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# Advancing biomaterials of human origin for tissue engineering

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ABSTRACT

Biomaterials have played an increasingly prominent role in the success of biomedical devices and in the development of tissue engineering, which seeks to unlock the regenerative potential innate to human tissues/organs in a state of deterioration and to restore or reestablish normal bodily function. Advances in our understanding of regenerative biomaterials and their roles in new tissue formation can potentially open a new frontier in the fast-growing field of regenerative medicine. Taking inspiration from the role and multicomponent construction of native extracellular matrices (ECMs) for cell accommodation, the synthetic biomaterials produced today routinely incorporate biologically active components to define an artificial *in vivo* milieu with complex and dynamic interactions that foster and regulate stem cells, similar to the events occurring in a natural cellular microenvironment. The range and degree of biomaterial sophistication have also dramatically increased as more knowledge has accumulated through materials science, matrix biology and tissue engineering. However, achieving clinical translation and commercial success requires regenerative biomaterials to be not only efficacious and safe but also cost-effective and convenient for use and production. Utilizing biomaterials of human origin as building blocks for therapeutic purposes has provided a facilitated approach that closely mimics the critical aspects of natural tissue with regard to its physical and chemical properties for the

*Abbreviations:* 3D, three-dimensional; ACI, autologous chondrocyte implantation; ACS, absorbable collagen sponge; AM, amniotic membrane; ASI, alternating solution immersion; ASCs, adipose-derived stem cells; BBIM, bioactive bone-inducing material; BM, basement membrane; BMC, bone marrow concentrate; BMPs, bone morphogenetic proteins; CaP, calcium phosphate; CBD-BMP-2, collagen-binding domain bone morphogenetic protein-2; CCC, cortical cancellous chips; CMC, carboxymethylcellulose; CNTF, ciliary neurotrophic factor; CS, chondroitin sulfate; CTA, complex tissue allotransplantation; DBM, demineralized bone matrix; DDM, demineralized dentin matrix; Dex-GMA, glycidyl methacrylate-derivatized dextran; DFDBAs, demineralized freeze-dried bone allografts; DMD, Duchenne muscular dystrophy; ECGF, epithelial cell growth factor; ECM, extracellular matrix; EDTA, ethylenediaminetetraacetic acid; EGF, epidermal growth factor; EGTA, ethylene glycol tetraacetic acid; EPCs, endothelial progenitor cells; ESCs, embryonic stem cells; FAM, fiber-assisted molding; FBS, fetal bovine serum; FDA, Food and Drug Administration; FDBAs, freeze-dried bone allografts; FGG, free gingival graft; GAGs, glycosaminoglycans; GMP, good manufacturing practice; HA, hyaluronic acid; HGF, hepatocyte growth factor; HIV, immunodeficiency virus; HLA, human leukocyte antigen; HS, heparin sulfate; HSCs, hematopoietic stem cells; ICBG, iliac crest bone graft; IGF, insulin-like growth factor; IVD, intervertebral disc; MMP2, matrix metalloproteinase 2; MSCs, mesenchymal stem cells; NCPs, non-collagen proteins; NF-κB, nuclear factor-κB; NF-gelatin, nanofibrous gelatin; NP, nucleus pulposus; PCL, poly(ε-caprolactone); PDAF, platelet-derived angiogenesis factor; PDEGF, platelet-derived endothelial growth factor; PDGFs, platelet-derived growth factors; PEG, polyethylene glycol; PF-4, platelet factor-4; PGA, polyglycolic acid; PL, platelet lysate; PLA, polylactic acid; PLGA, poly(lactic-*co*-glycolic acid); PRF, platelet-rich fibrin; PRGF, plasma rich in growth factor; PRP, platelet-rich plasma; RGD, arginine–glycine–aspartic acid; rhBMP-2, recombinant human bone morphogenetic protein-2; rhELR, recombinant human elastin-like polymer; SDF-1, stromal cell-derived factor-1; SDS, sodium dodecyl sulfate; SEM, scanning electron microscopy; SF, silk fibroin; SIS, small intestinal submucosa; SM, stromal matrix; SVF, stromal vascular fraction; TCP, tricalcium phosphate; TGF-β, transforming growth factor-β; VEGFs, vascular endothelial growth factors.

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orchestration of wound healing and tissue regeneration. In addition to directly using tissue transfers and transplants for repair, new applications of human-derived biomaterials are now focusing on the use of naturally occurring biomacromolecules, decellularized ECM scaffolds and autologous preparations rich in growth factors/non-expanded stem cells to either target acceleration/magnification of the body's own repair capacity or use nature's paradigms to create new tissues for restoration. In particular, there is increasing interest in separating ECMs into simplified functional domains and/or biopolymeric assemblies so that these components/constituents can be discretely exploited and manipulated for the production of bioscaffolds and new biomimetic biomaterials. Here, following an overview of tissue auto-/allo-transplantation, we discuss the recent trends and advances as well as the challenges and future directions in the evolution and application of human-derived biomaterials for reconstructive surgery and tissue engineering. In particular, we focus on an exploration of the structural, mechanical, biochemical and biological information present in native human tissue for bioengineering applications and to provide inspiration for the design of future biomaterials.



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