SciMedCentral

JSM Nanotechnology & Nanomedicine

Editorial

Regenerative Nanomedicine

Eap S[1,2], Keller L[1,2], Schiavi J[1,2], Fioretti F[1,2] and Benkirane-Jessel N[1,2]*

[1]INSERM (French National Institute of Health and Medical Research), UMR 1109, "Osteoarticular and Dental Regenerative Nanomedicine" team, 11 rue Humann, 67085 Strasbourg Cedex, France

[2]University of Strasbourg, Faculty of Dental Surgery of Strasbourg, France

Corresponding author

Benkirane-Jessel N, Leader, 1INSERM (French National Institute of Health and Medical Research), UMR 1109, "Osteoarticular and Dental Regenerative Nanomedicine" team, 11 rue Humann, 67085 Strasbourg Cedex, France, Email: nadia.jessel@inserm.fr

Submitted: 18 June 2013

Accepted: 18 June 2013

Published: 21 June 2013

Nanomedicine is the application of nanotechnology to medicine and healthcare. The field takes advantage of the physical, chemical and biological properties of materials at the nanometer scale to be used for diagnosis, treatment and follow-up of diseases. Given the immense potential impact of nanomedicine on public wellbeing and on economic growth, the field is of considerable strategic importance for medicine and healthcare.

Nanoscale materials should be designed according to the time-dependent requirements of target tissues to be regenerated in order to maximize the tissue-healing capacity of nano-devices. In spite of important progress in regenerative nanomedicine, there are still critical challenges for an advanced nanomedical approach to develop a clinical device. It may be necessary to mimic much of the complex, natural regenerative processes in order to repair diseased or damaged tissue.

Regeneration of dysfunctional or damaged tissues to restore their structure and function constitutes a main challenge in modern medicine. It can be addressed through the rapidly developing, multidisciplinary field of tissue engineering, which aims to form new functional tissue using optimal combinations of cells (autologous, allogeneic, xenogeneic, genetically engineered, or stem cells) and tailored biophysical and biochemical milieus capable of directing the organization, behaviour and functions of cells (e.g. adhesion, morphology, proliferation, differentiation). This approach requires the development of next-generation biomaterials that provide provisional bioactive 3-D scaffolds capable of guiding the spatially and temporally complex multicellular processes of tissue formation and regeneration [1-7].

Biomimetic matrices inspired from the intricate nanofibrillar architecture of natural extracellular matrix (ECM) components have already shown remarkable success in tissue engineering applications [5,8-10], allowing for instance, reconstruction of a dog urinary bladder [9], or regeneration after brain injury in a mouse stroke model [10]. However, it is established that durable tissue repair cannot be achieved with inert ECM-mimetic scaffolds. Ideally, scaffolds should also be equipped with bioactive molecules, including growth factors, angiogenic factors, differentiation factors and bone morphogenetic proteins to accelerate specific ECM production and tissue integration, or drugs to prevent adverse biological response such as sepsis or cancer recurrence [11]. To this end, strong benefits are expected from the combination of recent advances in (i) the design of nanoengineered ECM analogues [12-15], and (ii) strategies to enrich the surface of biomaterials with bioactive compounds [16-26].

Extracellular microenvironments play a critical role in the regulation of a range of cell behavior, including cell adhesion, proliferation, migration and differentiation [27,28]. In order to develop novel functional implants it is essential to construct suitable interfacial microenvironments—which both direct cell fates and improve interactions between cells and implant materials—on the surfaces of materials. With the advancement and convergence of materials science and biology, it is possible to construct biomimetic extracellular microenvironments on the surfaces of implants by combining functional drug-delivery systems with biomaterials [29,30]. Various strategies have been employed to construct extracellular microenvironments, such as functional proteins, fibrin hydrogels containing growth factor and anti-inflammatory drug-eluting multilayers[16-33]. We have also developed gene-stimulating microenvironments on titanium and poly(d,l-lactic acid) substrates via a layer-by-layer (LbL) assembly technique which were able to regulate cell functions, including the differentiation of mesenchymal stem cells (MSCs) [34,35].

The tissue-engineering approach is a promising strategy added in the field of bone regenerative medicine, which aims to generate new, cell-driven, functional tissues, rather than just to

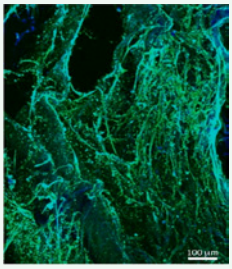

Figure 1 Electrospun nanofibers membrane of poly-ε-caprolactone visualization after 21 days of human Osteoblasts culture (Cells visualization in blue (nucleus /DAPI) and PLL^{FITC} labelled nanofibers in green): colonization and proliferation of osteoblasts into the nanofibers membrane.

implant non-living scaffolds. Three-dimensional porous scaffolds with specific architectures at the nano, micro and macro scale for optimum surface porosity and chemistry, which enhance cellular attachment, migration, proliferation and differentiation, are undergoing a continuous evaluation process.

References

1. Peppas NA, Langer R. New challenges in biomaterials. Science. 1994; 263: 1715-20.
2. Hubbell JA. Biomaterials in tissue engineering. Biotechnology (N Y). 1995;13: 565-76.
3. Griffith LG, Naughton G. Tissue engineering--current challenges and expanding opportunities. Science. 2002; 295:1009-14.
4. Chaikof EL, Matthew H, Kohn J, Mikos AG, Prestwich GD, Yip CM. Biomaterials and scaffolds in reparative medicine. Ann N Y Acad Sci. 2002; 961: 96-105.
5. Langer R, Tirrell DA. Designing materials for biology and medicine. Nature. 2004; 428: 487-92.
6. Yang C, Hillas PJ, Báez JA, Nokelainen M, Balan J, Tang J, Spiro R, Polarek JW. The application of recombinant human collagen in tissue engineering. BioDrugs. 2004; 18: 103-19.
7. Kumar G, Tison CK, Chatterjee K, Pine PS, McDaniel JH, Salit ML, Young MF, Simon CG Jr. The determination of stem cell fate by 3D scaffold structures through the control of cell shape. Biomaterials. 2011; 32: 9188-96.
8. Dvir T, Timko BP, Kohane DS, Langer R. Nanotechnological strategies for engineering complex tissues. Nat Nanotechnol. 2011; 6: 13-22.
9. Oberpenning F, Meng J, Yoo JJ, Atala A. De novo reconstitution of a functional mammalian urinary bladder by tissue engineering. Nat Biotechnol. 1999; 17: 149-55.
10. Park KI, Teng YD, Snyder EY. The injured brain interacts reciprocally with neural stem cells supported by scaffolds to reconstitute lost tissue. Nat Biotechnol. 2002; 20:1111-7.
11. Porter JR, Ruckh TT, Popat KC. Bone tissue engineering: a review in bone biomimetics and drug delivery strategies. Biotechnol Prog. 2009; 25: 1539-60.
12. Kenawy E, Layman JM, Watkins JR, Bowlin GL, Matthews JA, Simpson DG, Et al, Electrospinning of poly(ethylene-co-vinyl alcohol) fibers. Biomaterials. 2003; 24: 907-13.
13. Zhang S. Fabrication of novel biomaterials through molecular self-assembly. Nat Biotechnol. 2003; 21: 1171-8.
14. Barnes CP, Sell SA, Boland ED, Simpson DG, Bowlin GL. Nanofiber technology: designing the next generation of tissue engineering scaffolds. Adv Drug Deliv Rev. 2007; 59: 1413-33.
15. Smith LA, Liu X, Ma PX. Tissue Engineering with Nano-Fibrous Scaffolds. Soft Matter. 2008; 4: 2144-2149.
16. Yoo HS, Kim TG, Park TG. Surface-functionalized electrospun nanofibers for tissue engineering and drug delivery. Adv Drug Deliv Rev. 2009; 61: 1033-42.
17. Jessel N, Atalar F, Lavalle P, Mutterer J, Decher G, Schaaf P, et al. Bioactive Coatings Based on a Polyelectrolyte Multilayer Architecture Functionalized by Embedded Proteins. Advanced Materials. 2003; 15: 692-695.
18. Jessel N, Lavalle P, Meyer F, Audouin F, Frisch B, Schaaf P, et al. Control of monocyte morphology on and response to model surfaces for implants equipped with anti-inflammatory agents. Advanced Materials. 2004; 16: 1507-1511.
19. Benkirane-Jessel N, Schwinté P, Falvey P, Darcy R, Haïkel Y, Schaaf P, et al. Build-up of polypeptide multilayer coatings with anti-inflammatory properties based on the embedding of piroxicam-cyclodextrin complexes. Advanced Functional Materials. 2004; 14: 174.
20. Benkirane-Jessel N, Lavalle P, Hubsch E, Holl V, Senger B, Haikel Y, et al. Short-time timing of the biological activity of functionalized polyelectrolyte multilayers. Adv Funct Mater. 2005; 15: 648-54.
21. Jessel N, Oulad-Abdelghani M, Meyer F, Lavalle P, Haîkel Y, Schaaf P, et al. Multiple and time-scheduled in situ DNA delivery mediated by beta-cyclodextrin embedded in a polyelectrolyte multilayer.Proc Natl Acad Sci U S A. 2006; 103: 8618-21.
22. Lynn DM, Layers of opportunity: nanostructured polymer assemblies for the delivery of macromolecular therapeutics. Soft Matter. 2006; 2: 269-273.
23. Dierich M, Le Guen E, Messadeq N, Netter P, Schaaf P, Voegel JC, Jessel N. Bone formation mediated by growth factors embedded in a polyelectrolyte multilayer film. Adv Mater. 2007; 19: 693-697.
24. Kim BS, Park SW, Hammond PT. Hydrogen-bonding layer-by-layer-assembled biodegradable polymeric micelles as drug delivery vehicles from surfaces. ACS Nano. 2008; 2: 386-92.
25. Mendoza-Palomares C, Ferrand A, Facca S, Fioretti F, Ladam G, Kuchler-Bopp S, Regnier T, Mainard D, Benkirane-Jessel N. Smart hybrid materials equipped by nanoreservoirs of therapeutics. ACS Nano. 2012; 6: 483-90.
26. Decher G. Fuzzy Nanoassemblies: Toward Layered Polymeric Multicomposites. Science. 1997; 277: 1232-1237.
27. Lutolf MP, Hubbell JA. Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering. Nat Biotechnol. 2005; 23: 47-55.
28. Peng CW, Liu XL, Chen C, Liu X, Yang XQ, Pang DW, Zhu XB, Li Y. Patterns of cancer invasion revealed by QDs-based quantitative multiplexed imaging of tumor microenvironment. Biomaterials. 2011; 32: 2907-17.
29. Discher DE, Mooney DJ, Zandstra PW. Growth factors, matrices, and forces combine and control stem cells. Science. 2009; 324: 1673-7.
30. Kang Y, Kim S, Khademhosseini A, Yang Y. Creation of bony microenvironment with CaP and cell-derived ECM to enhance human bone-marrow MSC behavior and delivery of BMP-2. Biomaterials. 2011; 32: 6119-30.
31. Zhang Y, Xiang Q, Dong S, Li C, Zhou Y. Fabrication and characterization of a recombinant fibronectin/cadherin bio-inspired ceramic surface and its influence on adhesion and ossification in vitro. Acta Biomater. 2010; 6: 776-85.
32. Park JS, Yang HN, Woo DG, Jeon SY, Park KH. Chondrogenesis of human mesenchymal stem cells in fibrin constructs evaluated in vitro and in nude mouse and rabbit defects models. Biomaterials. 2011; 32: 1495-507.
33. Macdonald ML, Samuel RE, Shah NJ, Padera RF, Beben YM, Hammond PT. Tissue integration of growth factor-eluting layer-by-layer polyelectrolyte multilayer coated implants. Biomaterials. 2011; 32: 1446-5.
34. Hu Y, Cai KY, Luo Z, Zhang R, Yang L, Deng LH, et al. Biomaterials. 2009; 30: 3626
35. Cai KY, Hu Y, Luo Z, Kong T, Lai M, Sui XJ, et al. cell- specific gene transfection from a gene-functionalized poly(D,L-lactic acid) substrate fabricated by the layer-by-layer assembley technique. Angewandte Chemie International Edition. 2008; 47: 7479-7481.

Cite this article

Eap S, Keller L, Schiavi J, Fioretti F, Benkirane-Jessel N (2013) Regenerative Nanomedicine. JSM Nanotechnol Nanomed 1(1): 1001.