https://doi.org/10.52889/1684-9280-2021-2-57-17-23
UDC 617.3; 616-089.23; 61:57.086
IRSTI 76.29.41; 76.03.33

Review article

Cellular Technologies Evolution in the Treatment of Reparative Regeneration Disorders of Bone Tissue in Long Tubular Bones

Murat Baidarbekov

Head of the Department of Traumatology No.1, National Scientific Center of Traumatology and Orthopaedics named after Academician Batpenov N.D., Nur-Sultan, Kazakhstan. E-mail: baidarbekov_m@nscto.kz

Abstract

Autografts, allo- and xenografts are current treatment standards of reparative regeneration disorders of bone tissue in long tubular bones, but these approaches still show some disadvantages, such as limited availability of bone tissue for transplantation or immune reactions. Modern plastic materials have been studied in both in vitro and in vivo studies, showing promising results in terms of biocompatibility and biomechanical properties. In addition, bone repair implants have shown promising results in combination with drugs, growth factors and mesenchymal stem cells, which can interact to facilitate the deposition and mineralization of bone tissue. Among the various approaches to drug delivery, techniques with embedded nano - and micro particles containing drugs or biologically active substances occupy a special place. These innovative drug delivery systems have a number of advantages that differentiate them from other systems. In addition, the use of nano - and microparticles makes it possible to increase the efficiency and controlled release of the drug from the skin over time at appropriate therapeutic concentrations. These controlled delivery systems can effectively stimulate osteogenesis and accelerate bone regeneration without significant side effects. However, despite the promising results of preclinical studies, the implementation of the developed drug delivery systems requires additional clinical trials.

Keywords: cell technologies, reparative regeneration disorders, long tubular bones, bone tissue, autografts, allografts, xenografts.

Corresponding author: Murat Baidarbekov, Head of the Department of Traumatology No.1, National Scientific Center of Traumatology and Orthopaedics named after Academician Batpenov N.D., Nur-Sultan, Kazakhstan.
Postal code: Z00P5Y4
Address: Kazakhstan, Nur-Sultan, Abylai Khan Avenue, 15A
Phone: +77019450217
E-mail: baidarbekov_m@nscto.kz

J Trauma Ortho Kaz 2021; 2 (57): 17-23
Recieved: 05-05-2021
Accepted: 17-05-2021

Introduction

Currently, the problem of the treatment of long tubular bones repair bone regeneration disorders remains a current problem in modern traumatology and orthopaedics [1,2]. According to modern data, in the structure of the consequences of injuries to long tubular bones, defects and pseudarthrosis of the femur reach 10.7-30.8% of cases, of the lower leg bones – 15-50.6%, of the humerus – 0.4-30%. The resulting anatomical and functional disorders of the limb in the form of its shortening and deformation, persistent contractures of interfacing joints and neurotrophic disorders reach 11.6-44.9% of cases [3,4,5] and cause permanent disability, prolong hospitalization and rehabilitation of patients, which in turn leads to a significant economic problem [6,7,8].

Bone tissue has a high ability to recover from injury through complex and highly regulated biological processes. Although in some cases, such as extensive bone resections due to oncoprocesss, osteoporosis, osteomatization, osteomyelitis, AVN and atrophic degeneration, bone regeneration can be impaired [9].

A variety of existing methods of surgical treatment pseudo arthrosis of long bones has not solved the problem of the bone structures regenerative capacity due to the fact that the use of open surgical methods involves additional trauma to soft tissues, damaged limbs and possible complications, which is their disadvantage [10].

The aim of the review: to describe the modern aspects of the application of cell technologies in the treatment of reparative regeneration disorders of bone tissue in long tubular bones.

Autografts, Allogenetic grafts or Xenografts

In the development of cellular technology in the treatment of disorders of repair bone tissue regeneration, the introduction of bone defect replacement alternative methods for stimulation of bone regeneration has played a decisive role.

Affected bones can be reconstructed to normal using autografts, allogenetic grafts or xenografts [11].

Autologous grafts are the gold standard (Cypher and Grossman, 1996) in bone regeneration due to biocompatibility and osteoinductive and osteoconductive properties. However, autografts still show some disadvantages due to the limited amount of bone available for transplantation and the trauma associated with graft retrieval.

Allogeneic grafts or xenografts are an alternative to bone transplants, as they are similar to human bone tissue and do not require transplant removal from the patient [12]. Disadvantages of allograft are that chemical agents aggressive to bone tissue are often used in their cleaning processes [13]. Although there are, various processes for clearing allogeneic bone that provide security for all transplantation, the risk of immune response and disease transmission remains.

Xenografts are bones of animal origin, most often xenografts are cattle, horses and pigs. According to studies, bovine cancellous bone grafts are the closest xenograft to human bone to be regenerated, second only to autografts [14-17].

However, allo- and xenografts have disadvantages such as high cost, risk of infection, or immune reaction [18,19]. In addition, the processes of purification and sterilization of starting materials of animal origin lead to a deterioration in both mechanical and biological characteristics [20-23].

In addition to the above-mentioned biological grafts, various other implants are used in modern traumatology and orthopedics.

Porous implants have good biocompatibility with human bone tissue [24,25]. But their drawback is the need to stimulate and deliver growth factors to the damaged site [26].

Synthetic polymers are also promising materials

Synthetic polymers are also promising materials for bone stimulation due to their biomechanical and biodegradable properties. The best-studied synthetic polymers for bone regeneration are aliphatic polyesters such as polylactic acid, polycaprolactone and polyglycolic acid and their derivatives. Other synthetic polymers include polymethyl methacrylate, poly-e-caprolactone, polyhydroxybutyrate, polyethylene, polypropylene, polyurethane. These polymers are hydrolyzed in vivo and have the advantage of being easily adapted to different shapes according to the mechanical requirements of the specific bone defect being treated [27-29]. However, synthetic polymers have disadvantages such as the biodegradability of the material, which reduces their mechanical strength in vivo. Some polymers, such as polypropylene fumarate, have demonstrated a high resistance to compression, but their absorption results in the release of toxic acid compounds [30].

Modern literature also describes the use of natural polymers in stimulating human bone tissue, ensuring differentiation of mesenchymal stem cells into osteoblasts. Their advantage lies in their similarity to the native extracellular matrix due to their osteoinductive properties and biocompatibility. By chemical composition, natural polymers are divided into proteins (collagen, gelatin, fibrinogen, elastin) and polysaccharides (glycosaminoglycans, cellulose, amylose) [31,32]. Several ways have been proposed for the manufacture of natural polymeric materials: they can be obtained by cells, which are induced to form a native extracellular matrix, or directly obtained from decellularized bone tissue [33]. However, the mechanical properties and biodegradability of natural polymers are inferior to those of synthetic polymers [34]. In order to reduce the toxic effect of the drug and expand its activity, a deacetylated chitin derivative (chitosan) is used as a carrier for drug delivery, which can enhance the absorption of hydrophobic macromolecular drugs due to its mucoadhesive cationic nature [35]. Most often, modified chitosan is used, which is comparable in structure to heparin, which can favorably bind to the basic amino acids BMP-2 (Bone Morphogenetic Proteins). By improving sustained release, this interaction can enhance the biological activity

of BMP-2 for bone regeneration [36].

Inorganic implants are divided into metal and ceramic implants. In turn, metal implants are represented by silicon, gold and diamond nanoparticles. Silicon nanoparticles have a porous structure, which makes it possible to accelerate the release of a medicinal agent by increasing the resistance to diffusion of a medicinal agent. These nanoparticles are able to deliver anticancer drugs in a targeted manner and release them on demand in order to increase their cellular uptake without any premature release [37]. They can accelerate bone formation by increasing osteoblast activity and reduce bone resorption by decreasing osteoclast activity; for this reason, they are still a great option for treating osteoporosis [38]. Gold nanoparticles are suitable for controlled drug delivery, treatment and diagnosis of cancer processes [39]. These nanoparticles can inhibit the formation of osteoclasts, the function of the promoter of osteoclastogenesis and reduce the level of reactive oxygen species [40]. Gold nanoparticles can also be used to transport narcotic drugs. To induce osteogenic differentiation, they are able to provide mechanical stress on the membranes of mesenchymal stem cells in order to mitogenic-activated protein kinases [41,42]. Diamond nanoparticles are octahedral nanoscale carbon implants that are intracellular carriers of bioactive compounds due to their properties, such as: biocompatibility, small size and chemical interaction with a large surface [43]. These nanoparticles are expected to play a positive role in the proliferation and differentiation of osteoblasts [44].

Ceramic implants are valuable in the regeneration of bone tissue, as it contains an inorganic extracellular matrix composed of almost 70% hydroxyapatite and 30% collagen [45]. Calcium phosphate nanoparticles have excellent biocompatibility, biodegradability and structural similarity to the inorganic composition of bone minerals [46]. The most studied nanoparticles of calcium phosphate are hydroxyapatite, beta-tricalcium phosphate and biphasic calcium phosphate [47]. These nanoparticles are able to integrate into bone tissue and stimulate osteoblast differentiation, osteoblast growth and inorganic matrix deposition. However, the clinical use of nanoparticles of calcium phosphate is limited by their fragility, irregular absorption rates, and overall poor clinical results. In this way, the new bone tissue formed in the ceramic framework cannot withstand the mechanical load in the same way as the natural bone. More recently, it has been shown that doping a calcium phosphate backbone with various compounds can improve mechanical stability, biocompatibility and absorption rate [48,49].

The disadvantages of various osteoplastic materials and implants prompt researchers to search for new methods of bone grafting and bone graft substitutes. Currently, the main direction is the development and implementation into practice of composite biomaterials with osteogenic and osteoinductive properties, which include human stem or osteoprogenitor cells, as well as growth factors [50]. In this connection, in the field of tissue engineering, research is being actively pursued to create a new generation of osteoconductive biomaterials based on the use of bone morphogenetic recombinant proteins that have been approved (Food and Drug Administration) FDA is still in use in clinical practice to repair permanent fractures. Bone morphogenetic proteins (BMP) are one of the key factors in the reconstruction and restoration of damaged bone tissue. They have been shown to have powerful osteoinductive effects and are able to stimulate the formation of new bone tissue through the differentiation of mesenchymal stem cells into osteoblasts [52].

However, despite the high efficiency of recombinant BMPs, there are still some problems associated with their clinical use. First of all, this is due to the short life span of the BMP. The proteins injected into the site lose their biological activity in a short period of time and therefore use large doses of recombinant BMPs to achieve therapeutic effect in clinical practice [53]. For example, the effective dose for bone regeneration is 1.5 mg/ml of defect, which is 4-5 times the endogenous dose. Such high doses of recombinant BMP may diffuse from the injury site and cause side effects, including pathological bone growth and immune response [54]. In order to avoid these problems, there is a need to develop transport delivery systems with a controlled release of osteoconductive growth factors into bone damage. Although a number of polymer-based delivery systems have been developed for the treatment of bone defects, only a few have reached clinical use.

There are currently several commercial carriers for the delivery of osteoinductive growth factors such as OP-1, INFUSE®, InductOS® and AUGMENT® [8]. A number of prospective, randomized, multicenter studies have shown that OP-1 is safe, effective, and accelerates bone regeneration in the treatment of open tibial fractures [55,56].

As a result of numerous clinical trials from 2002 to 2017 to assess the safety, efficacy and dose-dependent effects of INFUSE® implantation in interbody fusion using recombinant BMP-2 and a collagen sponge had a significantly higher fusion rate compared to patients without recombinant BMP-2 [57,58].

Studies by Triplett, R.G et. all 2009, the use of recombinant BMP-2 and collagen sponge for maxillary sinus plasty compared with autogenous bone graft in 160 patients, efficiency and acceleration of bone tissue regeneration were noted, as well as the number of complications, such as prolonged paresthesias and pain in the area of graft collection [59]. In addition, the use of recombinant BMP-2 and a collagen sponge of two doses (1.5 mg/ml) in 80 patients showed an increase in bone tissue in the alveolar process [60].

Like BMP, platelet growth factor also plays an important role in bone regeneration [61]. Clinical studies have shown that injectable bone graft (Augment®, Wright Medical Technologies) is effective in ankle atrodesis [62,63], significantly reduces the fusion time (14.3-8.9 weeks) compared with an autograft (19.7-11,5 weeks). Good clinical results reached 91%.

In this way, existing polymer-based delivery systems available to accelerate osteanagenesis, have demonstrated good therapeutic potency in various clinical use.

Conclusion

Disorders of reparative regeneration of bone tissue of long tubular bones remains an urgent problem and requires improvement of treatment methods. Autografts, allo and xenografts are current treatment standards, but these approaches still show some disadvantages, such as limited availability of bone tissue for transplantation or immune reactions. Modern plastic materials have been studied in both *in vitro* and *in vivo* studies, showing promising results in terms of biocompatibility and biomechanical properties. In addition, bone repair implants

have shown promising results in combination with drugs, growth factors and mesenchymal stem cells, which can interact to facilitate the deposition and mineralization of bone tissue. Among the various approaches to drug delivery, techniques with embedded nano- and micro particles containing drugs or biologically active substances occupy a special place. These innovative drug delivery systems have a number of advantages that differentiate them from other systems. In addition, the use of nano - and microparticles makes it possible to increase the efficiency and controlled release of the drug from the skin over time at appropriate therapeutic concentrations. These controlled delivery systems can effectively stimulate osteogenesis and accelerate bone regeneration without significant side effects. However, despite the promising results of preclinical studies, the implementation of the developed drug delivery systems requires additional clinical trials.

Funding: This research received no external funding.

References

1. Olshansky S.J., Passaro D.J., Hershow R.C., Layden J. et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med. 2005; 352(11): 1138–1145. https://doi.org/10.1056/nejmsr043743.

2. Carrington J.L. Aging bone and cartilage: Cross-cutting issues. Biochem Biophys Res Commun. 2005; 328(3): 700–708. https://doi.org/10.1016/j.bbrc.2004.12.041.

3. Tzioupis C., Giannoudis P.V. Prevalence of long-bone non-unions. Injury. 2007; 38(2): S3-S9. https://doi.org/10.1016/S0020-1383(07)80003-9.

4. Gómez-Barrena E., Rosset P., Lozano D., Stanovici J. et al. Bone fracture healing: cell therapy in delayed unions and nonunions. Bone. 2015; 70: 93–101. https://doi.org/10.1016/j.bone.2014.07.033.

5. Ekegren C.L., Edwards E.R., De Steiger R., Gabbe B.J. Incidence, costs and predictors of non-union, delayed union and mal-union following long bone fracture. Int J Environ Res Public Health. 2018; 15: 15(12): 2845. https://doi.org/10.3390/ijerph15122845.

6. Борзунов Д.Ю. Несвободная костная пластика по Г.А. Илизарову в проблеме реабилитации больных с дефектами и ложными суставами длинных костей // Гений ортопедии. – 2011. – №2. – С. 21-26.

Borzunov D.Iu. Nesvobodnaia kostnaia plastika po G.A. Ilizarovu v probleme reabilitatsii bol'nykh s defektami i lozhnymi sustavami dlinnykh kostei (Non-free bone grafting according to G.A. Ilizarov in the problem of rehabilitation of patients with defects and pseudarthrosis of long bones) [in Russian]. Genii ortopedii. 2011; 2: 21-26.

7. Gruber R., Koch H., Doll B.A., Tegtmeier F. et al. Fracture healing in the elderly patient. Exp Gerontol. 2006; 41(11): 1080–1093. https://doi.org/10.1016/j.exger.2006.09.008.

8. Borrelli J., Pape C., Hak D., Hsu J. et al. Physiological challenges of bone repair. J Orthop Trauma. 2012; 26(12): 708–711. https://doi.org/10.1097/BOT.0b013e318274da8b.

9. Gao C., Deng Y., Feng P., Mao Z. et al. Current progress in bioactive ceramic scaffolds for bone repair and regeneration. Int J Mol Sci. 2014; 15(3): 4714–4732. https://doi.org/10.3390/ijms15034714.

10. Барабаш А.П., Барабаш Ю.А., Балаян В.Д., Тишков Н.В. и др. Лечение ложных суставов голени методом чрескостной фиксации с дистанционной стимуляцией регенераторного процесса // Политравма. – 2012. – №4. – С. 19-29.

Barabash A.P., Barabash Iu.A., Balaian V.D., Tishkov N.V. i dr. Lechenie lozhnykh sustavov goleni metodom chreskostnoi fiksatsii s distantsionnoi stimuliatsiei regeneratornogo protsessa (Treatment of leg false joints by means of transosseous fixation with remote stimulation of regenerative process) [in Russian]. Politravma. 2012; 4: 19-29.

11. Rasch A., Naujokat H., Wang F., Seekamp A. et al Evaluation of bone allograft processing methods: impact on decellularization efficacy, biocompatibility and mesenchymal stem cell functionality. PLoS One. 2019; 14: e0218404. https://doi.org/10.1371/journal.pone.0218404.

12. Delloye C., Cornu O., Druez V., Barbier O. Bone allografts: what they can offer and what they cannot. J Bone Joint Surg Br. 2007; 89(5): 574–579. https://doi.org/10.1302/0301-620X.89B5.19039.

13. Dumas A., Gaudin-Audrain C., Mabilleau G., Massin P. et al. The influence of processes for the purification of human bone allografts on the matrix surface and cytocompatibility. Biomaterials. 2006; 27(23): 4204–4211. https://doi.org/10.1016/j.biomaterials.2006.03.044.

14. Athanasiou V.T., Papachristou D.J., Panagopoulos A., Saridis A. et al. Histological comparison of autograft, allograft-DBM, xenograft, and synthetic grafts in a trabecular bone defect: an experimental study in rabbits. Med Sci Monit. 2010; 16(1): BR24-31.

15. Datta A., Gheduzzi S., Miles A.W. A comparison of the viscoelastic properties of bone grafts. Clin Biomech. 2006; 21(7): 761–766. https://doi.org/10.1016/j.clinbiomech.2006.03.009.

16. Capanna V., Milano G., Pagano E., Barba M. et al. Bone substitutes in orthopaedic surgery: From basic science to clinical practice. J Mater Sci Mater Med. 2014; 25(10): 2445–2461. http://dx.doi.org/10.1007%2Fs10856-014-5240-2.

17. Knofler W., Barth T., Graul R., Krampe D. Retrospective analysis of 10,000 implants from insertion up to 20 years-analysis of implantations using augmentative procedures. Int J Implant Dent. 2016; 2(1): 25. https://doi.org/10.1186/s40729-016-0061-3.

18. Ferracini R., Martínez Herreros I., Russo A., Casalini T. et al. Scaffolds as structural tools for bone-targeted drug delivery. Pharmaceutics. 2018; 10(3): 122. https://doi.org/10.3390/pharmaceutics10030122.

19. Ho-Shui-Ling A., Bolander J., Rustom L.E., Johnson A.W. et al. Bone regeneration strategies: Engineered scaffolds, bioactive molecules and stem cells current stage and future perspectives. Biomaterials. 2018; 180: 143–162. https://doi.org/10.1016/j.biomaterials.2018.07.017.

20. Ceccarelli G., Presta R., Benedetti L., Gabriella M. et al. Emerging perspectives in scaffold for tissue engineering in oral surgery. Stem Cells Int. 2017; 2017: 4585401. https://doi.org/10.1155/2017/4585401.

21. Colaço H.B., Shah Z., Back D., Davies A. et al. Xenograft in orthopaedics. Orthop Trauma. 2015; 29(4): 253–260. https://doi.org/10.1016/j.mporth.2015.06.001.

22. Pertici G., Rossi F., Casalini T., Perale G. Composite polymer-coated mineral grafts for bone regeneration: Material

characterisation and model study. Ann Oral Maxillofac Surg. 2014; 2(1): 4. ISSN 2052-7837.

23. Stacchi C., Lombardi T., Perinetti G., Traini T. et al. New bone formation after transcrestal sinus floor elevation was influenced by sinus cavity dimensions: A prospective histologic and histomorphometric study. Clin Oral Implants Res. 2018; 29(5): 465–479. https://doi.org/10.1111/clr.13144.

24. Murphy C.M., Haugh M.G., O'Brien F.J. The effect of mean pore size on cell attachment, proliferation and migration in collagen-glycosaminoglycan scaffolds for bone tissue engineering. Biomaterials. 2010; 31(3): 461–466. https://doi.org/10.1016/j.biomaterials.2009.09.063.

25. Tu J., Wang H., Li H., Dai K. et al. The in vivo bone formation by mesenchymal stem cells in zein scaffolds. Biomaterials. 2009; 30(26): 4369–4376. https://doi.org/10.1016/j.biomaterials.2009.04.054.

26. Gu W., Wu C., Chen J., Xiao Y. Nanotechnology in the targeted drug delivery for bone diseases and bone regeneration. Int J Nanomed. 2013; 8: 2305–2317. https://doi.org/10.2147/ijn.s44393.

27. Ali Akbari Ghavimi S., Ebrahimzadeh M.H., Solati-Hashjin M., Abu Osman N.A. Polycaprolactone/starch composite: Fabrication, structure, properties, and applications. J Biomed Mater Res A. 2015; 103(7): 2482–2498. https://doi.org/10.1002/jbm.a.35371.

28. Athanasiou K.A., Agrawal C.M., Barber F.A., Burkhart S.S. Orthopaedic applications for PLA-PGA biodegradable polymers. Arthroscopy. 1998; 14(7): 726–737. https://doi.org/10.1016/S0749-8063(98)70099-4.

29. Ghassemi T., Shahroodi A., Ebrahimzadeh M.H., Mousavian A. et al. Current concepts in scaffolding for bone tissue engineering. Arch Bone Jt Surg. 2018; 6(2): 90–99. https://dx.doi.org/10.22038/abjs.2018.26340.1713.

30. Yan J., Li J., Runge M.B., Dadsetan M. et al. Cross-linking characteristics and mechanical properties of an injectable biomaterial composed of polypropylene fumarate and polycaprolactone co-polymer. J Biomater Sci Polym Ed. 2011; 22(4-6): 489–504. https://doi.org/10.1163/092050610X487765.

31. Ghassemi T., Shahroodi A., Ebrahimzadeh M.H., Mousavian A. et al. Current concepts in scaffolding for bone tissue engineering. Arch Bone Jt Surg. 2018; 6(2): 90–99. https://dx.doi.org/10.22038/abjs.2018.26340.1713. Повторяется в 29 ссылке

32. Moradi A., Ataollahi F., Sayar K., Pramanik S. et al. Chondrogenic potential of physically treated bovine cartilage matrix derived porous scaffolds on human dermal fibroblast cells. J Biomed Mater Res A. 2016; 104(1): 245–256. https://doi.org/10.1002/jbm.a.35561.

33. Pei M., Li J.T., Shoukry M., Zhang Y. A review of decellularized stem cell matrix: A novel cell expansion system for cartilage tissue engineering. Eur Cell Mater. 2011; 22: 333–343. https://doi.org/10.22203/ecm.v022a25.

34. Yarlagadda P.K., Chandrasekharan M., Shyan J.Y. Recent advances and current developments in tissue scaffolding. Biomed Mater Eng. 2005; 15(3):159-177.

35. Russo E., Gaglianone N., Baldassari S., Parodi B. et al. Preparation, characterization and in vitro antiviral activity evaluation of foscarnet-chitosan nanoparticles. Colloids and Surfaces B: Biointerfaces. 2014; 118: 117–125. https://doi.org/10.1016/j.colsurfb.2014.03.037.

36. Cao L., Werkmeister J.A., Wang J., Glattauer V. et al. Bone regeneration using photocrosslinked hydrogel incorporating rhbmp-2 loaded 2-n, 6-o-sulfated chitosan nanoparticles. Biomaterials. 2014; 35(9): 2730–2742. https://doi.org/10.1016/j.biomaterials.2013.12.028.

37. Wang Y., Zhao Q., Han N., Bai L. et al. Mesoporous silica nanoparticles in drug delivery and biomedical applications. Nanomedicine. 2015; 11(2): 313–327. https://doi.org/10.1016/j.nano.2014.09.014.

38. Cheng H., Chawla A., Yang Y., Li Y. et al. Development of nanomaterials for bone-targeted drug delivery. Drug Discov Today. 2017; 22(9): 1336–1350. https://doi.org/10.1016/j.drudis.2017.04.021.

39. Cabuzu D., Cirja A., Puiu R., Grumezescu A.M. Biomedical applications of gold nanoparticles. Curr Top Med Chem. 2015; 15(16): 1605–1613. https://doi.org/10.2174/1568026615666150414144750.

40. Sul O.J., Kim J.C., Kyung T.W., Kim H.J. et al. Gold nanoparticles inhibited the receptor activator of nuclear factor-kappab ligand (RANKL)-induced osteoclast formation by acting as an antioxidant. Biosci Biotechnol Biochem. 2010; 74(11): 2209–2213. https://doi.org/10.1271/bbb.100375.

41. Ghosh P., Han G., De M., Kim C.K. et al. Gold nanoparticles in delivery applications. Adv Drug Deliv Rev. 2008; 60(1): 1307–1315. https://doi.org/10.1016/j.addr.2008.03.016.

42. Yi C., Liu D., Fong C.C., Zhang J. et al. Gold nanoparticles promote osteogenic differentiation of mesenchymal stem cells through p38 MAPK pathway. ACS Nano. 2010; 4(11): 6439–6448. https://doi.org/10.1021/nn101373r.

43. Cheng H., Chawla A., Yang Y., Li Y. et al. Development of nanomaterials for bone-targeted drug delivery. Drug Discov Today. 2017; 22(9): 1336–1350. https://doi.org/10.1016/j.drudis.2017.04.021. Повторяется в 38 ссылке.

44. Zhang Q., Mochalin V.N., Neitzel I., Knoke I.Y. et al. Fluorescent PLLA-nanodiamond composites for bone tissue engineering. Biomaterials. 2011; 32(1): 87–94. https://doi.org/10.1016/j.biomaterials.2010.08.090.

45. Biltz R.M., Pellegrino E.D. The chemical anatomy of bone. I. A comparative study of bone composition in sixteen vertebrates. J Bone Jt Surg Am. 1969; 51(3): 456–466.

46. Bose S., Tarafder S. Calcium phosphate ceramic systems in growth factor and drug delivery for bone tissue engineering: A review. Acta Biomater. 2012; 8(4): 1401–1421. https://doi.org/10.1016/j.actbio.2011.11.017.

47. Ambre A.H., Katti D.R., Katti K.S. Biomineralized hydroxyapatite nanoclay composite scaffolds with polycaprolactone for stem cell-based bone tissue engineering. J Biomed Mater Res A. 2015; 103(6): 2077–2101. https://doi.org/10.1002/jbm.a.35342.

48. Fielding G.A., Bandyopadhyay A., Bose S. Effects of silica and zinc oxide doping on mechanical and biological properties of 3D printed tricalcium phosphate tissue engineering scaffolds. Dent Mater. 2012; 28(2): 113–122. https://doi.org/10.1016/j.dental.2011.09.010.

49. Alves C.D., Jansen J.A., Leeuwenburgh S.C. Synthesis and application of nanostructured calcium phosphate ceramics for bone regeneration. J Biomed Mater Res B. 2012; 100B(8): 2316–2326. https://doi.org/10.1002/jbm.b.32794.

50. Oryan A., Alidadi S., Moshiri A., Maffulli N. Bone regenerative medicine: classic options, novel strategies, and future

directions. J Orthop Surg Res. 2014; 9(1): 18. https://doi.org/10.1186/1749-799x-9-18.

51. Granjeiro J.M., Oliveira R.C., Bustos-Valenzuela J.C., Sogayar M.C. et al. Bone morphogenetic proteins: from structure to clinical use. Braz J Med Biol Res. 2005; 38(10): 1463-73. https://doi.org/10.1590/s0100-879x2005001000003.

52. Gautschi O.P., Frey S.P., Zellweger R. Bone morphogenetic proteins in clinical applications. ANZ J Surg. 2007; 77(8): 626-31. https://doi.org/10.1111/j.1445-2197.2007.04175.x.

53. Carter T.G., Brar P.S., Tolas A., Beirne O.R. Off-label use of recombinant human bone morphogenetic protein-2 (rhBMP-2) for reconstruction of mandibular bone defects in humans. J Oral Maxillofac Surg. 2008; 66(7): 1417-25. https://doi.org/10.1016/j.joms.2008.01.058.

54. McKay B., Sandhu H.S. Use of recombinant human bone morphogenetic protein-2 in spinal fusion applications. Spine. 2002; 27(1 (Suppl 1)): S66-85.

55. El Bialy I., Jiskoot W., Nejadnik M.R. Formulation, Delivery and Stability of Bone Morphogenetic Proteins for Effective Bone Regeneration. Pharm Res. 2017; 34(6): 1152–1170. http://dx.doi.org/10.1007%2Fs11095-017-2147-x.

56. White A.P., Vaccaro A.R., Hall J.A., Whang P.G. et al. Clinical applications of BMP-7/OP-1 in fractures, nonunions and spinal fusion. Int Orthop. 2007; 31: 735–741. https://doi.org/10.1007/s00264-007-0422-x.

57. Ristiniemi J., Flinkkilä T., Hyvönen P., Lakovaara M. et al. RhBMP-7 accelerates the healing in distal tibial fractures treated by external fixation. J Bone Jt Surg Br. 2007; 89(2): 265–272. https://doi.org/10.1302/0301-620X.89B2.18230.

58. Wen Y.D., Jiang W.M., Yang H.L., Shi J.H. Exploratory meta-analysis on dose-related ecacy and complications of rhBMP-2 in anterior cervical discectomy and fusion: 1,539,021 cases from 2003 to 2017 studies. J Orthop Transl. 2020; 24: 166–174. https://doi.org/10.1016/j.jot.2020.01.002.

59. Triplett R.G., Nevins M., Marx R.E., Spagnoli D.B. et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. J Oral Maxillofac Surg. 2009; 67(9): 1947–1960. https://doi.org/10.1016/j.joms.2009.04.085.

60. Fiorellini J.P., Howell T.H., Cochran D., Malmquist J. et al. Randomized study evaluating recombinant human bone morphogenetic protein-2 for extraction socket augmentation. J Periodontol. 2005; 76(4): 605–613. https://doi.org/10.1902/jop.2005.76.4.605.

61. Hollinger J.O., Hart C.E., Hirsch S.N., Lynch S. et al. Recombinant human platelet-derived growth factor: Biology and clinical applications. J Bone Jt Surg Am. 2008; 90(Suppl. 1): 48–54. https://doi.org/10.2106/jbjs.g.01231.

62. Min S.H., Kang N.E., Song S.I., Lee J.K. Regenerative effect of recombinant human bone morphogenetic protein-2/absorbable collagen sponge (rhBMP-2/ACS) after sequestrectomy of medication-related osteonecrosis of the jaw (MRONJ). J Korean Assoc Oral Maxillofac Surg. 2020; 46(3): 191–196. https://doi.org/10.5125/jkaoms.2020.46.3.191.

63. Kim M.S., Kim K.J., Kim B.J., Kim C.H. et al. Immediate reconstruction of mandibular defect after treatment of medication-related osteonecrosis of the jaw (MRONJ) with rhBMP-2/ACS and miniplate: Review of 3 cases. Int J Surg Case Rep. 2020; 66: 25–29. https://doi.org/10.1016/j.ijscr.2019.11.038.

Ұзын түтікшелі сүйектердің сүйек тінінің репаративті регенерациялық бұзылыстарын емдеудегі жасушалық технологиялардың эволюциясы

Байдарбеков М.Ө.

№1 травматология бөлімшесінің меңгерушісі, Академик Батпенов Н.Ж. атындағы ұлттық ғылыми травматология және ортопедия орталығы,

Нұр-Сұлтан, Қазақстан. E-mail: baidarbekov_m@nscto.kz

Түйіндеме

Аутотрансплантаттар, алло- және ксенотрансплантаттар ұзын сүйектердегі сүйек тінінің репаративті регенерациясының бұзылыстарын емдеудің заманауи стандарты болып табылады. Алайда бұл тәсілдердің сүйек тінінің трансплантация үшін қолжетімділігінің шектеулі болуы немесе иммундық жауаптардың орын алуы секілді кейбір кемшіліктері бар. Сондай-ақ, қазіргі қолданылып жүрген пластмассалық материалдар in vitro және in vivo зерттеліп, биоүйлесімділік және биомеханикалық қасиеттері бойынша оң нәтижелер көрсеткен. Сүйек тінін қалпына келтіру үшін қолданылатын имплантаттар да сүйектің тұнуы мен минералдануын жеңілдету үшін өзара әрекеттесе алатын дәрілік заттармен, өсу факторларымен және мезенхималық дің жасушаларымен үйлескенде оң нәтиже көрсетті. Нано- және микробөлшектерді тиімді емдік концентрацияда пайдалану олардың уақыт өте келе теріден босап шығарылу қасиетін арттыруға мүмкіндік береді. Бұл жүйелер остеогенез процесін күшейтіп, сүйек регенерациясын жылдамдатады. Дегенмен, клиникаға дейінгі зерттеулердің оң нәтижелеріне қарамастан, бұл жүйелерді пайдалану әлі де болса қосымша клиникалық сынақтардан өтуді қажет етеді.

Түйін сөздер: жасушалық технологиялар, репаративті регенерация бұзылыстары, ұзын түтікшелі сүйектер, сүйек тіндері, аутотрансплантат, аллотрансплантат, ксенотрансплантат.

Эволюция клеточных технологий в лечении нарушений репаративной регенерации костной ткани длинных трубчатых костей

Байдарбеков М.У.

Заведующий отделением травматологии №1, Национальный научный центр травматологии и ортопедии имени академика Батпенова Н.Д., Нур-Султан, Казахстан. E-mail: baidarbekov_m@nscto.kz

Резюме

Аутотрансплантаты, алло- и ксенотрансплантаты являются текущими стандартами лечения нарушений репаративной регенерации костной ткани длинных трубчатых костей, но эти подходы все еще имеют некоторые недостатки, такие как ограниченная доступность костной ткани для трансплантации или иммунные реакции. Современные пластмассовые материалы изучались как in vitro, так и in vivo, и показали многообещающие результаты с точки зрения биосовместимости и биомеханических свойств. Кроме того, имплантаты, применяемые для восстановления костной ткани, показали положительные результаты в сочетании с лекарствами, факторами роста и мезенхимальными стволовыми клетками, которые могут взаимодействовать, облегчая отложение и минерализацию костной ткани. Использование нано- и микрочастиц дает возможность повысить эффективность и контролируемое высвобождение вещества из кожи с течением времени при соответствующих терапевтических концентрациях. Эти системы контролируемой доставки могут эффективно стимулировать остеогенез и ускорять регенерацию костей без значительных побочных эффектов. Однако, несмотря на многообещающие результаты доклинических исследований, применение данных систем требует дополнительных клинических испытаний.

Ключевые слова: клеточные технологии, нарушения репаративной регенерации, длинные трубчатые кости, костная ткань, аутотрансплантаты, аллотрансплантаты, ксенотрансплантаты.