

**Title Page: Biochemistry of Mitochondrial Quality Control**

“Biochemistry of Mitochondrial Quality Control” handling editor “Prof Jeremy W Chambers”

**Review Article**

Enhanced Cell Mitochondrial Activity using Electrospun Nanofibers

Valencia Jacobs<sup>1,2,3,4\*</sup>

<sup>1</sup>CSIR Materials Science and Manufacturing, Polymers & Composites, P.O. Box  
1124, Port Elizabeth 6000, South Africa

<sup>2</sup>Department of Chemistry, Faculty of Science, Nelson Mandela Metropolitan  
University, Port Elizabeth, South Africa

<sup>3</sup>UNESCO-UNISA AFRICA Chair in Nanosciences/Nanotechnology, University of  
South Africa, Muckleneuk Ridge, Pretoria, South Africa

<sup>4</sup>Nanosciences African Network, iThemba LABS-National Research Foundation,  
Somerset West, Western Cape Province, South Africa

---

\* Corresponding Author address: Valencia Jacobs, CSIR Materials Science and  
Manufacturing, Polymers & Composites, P.O. Box 1124, Port Elizabeth 6000, South  
Africa, Tel: +27(0)41 508 3229; Fax: +27(0)41 583 2325

Email: [vjacobs@csir.co.za](mailto:vjacobs@csir.co.za)

**Abstract:** Research in tissue engineering related to the improved processes using nanofiber scaffolds has seen considerable progress in the last decade in the regeneration and construction of a number of artificial tissue types. These designs are generally viewed from the perspective of possible sources for clinical implant and transplant materials. Nowadays, advancement in engineering of tissues often referred to as three-dimensional (3D) cell culture provides enhanced activities owing to the 3D systems that readily imitate the *in vivo* setting for differentiated organs, than a typical 2D cell culture. Electrospinning has been useful in producing nanofibrous scaffolds with large surface area and high pore volume that has the potential to mimic the morphology of a tissue extracellular matrix and hence promoting cell attachment, proliferation and differentiation. This review reports improved processes of tissue revitalization utilizing electrospun nanofibrous scaffolds. Different tissue engineering approaches including their advantages have been discussed. Also, various biomaterials from both synthetic and natural origin have been elaborated.

**Keywords:** Cell activity; Electrospinning; Biomaterials; Tissue Engineering

**Abbreviations:** **PCL:** polycaprolactone; **PLA:** polylactic acid; **PHB:** polyhydroxybutyrate; **ECM:** extracellular matrix

### **Introduction:**

It is becoming apparent that biomaterials have a critical role to play in the development and evolution of regenerative medicine. Tissue engineering is one interdisciplinary area that combines the principles of engineering and life sciences to advance biological substances that restore, maintain and revitalize the damaged tissues and organs [1-3]. To replace diseased, defected, or lost cartilage tissue and to restore natural tissue functions during regeneration process, biomaterial and biomechanical considerations should be incorporated into a designed [4]. In the past, a large focus was on the development of biomaterials scaffolds for permanent tissue replacement. Among the few types of polyester onto which human cells can either differentiate, divide or both, biocompatible

and biodegradable PCL, PLA and PHB have been successfully electrospun into nanofiber scaffolds [1]. However, electrospun nanofibrous scaffolds are of great interest in tissue engineering due to their interconnected pores, their high surface area to volume ratio and architectural similarity to the native ECM [4]. These properties enable electrospun scaffolds to stimulate cell mitochondrial activities including cell adhesion, proliferation and differentiation but also improve spatial organization on the mesoscopic scale [1, 5-9].

### **Tissue Engineering Approaches**

Generally, engineered tissue is normally composed of primary or immortalized cells that are organized and cultured on the surface or inside a three-dimensional (3D) scaffold composed of either extracellular matrix proteins or analogous biomaterials [10]. However, utilizing regenerated tissue in biomedical research is to bridge the gap between traditional two-dimensional (2D) cell culture and the *in vivo* setting, thus, creating an environment that more closely represents the complex 3D structure of intrinsic tissue. In this tactic, the *in vitro* phenotype of cells in a 3D model, surrounded by extracellular matrix and other cells offers the ability to measure phenotypes that cannot be measured in 2D cell cultures and therefore in some cases will be more relevant to the *in vivo* situation [11, 12]. Another powerful advantage of 3D systems is to apply a high-throughput method to perform phenotypic measurement of traits typically limited to organ systems in analogous to 2D culture models. Furthermore, electrospinning has proven to be one of the significant methods for fiber-based 3D scaffold production [13].

### **Electrospun Nanofibrous Scaffolds**

Polymeric biomaterials and their blends have been widely utilized in biomaterials research due to their biodegradability. PCL, a hydrophobic polymer, is a well-known biocompatible polymer that has been successfully fabricated via electrospinning technology [14-16]. Electrospun PCL blends include natural biopolymers such as gelatin, chitosan and lecithin. However, PCL-gelatin blend can improve cell and neurite growth whereas PCL-chitosan blend promotes cell growth and expansion [17].

### Discussion and Conclusions

The presence of high porous networks and large surface area in the morphology of electrospun nanofibrous scaffolds can promote cell regeneration, proliferation and differentiation. Various approaches for tissue regeneration using a 3D *in vitro* model surrounded by extracellular matrix offers the ability to measure phenotypes that cannot be measured in 2D cell cultures.

### References

1. Daranarong D, Chan RTH, Wanandy NS, Molloy R, Punyodom W, Foster LJR. Electrospun Polyhydroxybutyrate and Poly(L-lactide-co- $\epsilon$ -caprolactone) Composites as Nanofibrous Scaffolds. *BioMed Res.* 2014, Article ID 741408, 12 pages. doi:10.1155/2014/741408.
2. Atala A, Mooney DJ, *Synthetic Biodegradable Polymer Scaffolds*, Birkhauser, Boston, Mass, USA, 1997.
3. Shalak R, Fox CF. Preface, in *Tissue Engineering*. Tissue Engineering, Liss, New York, NY, USA, 1988.
4. Jeong SI, Jeon O, Krebs MD, Hill MC, Alsberg E. Biodegradable photo-crosslinked alginate nanofibre scaffolds with tuneable physical properties, cell adhesivity and growth factor release. *Eur Cells Mater.* 2012; 24: 331-343.
5. Feng S, Shen X, Fu Z, Shao M. Preparation and Characterization of Gelatin–Poly (L-lactic) Acid/Poly(hydroxybutyrate-co-hydroxyvalerate) Composite. *Nanofibrous Scaffolds, J Macromol Sci Part B: Physics.* 2011; 50: 1705-1713.
6. Mooney DJ, Langer RS. *The Biomedical Engineering Handbook*, edited by Bronzino JD, CRC Press, 1995.
7. Shih Y-RV, Chen CN, Tsai SW, Yang JW, Lee OK. Growth of mesenchymal stem cells on electrospun type I collagen nanofibers, *Stem Cells.* 2006; 24: 2391–2397.
8. Prabhakaran MP, Venugopal J, Chan CK, Ramakrishna S, Surface modified electrospun nanofibrous scaffolds for nerve tissue engineering. *Nanotechnology.* 2008; 19: Article ID 455102.
9. Venugopal J, Low S., Choon AT, Kumar AB, Ramakrishna S., Electrospun-modified

nanofibrous scaffolds for the mineralization of osteoblast cells. *J Biomed Mater Res A*, 2008; 85: 408–417.

10. Petersen MC, Lazar J, Jacob HJ, Wakatsuki T. Tissue engineering: a new frontier in physiological genomics. *Physiol Genomics*. 2007; 32: 28-32.

11. Asnes CF, Marquez JP, Elson EL, Wakatsuki T. Reconstitution of the Frank-Starling mechanism in engineered heart tissues. *Biophys J*. 2006; 91: 1800–1810.

12. Liu H, Fan H, Cui Y, Chen Y, Yao K, Goh JC. Effects of the controlled-released basic fibroblast growth factor from chitosan-gelatin microspheres on human fibroblasts cultured on a chitosan-gelatin scaffold. *Biomacromolecules*. 2007; 8: 1446–1455.

13. Cholewa W-M, Langer K, Szymanowski K, Glodek A, Jankowska A, Warcholet W. et al. An efficient 3d cell culture method on biomimetic nanostructured grids. 2013; *PLoS ONE* 8(9): e72936.

14. Santos Jr AR. Bioresorbable polymers for tissue engineering. *Tissue Engineering*, Eberli D (Ed.), ISBN: 978-953-307-079-7.

15. Törmälä P, Pohjonen T, Rokkanen P. Bioabsorbable polymers: materials technology and surgical applications. *Proc Instn Mech Eng Part H - J Eng Med*. 1998; 212: 101-111.

16. Barbanti, S.H.; Zavaglia, C.A.C. & Duek, E.A.R. Polímeros bioreabsorvíveis na engenharia de tecidos. *Polímeros: Ciência e Tecnologia*. 2005; 15: 13-21.

17. Sell SA, Wolfe PS, Garg K, McCool JM, Rodriguez IA, Bowlin GL. The use of natural polymers in tissue engineering: a focus on electrospun extracellular matrix analogues. *Polymers*. 2010; 2: 522-553.