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Review Article

Harnessing Electricity in Biosystems- A Functional Tool for Tissue Engineering Applications

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Abstract

Tissue engineering aims to provide the necessary structural architecture and biophysical stimuli to support functioning of the target tissue. Native electricity has been demonstrated to guide the development and regeneration of a variety of tissues. Manipulation of this electricity through the external devices or the microenvironment surrounding the cell can potentially modulate function of individual cells, tissues and entire organs. This review highlights the recent progress made in utilization of electricity in tissue engineering and regenerative medicine applications.

Keywords: Tissue engineering; Bioelectricity; Endogenous electric field; Ion current; Surface charge

Introduction

Tissue engineering is a promising strategy to generate tissue suitable for recovery or replacement of native tissue. It involves different approaches to mimic the microenvironment of the native tissue via a variety of material, chemical, mechanical and electrical stimuli [1-6], with the ultimate goal to enhance the single cell function, improve cell-cell and cell-extracellular matrix interactions in the damaged tissue and restore tissue function. Studies have revealed the importance of electricity as one of the native regulators of cell functions. Electricity in the form of electrical fields, currents or charges provides spatial and temporal regulation of cellular activities ranging from embryonic development to regeneration of injured tissue [7-9]. *Electrical fields* are key for functioning of ion channels and pumps. These molecules are expressed within the cell membrane and generate the electric field on the order of 107 mV/ mm across the membrane [10]. *Electric currents* are induced by the transport of ions and separation of charges along the tissue and can regulate tissue physiological response [11,12]. For example, in the normal skin, there is a native trans-epithelial electric potential difference of ~ 40-70 mV that forms across the epithelial layer [13]. When the skin is injured, the trans-epithelial electric potential drops at the center of the wound site. As a result, a potential difference develops between the center of the wound and the surrounding tissues, giving rise to an electric field on the order of 100mV/mm that guides the cells to the site of injury and helps heal the wound [14,15]. *Electrostatic interactions* are key regulators of major cell functions such as adhesion, cell interactions with signals on the extracellular surfaces, and may even participate in immune function and infection prevention [9,16-18]. Overall, modulation of native electricity is a promising approach to regulate single cell function as well as cell-cell and cell-extracellular interactions and to activate appropriate cell signaling pathways. On a practical level, this can be achieved by (a) using charged surfaces to regulate electrostatic interactions, (b) delivering electricity through fabricated conductive scaffolds, or (c) application of external electricity to cells and tissues using custom made devices to locally induce electric field or generate electric current. Here we review recent advances in the use of external electricity as a tool for tissue engineering.

Charged Surfaces

Development of tissue from multicellular organisms during growth or repair relies on cell adhesion process which can be influenced by electrostatic charges [9,19]. Therefore, manipulation of substrate charge, for example, by coating the implant to enhance cell adhesion is a promising strategy to control cell movement, assembly and responses in tissue engineering applications. One of the most effective materials that can be used for surface coating is hydroxyapatite (HAp). Following deposition on the surface, it can be polarized by applying a DC electric field at high temperature, which results in high charge storage capacity. The polarity of the induced surface charge depends on the polarity of the applied DC electric field [20,21]. It has been shown that this surface charge can accelerate or decelerate cell adhesion and growth on the charged surfaces through attraction or repulsion of positive ions, specifically, divalent cations in the cell culture medium [9,22]. These cations enable interactions between the surface and negatively charged cell membrane and play an important role in formation of focal adhesions [23]. In practical applications, HAp coating is often applied on a titanium substrate, which is commonly used in dental and orthopedic implants [24]. Experiments with bone cells demonstrated that on negatively charged HAp coated titanium, cell proliferation and expression of vinculin (one of the major players in cell adhesion process) were enhanced, while on positively charged titanium, these responses were inhibited during the early stage of culture [25,26]. Thus, an improved adhesive property accelerates the tissue growth on implants. On the other hand, the decreased adhesion due to positive-charge coating can be used to regulate cell morphology. Another example of regulation of cell behavior via control of the substrate surface charge is polyion complex nanoparticles (PIC) coated polystyrene [27]. PIC nanoparticles are formed by mixing a cationic homopolymer (N,N-dimethylaminoethyl methacrylate) with anionic plasmid DNA at various charge ratios which can be adjusted to negative or positive

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coating [28]. Studies showed that adipose-derived stromal progenitor cells (ADSCs) cultured on PIC coated polystyrene change their morphology by altering the charge of the coating [27]. ADSCs show good adhesion with spindle-spread shape on negatively charged PIC-coated surface, while on the positively charged PIC surface, the cells change their morphology to form capillary-like networks. This finding is especially important for tissue engineering applications, where development of transplants with induced capillaries to introduce nutrient into transplanted tissue is necessary to prevent ischaemia [29].

An important consideration in the development of the strategies to control cell behavior via regulation of the surface charge is that changing the substrate charge may modify other properties of the surface, such as rigidity or even chemistry, which in turn can further affect cell adhesion process [27]. This consideration becomes critical for the soft substrates like hydrogels, where several studies demonstrated that the substrate charge density can strongly affect cell attachment. Thus, osteoblast and fibroblast attachment and spreading on the positively charged HEMA or PEG hydrogels are significantly higher than on the negatively charged hydrogels [30]. Positively charged hydrogels (i.e. oligo-(polyethylene glycol) fumarate (OPF)) also support attachment of rat dorsal root ganglion explants and enhance the neurite outgrowth, in contrast to the unmodified hydrogels [31]. These results are encouraging and suggest that hydrogels with incorporated charges can be used to manipulate cell attachment for engineering of hard or soft tissue for clinical applications.

In addition to their use as a substrate to control cell adhesion, charged surfaces can also be utilized as antibacterial and antibiofilm substrates. Bacterial infection can be the critical factor in determining the outcome of a variety of implants [32,33]. Bacteria surface is negatively charged (in a neutral medium); therefore, initial adhesion of bacteria is expected to be prevented on negatively charged surfaces and promoted on positively charged surfaces. Similarly, surface growth of bacteria can be minimized or prevented by the charge of the surface [34]. For example, it has been shown that E.coli forms a spare and mushroom-like biofilm on negatively charged surface, whereas on the positively charged surface, the E. coli biofilm is dense and homogeneous [35]. Similarly, positively charged poly (methacrylate) (PMMA/TMAEMA-Cl) has shown to support adhesion, but not bacterial growth, thus resulting in an antimicrobial effect on Gram-negative bacteria [36]. These results suggest potential regulatory role for the surface charge of implants in lowering the risk of infection and prevention of implant failure, as well as enhancing cell growth for a variety of applications.

Conductive Polymer Scaffolds

Electrically conductive polymers (i.e. polypyrrole (PPy), polyaniline (PANi), polythiophene (PT), etc.) are biocompatible materials, which have physical and chemical properties of organic polymers and electrical properties of metals. As a result, these materials can deliver electricity directly to the cells attached to their surface [37-39]. Studies have shown that relatively small electrical field (50 mV/mm) delivered by these conductive polymers can upregulate the growth and enhance viability and cellular cytokine production of human fibroblasts [40,41]. Similarly, stimulation of vascular smooth muscle cells cultured on these conductive polymers by sinusoidal electrical field (5, 500 HZ) leads to enhanced cell proliferation and protein expression [42].

Among polymeric bio-substrates, nanofibrous scaffolds (i.e. scaffolds made from nano-scale polymer fibers) provide the best support for cell survival and growth due to their specific fiber size and alignment, as well as porous structure [43]. However, conductive polymer nanofibers may be especially effective in modulating cell functions, because these materials are able to both mimic the three-dimensional architecture of natural extracellular matrix and to deliver appropriate electrical signals to the cells. Indeed, studies have reported that this combined stimulation results in significantly enhanced rate of neurite outgrowth in dorsal root ganglia [44,45]. Similarly, conductive fibers have been shown to stimulate myoblast differentiation [46,47]. In general, these findings suggest that utilizing the complex bio-surfaces that are made from the conductive polymers may be the best approach to modulate substrate or scaffold properties for cell adhesion and growth.

Electrical Stimulation Devices

The electrical stimulation devices are designed to apply external electrical currents or fields to alter the native cell electricity. Endogenous electrical current plays an important role such as directing cell migration during tissue repair and angiogenesis (blood vessel formation and growth) [15,48,49]. To mimic this current in vitro, a device has been designed which applies electrical currents (100-500 mV/mm) generated by two salt bridges to cells cultured in a chamber filled with the cell culture medium [50]. The direct electrical current in the medium induces cell responses such as directional cell migration, elongation and reorganization of actin cytoskeleton in a wide variety of microvascular and macrovascular cells [51,52]. Application of this electrical current has been shown to enhance growth factor expression, activate signaling pathways and upregulate angiogenic factors in different cell types such as lens epithelial cells, endothelial cells, keratinocytes and fibroblasts [51,53-59].The electric field-directed cell migration has been demonstrated in collective migration of epithelial monolayers as well as 3D environment of spinal cord for neural progenitor cells [60,61].

In addition to endogenous direct current, electrical pulses are essential regulators of organ function, specifically heart function. Cardiomyocytes are continuously subjected to electrical signals that regulate their contractions [62]. To mimic the native pulse in vitro, a device has been designed that delivers rectangular-wave pulses with millisecond pulse width to the culture medium [63]. The application of electrical stimulation enhances the contractile behavior and increases the amplitude of contractions in cardiac myocytes [64]. Electrical stimulation of cardiomyocytes also increases expression of cardiac specific genes and transcripts. Importantly for biophysical and engineering applications, electrical stimulation acts through the mechanisms that differ from mechanical stretching [62]. Cardiomyocytes are electrically coupled, and the ionic wave (e.g. Ca^{2+}, K^{+}) between the cells acts as a regulator of their function. Therefore, stimulation and monitoring of a pair of cardiomyocytes is required for cardiac cell based therapy [65]. Another approach is the use of multi-unit electrode arrays, which allows localization of electrical stimulation on the single and multiple cell level to investigate the

propagation of ionic waves between adjacent cells in response to electrical stimulation. These devices are composed of microfabricated PDMS microchannels with embedded or patterned electrodes to deliver millisecond pulsed electric field to cells [66,67].

In addition to short pulses-based stimulation, radio frequency electric field has also been employed to regulate cellular functions. In this method, cells are exposed to electric field at frequency of 2.4 GHz. Radio electric asymmetric conveyer (REAC) stimulates the cells through the cell culture medium [68].

REAC exposure for 24-48 hrs enhances the expression of cardiac, skeletal and neuronal lineage-restricted marker proteins in mouse embryonic stem cells; with the increased gene expression is retained for 2-7 days after stimulus removal [68]. Human dermal fibroblasts exposed to REAC show increased transcription of tissue restricted genes for cardiac reprogramming, skeletal myogenesis and neurogenesis [69]. REAC exposed human adipose derived stem cells (hASCs) show increase in the expression of the lineage restricted genes and proteins in both transcriptional and protein expression level [70]. These findings suggest a great promise of the REAC-based approach towards achievement of complex lineages for regenerative medicine, with an important advantage of cell stimulation without the use of chemical agonists, thus avoiding potentially significant side effects.

Another approach which has been introduced for electrical stimulation of the mammalian cells is based on a non-contact method of inducing electric field in cells and culture medium [71]. The stimulation device is composed of a cavity resonator fed by a coaxial microwave line to stimulate cells with low amplitude (~100mV/mm), high frequency (7.5 GHz) electric field during cell culture on native or synthetic scaffolds or substrates. The high frequency electric field enhances angiogenic endothelial cell responses, including capillary morphogenesis, vascular endothelial growth factor expression and MAPK/ERK intracellular pathway activation of endothelial cells [71]. This method induces electric field in the cell membrane and cytoplasm without any physical contact between the electrodes and the medium. The non-contact electric field-based technology may present an attractive alternative or adjuvant therapy to standard treatments of chronic wounds or vascular tissue regeneration by integrating engineering and biological principles to stimulate cellular responses in the wound using extracellular signal with no systemic drug-associated side effects [72-75].

The devices described above generate low amplitude electric field to induce electric field in the cell membrane. The induced field is usually smaller than the natural electric field due to the electric potential difference across the cell membrane and therefore does not damage the cell. Electroporation is a technique to induce very high magnitude electric field in the cell membrane using pulse generators [76]. Application of high magnitude pulsed electric field forms nanoscale pores in the membrane and permeabilizes the cell [77]. Electroporation could be reversible or irreversible depending on the electric field amplitude and duration [78,79]. Reversible electroporation has been used to introduce drugs and genes through the pores into the cells [80-83]. Irreversible electroporation opens permanent pores in the membrane of targeted cells and can be used to obtain decellularized tissue scaffolds. This approach allows preservation of the intact extracellular matrix (ECM) for subsequent use in the tissue engineering applications.

For example, the decellularized artery obtained using this technique has no vascular muscle cell layer, but is able to support growth of endothelial cells along the lumen, thus demonstrating that the ECM is not harmed following the electrical treatment [84]. In another study, an epithelial layer was formed on the decellularized small intestine tissue following in vivo stimulation, indicating that ECM of the intestine remains fully functional following electrical treatment [85].

Conclusion

The goal of this review is to emphasize the beneficial use of electricity for tissue engineering and related applications and describe the recent advances in the field. The studies discussed above demonstrate that application of electricity via a variety of approaches advances our understanding of native electricity and makes it possible to manipulate and control cell functions, thus creating the foundation for future therapies. Application of external electricity in the form of current, field or electrostatic charges stimulates cell's natural capacity to enhance the development of new tissue. This electrical signal together with chemical and mechanical signals provided by tissue engineering methods can help the injured tissue to restore the normal function and prevent infection. The developed innovative methods and devices show great promise toward development of valid clinical and therapeutic applications for neuronal regeneration, vascular and cardiovascular therapies, wound healing, pain relief, bone fracture healing, drug delivery and cancer treatment. The described devices are custom-designed and individually made to satisfy the requirements for each particular application. Although these studies resulted in significant scientific advances, the mechanisms of the electric field effects on cell and tissue repair remain poorly understood [73]. As a result, technological progress in developing electric field-based therapies has been slow, impeded by the lack of standardized protocols and a large variability in electric field application modes [74,75,86]. Therefore, future studies will need to focus on general mechanisms of electric field interactions with live cells and tissues and development of standardized methods for stimulation, to enable further field parameter optimization for a variety of therapies.

References

1. Langer R, Vacanti JP. Tissue engineering. Science. 1993; 260: 920-926.
2. Hubbell JA. Biomaterials in tissue engineering. Biotechnology (N Y). 1995; 13: 565-576.
3. Song Y, Kamphuis MM, Zhang Z, Sterk LM, Vermes I, Poot AA, et al. Flexible and elastic porous poly (trimethylene carbonate) structures for use in vascular tissue engineering. Acta Biomater. 2010; 6: 1269-1277.
4. Hasan A, Memic A, Annabi N, Hossain M, Paul A, Dokmeci MR, et al. Electrospun scaffolds for tissue engineering of vascular grafts. Acta Biomater. 2014; 10: 11-25.
5. Hong JK, Madihally SV. Next generation of electrosprayed fibers for tissue regeneration. Tissue Eng Part B Rev. 2011; 17: 125-142.
6. Langer R. Biomaterials and biomedical engineering. Chemical Engineering Science. 1995; 50: 4109-4121.
7. Nuccitelli R. Endogenous electric fields in embryos during development, regeneration and wound healing. Radiat Prot Dosimetry. 2003; 106: 375-383.
8. Nuccitelli R. A role for endogenous electric fields in wound healing. Curr Top Dev Biol. 2003; 58: 1-26.

9. Funk RH, Monsees TK. Effects of electromagnetic fields on cells: physiological and therapeutical approaches and molecular mechanisms of interaction. A review. Cells Tissues Organs. 2006; 182: 59-78.

10. Warshaviak DT, Muellner MJ, Chachisvilis M. Effect of membrane tension on the electric field and dipole potential of lipid bilayer membrane. Biochim Biophys Acta. 2011; 1808: 2608-2617.

11. Levin M, Stevenson CG. Regulation of cell behavior and tissue patterning by bioelectrical signals: challenges and opportunities for biomedical engineering. Annu Rev Biomed Eng. 2012; 14: 295-323.

12. Geddes LA, Hoff HE. The discovery of bioelectricity and current electricity The Galvani-Volta controversy. IEEE Spectr. 1971; 8: 38-46.

13. Vanhaesebroeck B. Charging the batteries to heal wounds through PI3K. Nat Chem Biol. 2006; 2: 453-455.

14. McCaig CD, Rajnicek AM, Song B, Zhao M. Controlling cell behavior electrically: current views and future potential. Physiol Rev. 2005; 85: 943-978.

15. Zhao M. Electrical fields in wound healing-An overriding signal that directs cell migration. Semin Cell Dev Biol. 2009; 20: 674-682.

16. Bennett KM, Walker SL, Lo DD. Epithelial Microvilli Establish an Electrostatic Barrier to Microbial Adhesion. Infect Immun. 2014; 82: 2860-2871.

17. Tran PL, Gamboa JR, McCracken KE, Riley MR, Slepian MJ, Yoon JY, et al. Nanowell-trapped charged ligand-bearing nanoparticle surfaces: a novel method of enhancing flow-resistant cell adhesion. Adv Healthc Mater. 2013; 2: 1019-1027.

18. Gottenbos B, van der Mei HC, Klatter F, Grijpma DW, Feijen J, Nieuwenhuis P, et al. Positively charged biomaterials exert antimicrobial effects on gram-negative bacilli in rats. Biomaterials. 2003; 24: 2707-2710.

19. Benoit M, Gabriel D, Gerisch G, Gaub HE. Discrete interactions in cell adhesion measured by single-molecule force spectroscopy. Nat Cell Biol. 2000; 2: 313-317.

20. Samavedi S, Whittington AR, Goldstein AS. Calcium phosphate ceramics in bone tissue engineering: a review of properties and their influence on cell behavior. Acta Biomater. 2013; 9: 8037-8045.

21. Ohgaki M, Kizuki T, Katsura M, Yamashita K. Manipulation of selective cell adhesion and growth by surface charges of electrically polarized hydroxyapatite. J Biomed Mater Res. 2001; 57: 366-373.

22. Ueda MJ, Takeichi M. Two mechanisms in cell adhesion revealed by effects of divalent cations. Cell Struct Funct. 1976; 1: 377-388.

23. Searles GE, Dixon WT, Thomas PD, Jimbow K. Divalent cations control cell-substrate adhesion and laminin expression in normal and malignant human melanocytes in early and late stages of cellular differentiation. J Invest Dermatol. 1995; 105: 301-308.

24. Guo CY, Matinlinna JP, Tang AT. Effects of surface charges on dental implants: past, present, and future. Int J Biomater. 2012; 2012: 381535.

25. Bodhak S, Bose S, Bandyopadhyay A. Electrically polarized HAp-coated Ti: in vitro bone cell-material interactions. Acta Biomater. 2010; 6: 641-651.

26. Kuroda K, Okido M. Hydroxyapatite coating of titanium implants using hydroprocessing and evaluation of their osteoconductivity. Bioinorg Chem Appl. 2012; 2012: 730693.

27. Iwai R, Nemoto Y, Nakayama Y. The effect of electrically charged polyion complex nanoparticle-coated surfaces on adipose-derived stromal progenitor cell behaviour. Biomaterials. 2013; 34: 9096-9102.

28. Iwai R, Kusakabe S, Nemoto Y, Nakayama Y. Deposition gene transfection using bioconjugates of DNA and thermoresponsive cationic homopolymer. Bioconjug Chem. 2012; 23: 751-757.

29. Hashizume R, Fujimoto KL, Hong Y, Guan J, Toma C, Tobita K, et al. Biodegradable elastic patch plasty ameliorates left ventricular adverse remodeling after ischemia-reperfusion injury: A preclinical study of a porous polyurethane material in a porcine model. Journal of Thoracic and Cardiovascular Surgery. 2013; 146: 391-399.

30. Schneider GB, English A, Abraham M, Zaharias R, Stanford C, Keller J, et al. The effect of hydrogel charge density on cell attachment. Biomaterials. 2004; 25: 3023-3028.

31. Dadsetan M, Knight AM, Lu L, Windebank AJ, Yaszemski MJ. Stimulation of neurite outgrowth using positively charged hydrogels. Biomaterials. 2009; 30: 3874-3881.

32. Bergmann PA, Tamouridis G, Lohmeyer JA, Mauss KL, Becker B, Knobloch J, et al. The effect of a bacterial contamination on the formation of capsular contracture with polyurethane breast implants in comparison with textured silicone implants: An animal study. J Plast Reconstr Aesthet Surg. 2014; 4: 00282-00284.

33. Porter JA, von Fraunhofer JA. Success or failure of dental implants? A literature review with treatment considerations. Gen Dent. 2005; 53: 423-432.

34. Desrousseaux C, Sautou V, Descamps S, Traoré O. Modification of the surfaces of medical devices to prevent microbial adhesion and biofilm formation. J Hosp Infect. 2013; 85: 87-93.

35. Terada A, Okuyama K, Nishikawa M, Tsuneda S, Hosomi M. The effect of surface charge property on Escherichia coli initial adhesion and subsequent biofilm formation. Biotechnol Bioeng. 2012; 109: 1745-1754.

36. Gottenbos B, Grijpma DW, van der Mei HC, Feijen J, Busscher HJ. Antimicrobial effects of positively charged surfaces on adhering Gram-positive and Gram-negative bacteria. J Antimicrob Chemother. 2001; 48: 7-13.

37. Balint R, Cassidy NJ, Cartmell SH. Conductive polymers: towards a smart biomaterial for tissue engineering. Acta Biomater. 2014; 10: 2341-2353.

38. Guo B, Glavas L, Albertsson AC. Biodegradable and electrically conducting polymers for biomedical applications. Progress in Polymer Science. 2013; 38: 1263-1286.

39. Lee JY. Electrically conducting polymer-based nanofibrous scaffolds for tissue engineering applications. Polymer Reviews. 2013; 53: 443-459.

40. Shi G, Zhang Z, Rouabhia M. The regulation of cell functions electrically using biodegradable polypyrrole-polylactide conductors. Biomaterials. 2008; 29: 3792-3798.

41. Shi G, Rouabhia M, Wang Z, Dao LH, Zhang Z. A novel electrically conductive and biodegradable composite made of polypyrrole nanoparticles and polylactide. Biomaterials. 2004; 25: 2477-2488.

42. Rowlands AS, Cooper-White JJ. Directing phenotype of vascular smooth muscle cells using electrically stimulated conducting polymer. Biomaterials. 2008; 29: 4510-4520.

43. Patel S, Kurpinski K, Quigley R, Gao H, Hsiao BS, Poo MM. Bioactive nanofibers: synergistic effects of nanotopography and chemical signaling on cell guidance. Nano Lett. 2007; 7: 2122-2128.

44. Goh YF, Shakir I, Hussain R. Electrospun fibers for tissue engineering, drug delivery, and wound dressing. Journal of Materials Science. 2013; 48: 3027-3054.

45. Xie J, Macewan MR, Willerth SM, Li X, Moran DW, Sakiyama-Elbert SE, et al. Conductive Core-Sheath Nanofibers and Their Potential Application in Neural Tissue Engineering. Adv Funct Mater. 2009; 19: 2312-2318.

46. Jun I, Jeong S, Shin H. The stimulation of myoblast differentiation by electrically conductive sub-micron fibers. Biomaterials. 2009; 30: 2038-2047.

47. Ku SH, Lee SH, Park CB. Synergic effects of nanofiber alignment and electroactivity on myoblast differentiation. Biomaterials. 2012; 33: 6098-6104.

48. Robinson KR, Messerli MA. Left/right, up/down: the role of endogenous electrical fields as directional signals in development, repair and invasion. Bioessays. 2003; 25: 759-766.

49. Reid B, Song B, McCaig CD, Zhao M. Wound healing in rat cornea: the role of electric currents. FASEB J. 2005; 19: 379-386.

50. Song B, Gu Y, Pu J, Reid B, Zhao Z, Zhao M, et al. Application of direct current electric fields to cells and tissues in vitro and modulation of wound electric field in vivo. Nat Protoc. 2007; 2: 1479-1489.

51. Zhao M, Bai H, Wang E, Forrester JV, McCaig CD. Electrical stimulation directly induces pre-angiogenic responses in vascular endothelial cells by signaling through VEGF receptors. J Cell Sci. 2004; 117: 397-405.

52. Li X, Kolega J. Effects of direct current electric fields on cell migration and actin filament distribution in bovine vascular endothelial cells. J Vasc Res. 2002; 39: 391-404.

53. Wang E, Zhao M, Forrester JV, McCaig CD. Electric fields and MAP kinase signaling can regulate early wound healing in lens epithelium. Invest Ophthalmol Vis Sci. 2003; 44: 244-249.

54. Wang E, Zhao M, Forrester JV, McCaig CD. Bi-directional migration of lens epithelial cells in a physiological electrical field. Exp Eye Res. 2003; 76: 29-37.

55. Zhao M, Pu J, Forrester JV, McCaig CD. Membrane lipids, EGF receptors, and intracellular signals colocalize and are polarized in epithelial cells moving directionally in a physiological electric field. The FASEB J. 2002; 16: 857-859.

56. Bai H, Forrester JV, Zhao M. DC electric stimulation upregulates angiogenic factors in endothelial cells through activation of VEGF receptors. Cytokine. 2011; 55: 110-115.

57. Pullar CE, Baier BS, Kariya Y, Russell AJ, Horst BA, Marinkovich MP, et al. Beta4 integrin and epidermal growth factor coordinately regulate electric field-mediated directional migration via Rac1. Mol Biol Cell. 2006; 17: 4925-4935.

58. Zhao M, Song B, Pu J, Wada T, Reid B, Tai G, et al. Electrical signals control wound healing through phosphatidylinositol-3-OH kinase-gamma and PTEN. Nature. 2006; 442: 457-460.

59. Guo A, Song B, Reid B, Gu Y, Forrester JV, Jahoda CA, et al. Effects of physiological electric fields on migration of human dermal fibroblasts. J Invest Dermatol. 2010; 130: 2320-2327.

60. Cohen DJ, Nelson WJ, Maharbiz MM. Galvanotactic control of collective cell migration in epithelial monolayers. Nat Mater. 2014; 13: 409-417.

61. Meng X, Li W, Young F, Gao R, Chalmers L, Zhao M, et al. Electric field-controlled directed migration of neural progenitor cells in 2D and 3D environments. J Vis Exp. 2012.

62. Martherus RS, Vanherle SJ, Timmer ED, Zeijlemaker VA, Broers JL, Smeets HJ, et al. Electrical signals affect the cardiomyocyte transcriptome independently of contraction. Physiol Genomics. 2010; 42A: 283-289.

63. Johnson TB, Kent RL, Bubolz BA, McDermott PJ. Electrical stimulation of contractile activity accelerates growth of cultured neonatal cardiocytes. Circ Res. 1994; 74: 448-459.

64. Radisic M, Park H, Shing H, Consi T, Schoen FJ, Langer R, et al. Functional assembly of engineered myocardium by electrical stimulation of cardiac myocytes cultured on scaffolds. Proc Natl Acad Sci U S A. 2004; 101: 18129-18134.

65. Klauke N, Smith G, Cooper JM. Microfluidic systems to examine intercellular coupling of pairs of cardiac myocytes. Lab Chip. 2007; 7: 731-739.

66. Klauke N, Smith GL, Cooper J. Stimulation of single isolated adult ventricular myocytes within a low volume using a planar microelectrode array. Biophys J. 2003; 85: 1766-1774.

67. Klauke N, Smith GL, Cooper J. Extracellular recordings of field potentials from single cardiomyocytes. Biophys J. 2006; 91: 2543-2551.

68. Maioli M, Rinaldi S, Santaniello S, Castagna A, Pigliaru G, Gualini S, et al. Radiofrequency energy loop primes cardiac, neuronal and skeletal muscle differentiation in mouse embryonic stem cells: a new tool for improving tissue regeneration. Cell Transplant. 2012; 21: 1225-1233.

69. Maioli M, Rinaldi S, Santaniello S, Castagna A, Pigliaru G, Gualini S, et al. Radio electric conveyed fields directly reprogram human dermal skin fibroblasts toward cardiac, neuronal, and skeletal muscle-like lineages. Cell Transplantation. 2013; 22: 1227-1235.

70. Maioli M, Rinaldi S, Santaniello S, Castagna A, Pigliaru G, Delitala A, et al. Radio Electric Asymmetric Conveyed Fields and Human Adipose-Derived Stem Cells Obtained with a Non-Enzymatic Method and Device: A Novel Approach to Multipotency. Cell Transplant. 2013; 30.

71. Sheikh AQ, Taghian T, Hemingway B, Cho H, Kogan AB, Narmoneva DA, et al. Regulation of endothelial MAPK/ERK signalling and capillary morphogenesis by low-amplitude electric field. J R Soc Interface. 2013; 10: 20120548.

72. Larsen JA, Overstreet J. Pulsed radio frequency energy in the treatment of complex diabetic foot wounds: two cases. J Wound Ostomy Continence Nurs. 2008; 35: 523-527.

73. Markov MS. Expanding use of pulsed electromagnetic field therapies. Electromagn Biol Med. 2007; 26: 257-274.

74. Isseroff RR, Dahle SE. Electrical Stimulation Therapy and Wound Healing: Where Are We Now? Adv Wound Care (New Rochelle). 2012; 1: 238-243.

75. Thakral G, Kim PJ, LaFontaine J, Menzies R, Najafi B, Lavery LA, et al. Electrical stimulation as an adjunctive treatment of painful and sensory diabetic neuropathy. J Diabetes Sci Technol. 2013; 7: 1202-1209.

76. Schoenbach KH, Peterkin FE, Alden Iii RW, Beebe SJ. The effect of pulsed electric fields on biological cells: experiments and applications. IEEE Transactions on Plasma Science. 1997; 25: 284-292.

77. Schoenbach KH, Joshi RP, Kolb JF, Chen N, Stacey M, Blackmore PF, et al. Ultrashort electrical pulses open a new gateway into biological cells. Proceedings of the IEEE. 2004; 92: 1122-1136.

78. Weaver JC, Chizmadzhev YA. Theory of electroporation: A review. Bioelectrochemistry and Bioenergetics. 1996; 41: 135-160.

79. Gehl J. Electroporation: theory and methods, perspectives for drug delivery, gene therapy and research. Acta Physiol Scand. 2003; 177: 437-447.

80. Widera G, Austin M, Rabussay D, Goldbeck C, Barnett SW, Chen M, et al. Increased DNA vaccine delivery and immunogenicity by electroporation in vivo. J Immunol. 2000; 164: 4635-4640.

81. Banga AK, Prausnitz MR. Assessing the potential of skin electroporation for the delivery of protein- and gene-based drugs. Trends Biotechnol. 1998; 16: 408-412.

82. Charoo NA, Rahman Z, Repka MA, Murthy SN. Electroporation: an avenue for transdermal drug delivery. Curr Drug Deliv. 2010; 7: 125-136.

83. Denet AR, Vanbever R, Préat V. Skin electroporation for transdermal and topical delivery. Adv Drug Deliv Rev. 2004; 56: 659-674.

84. Phillips M, Maor E, Rubinsky B. Principles of tissue engineering with nonthermal irreversible electroporation. Journal of Heat Transfer. 2011; 133.

85. Phillips MA, Narayan R, Padath T, Rubinsky B. Irreversible electroporation on the small intestine. Br J Cancer. 2012; 106: 490-495.

86. Strauch B, Herman C, Dabb R, Ignarro LJ, Pilla AA. Evidence-based use of pulsed electromagnetic field therapy in clinical plastic surgery. Aesthet Surg J. 2009; 29: 135-143.

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