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Combined use of plasmid drug pCMV-VEGFA and autodermoplasty for stimulation of skin defects healing in the experiment

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Abstract

© 2018 Human Stem Cell Institute. All rights reserved. To find effective ways to stimulate chronic skin wounds healing (including deep burns, diabetic and trophic ulcers) is an actual multidisciplinary task. The aim of our study was to assess the potential of using autodermoplasty in combination with plasmid drug pCMV-VEGFA to optimize skin defects repair in the experiment. Autodermoplasty was performed on Wistar rats. The size of the skin flap was 22 cm. Immediately after surgery the animals of the test group (n=8) underwent intradermal injection in the periphery of autotransplant with 1 ml solution containing 0.3 mg of supercoiled plasmid DNA pCMV-VEGFA, rats of the control group (n=8) received 1 ml of 0.9 % NaCl. The results were analyzed in 3, 6, 9 12, 18 days using macroscopic evaluation, laser Doppler flowmetry, histological methods. Macroscopically in the test group necrosis of the transplanted skin flap was found at later periods of observation, in one case complete survival of autotransplant was observed. The results of laser Doppler flowmetry in the group with plasmid DNA did not have statistically significant differences with control. The wound defect diameter in the test group at 12 days was 5,52± 4.80 mm, in the control 12,45±0,82 mm (p=0,03); 2,53±of 2,94 mm and 4,23±3,5 mm (p=0,067) at 18 days, respectively. At 18 days, the average number of vessels under the flap in the central zone were: of 26±2,9 in the test group and 20±8 in control; it the peripheral zone 27±3,4 and of 12,1±3,9 (p=0,035), respectively; in the skin muscle 21,2±of 3,9 and 12,4±3,6 (p=0,04), respectively. Thus, the use of plasmid drug pCMV-VEGFA improved the skin healing after autodermoplasty.

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Keywords

Autodermoplasty, Gene Therapy, Skin, Vascular Endothelial Growth factor, VEGFA gene

References

[1] Andrews K.L., Houdek M, Kiemele L. Wound management of chronic diabetic foot ulcers: From the basics to regenerative medicine. Prosthet. Orthot. Int. 2015; 39(I): 29-39.

[2] Kim H.S., Yoo H. In vitro and in vivo epidermal growth factor gene therapy for diabetic ulcers with electrospun fibrous meshes. Acta. Biomater. 2013; 9(VII): 7371-80.

[3] Global report on diabetes. Geneva: World Health Organization, 2016; 34-42.

[4] Lal B.K. Venous ulcers of the lower extremity: Definition, epidemiology, economic and social burdens. Semin. Vasc. Surg. 2015; 28(I): 3-5.

[5] Weledji E.P., Fokam P. Treatment of the diabetic foot-to amputate or not BMC Surg. 2014; 83-7.

[6] Alexiadou K.I., Doupis J. Management of diabetic foot ulcers. Diabetes Ther. 2012; 3: 4-6.

[7] Kang N.R., Hai Y, Liang F, et al. Preconditioned hyperbaric oxygenation protects skin flap grafts in rats against ischemia/reperfusion injury. Mol. Med. Report. 2014; 9(VI): 2124-30.

[8] Mao A.S., Mooney D. Regenerative medicine: Current therapies and future directions. Proc. Natl. Acad. Sci. 2015; 112: 14452-59.

[9] Talebi M.I., Palizban A. Viral and nonviral delivery systems for gene delivery. Adv. Biomed. Res. 2012; 1: 27-30.

[10] Martino M.M., Tortelli F., Mochizuki M., et al. Engineering the growth factor microenvironment with fibronectin domains to promote wound and bone tissue healing. Sci. Transl. Med. 2011; 3: 20-5.

[11] Mayer H.L., Bertram H., Lindenmaier W., et al. Vascular endothelial growth factor (VEGF-A) expression in human mesenchymal stem cells: Autocrine and paracrine role on osteoblastic and endothelial differentiation. J. Cell Biochem. 2005; 2: 30-34.

[12] Detmar M.A. The role of VEGF and thrombospondins in skin angiogenesis. Dermatol. Sci. 2000; 24: 78-84.

[13] Eckhart L.F. Cell death by cornification. Biochim. Biophys. Acta. 2013; 18: 34-45.

[14] Martino M.M., Brkic S., Bovo E., et al. Extracellular matrix and growth factor engineering for controlled angiogenesis in regenerative medicine. Front. Bioeng. Biotechnol. 2015; 4: 45-60.

[15] Martino M.M., Tortelli F., Mochizuki M., et al. Engineering the growth factor microenvironment with fibronectin domains to promote wound and bone tissue healing. Sci. Transl. Med. 2011; 1: 20-5.

[16] Kenna C.C., Ojeda A., Spurlin J. Sema3A maintains corneal avascularity during development by inhibiting Vegf induced angioblast migration. Dev. Biol. 2013; 10-5.

[17] Gould S.J., Subramani S. Firefly luciferase as a tool in molecular and cell biology. Analytical Biochemistry. 1988; 175(I): 5-13.