bioactive materials. Grafting of adhesion associated ligands onto a Polyethylene glycol (PEG) based polymer has been used as model in studying the influence of surface properties on adhesive cells[22,23]. These studies indicated that a higher density of Arg-Gly-Glu based adhesive epitope (RGD) is essential for triggering a pleiotropic cellular response to the adhesion, which is manifested by an increase in cell spreading, the activation of survival signaling pathways and the activation of focal adhesion assembly[6].

The hydrophobicity control protein adsorption and receptor-ligand accessibility, which in turn controls cell adhesion. Strongly hydrophobic surfaces lead to protein unfolding upon strong interaction with the surface, known as relaxation, resulting in a loss of biological activity[24] and associated inhibition of integrin binding[25]. Protein adsorption on hydrophilic surfaces tends to be weaker, and