

## Regenerative medicine for the reconstruction of hard tissue defects in oral and maxillofacial surgery

Young-Kyun Kim, D.D.S., PhD., Editor-in-Chief of JKAOMS

*Department of Oral and Maxillofacial Surgery, Section of Dentistry,  
Seoul National University Bundang Hospital, Seongnam, Korea*

As the most ideal bone graft material to reconstruct hard tissue with defects, autogenous bone provides excellent bone healing capacity in terms of osteogenesis, osteoinduction, and osteoconduction. Note, however, that patients and clinicians tend to avoid using it due to problems including limited amount and donor site complications. As a result, allograft, xenograft, and alloplastic material (synthetic bones) were developed and applied in clinical surgeries for a long time, yet they do not have the same bone healing capacity as that of autogenous bone<sup>1</sup>.

In the early stage, hydroxyapatite-type synthetic bone was used frequently for ridge augmentation to maintain full denture and for the reconstruction of tissue with defects after cyst enucleation. In addition, various synthetic bones such as bioglass,  $\beta$ -tricalcium phosphate (TCP), hard tissue replacement material (HTR), and calcium sulfate were developed and commercialized. Note, however, that synthetic bones only provide osteoconduction capacity and actually have many disadvantages in bony remodeling. As a result, xenograft bone with enhanced osteoconduction capacity such as BioOss (Geistlich Pharma AG, Wolhausen, Switzerland) was developed, and good clinical results have been recorded for several decades<sup>1,2</sup>. Meanwhile, since Urist<sup>3</sup> discovered bone morphogenic protein in the 1960s, many research studies to extract bone morphogenic protein and various growth factors from teeth or osseous tissue to apply in clinical situations have been conducted. Based on such research, allograft materials with excellent osteoinduction were developed and used as substitute for autogenous bone.

Recently, regenerative medicine has been developed remarkably not only in dentistry but in other medical departments as well. Tissue engineering as one field of regenerative medicine is a method of reconstructing tissues and organs with massive defects and recovering their function using biological cells. Moreover, in *Korean Assoc Oral Maxillofac Surg*, many research studies on regenerative medicine have

been published since long ago.

Since 1965 when Urist<sup>3</sup> suggested the concept of osteoinduction by bone morphogenic protein (BMP) in cortical bone, many researchers have attempted to extract BMP from teeth or osseous tissue for application in clinical situations. Note, however, that the extraction of a sufficient amount and application in clinical situations were very difficult<sup>4,6</sup>. Nonetheless, various BMPs (recombinant human BMP, rhBMP) have been recently manufactured by gene recombination based on the cell of mammals or colon bacillus<sup>7-9</sup>.

Growth factor is very important in bony remodeling and healing because it significantly influences the activity of osteoblast. The growth factor related to the regeneration of osseous tissue includes PDGF, VEGF, TGF- $\beta$ , AFGF,  $\beta$ -FGF, IGF-I, IGF-II, EGF, etc., and many research studies were reported in the *J Korean Assoc Oral Maxillofac Surg*<sup>10-19</sup>.

For stem cells, since Choi et al.<sup>20</sup> reported the differentiation of adult canine bone marrow stem cells into neurons in 2003, many research studies on stem cells derived from human cord blood, buccal fat pad, adipose tissue, impacted wisdom teeth, skin, pulp, periodontal ligament, and dental follicle have been reported<sup>21-26</sup>.

Achieving successful reconstruction by applying bone growth enzyme, BMP, and stem cells on defects requires a carrier (scaffold) to transfer them. The ideal scaffold must have a bony restorative effect by itself and encourage the maximum emission of bone growth factor and stem cells in the target area. Many researchers have conducted various research studies to develop an ideal scaffold<sup>27-29</sup>.

Autogenous tooth bone graft material was developed and utilized in 2008. It provides excellent bone healing capacity in terms of osteoinduction and osteoconduction because it contains minerals most similar to those of the human alveolar bone as well as type I collagen and a variety of proteins<sup>30-33</sup>.

In conclusion, a new material whose functions are very

similar to autogenous bone will be developed and commercialized soon by many researchers based on research studies on regenerative medicine. Therefore, good research on regenerative medicine should be reported in *J Korean Oral Maxillofac Surg*.

## References

- Kim YK. Clinical application and classification of bone graft material according to component. *J Korean Dent Assoc* 2010;48:263-74.
- Kim YK. Systematic classification and application of alloplastic bony substitutes and autogenous teeth bone graft material. *J Korean Acad Implant Dent* 2009;28:7-88.
- Urist MR. Bone: formation by autoinduction. *Science* 1965;150:893-9.
- Chae YP, Lee JH, Kim SK, Yeo HH. A histologic study on the repair of rat calvarial critical size defect with bovine bone morphogenetic protein (b-BMP). *J Korean Assoc Oral Maxillofac Surg* 1997;23:290-303.
- Kim BR, Lee JH, Kim JW. Comparison of bone inducing process of porcine bone matrix-derived BMP combined with the following, freeze-dried allogeneic bone, surface demineralized allogeneic bone, and demineralized allogeneic bone powder in rats. *J Korean Assoc Oral Maxillofac Surg* 1998;24:380-95.
- Oh DW, Lee SH, Shin HI. Histologic evaluation of the ectopic bone formation induced by partially purified BMP-fibrous glass membrane complex. *J Korean Assoc Oral Maxillofac Surg* 1996;22:86-100.
- Nam JH, Park JC, Yu SB, Chung YI, Tae GY, Kim JJ, et al. Bone regeneration with MMP sensitive hyaluronic acid-based hydrogel, rhBMP-2 and nanoparticles in rat calvarial critical size defect (CSD) model. *J Korean Assoc Oral Maxillofac Surg* 2009;35:137-45.
- Kim SJ, Kim MR, Oh JS, Han I, Shin SW. Effects of polycaprolactone-tricalcium phosphate, recombinant human bone morphogenetic protein-2 and dog mesenchymal stem cells on bone formation: Pilot study in dogs. *Yonsei Med J* 2009;50:825-31.
- Lee JH, Kim CS, Choi KH, Jung UW, Yun JH, Choi SH, et al. The induction of bone formation in rat calvarial defects and subcutaneous tissues by recombinant human BMP-2, produced in *Escherichia coli*. *Biomaterials* 2010;31:3512-9.
- Kim JH, Lee SC. Immunohistochemical profile of basic fibroblast growth factor (bFGF) in growing rat T-M joint. *J Korean Assoc Oral Maxillofac Surg* 2001;27:1-8.
- Song SI, Kim MJ. Growth inhibition in head and neck cancer cell lines by gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor. *J Korean Assoc Oral Maxillofac Surg* 2009;35:287-93.
- Suh JD, Myung H, Kang N, Choung PH. The effects of insulin-like growth factor I (IGF-I) on expression of vascular endothelial growth factor (VEGF) mRNA in MG-63 osteoblastlike cells. *J Korean Assoc Oral Maxillofac Surg* 2005;31:363-9.
- Park BW, Byun JH, Hah YS, Kim DR, Chung IK, Kim JR, et al. Expression of vascular endothelial growth factor receptors in tumor and stromal cells of tongue squamous cell carcinoma. *J Korean Assoc Oral Maxillofac Surg* 2007;33:11-9.
- Han SJ, Lee JH. Anti-tumor effects of vascular endothelial growth factor inhibitor on oral squamous cell carcinoma cell Lines. *J Korean Assoc Oral Maxillofac Surg* 2009;35:66-73.
- Min BG, Lee SK, Park YW. Immunohistochemical detection of growth factors and extracellular matrix proteins in the degenerating tissues of pre- and postnatal human cleft lip and palate. *J Korean Assoc Oral Maxillofac Surg* 2002;28:421-33.
- Lee SG, Kim KH. Production of transforming growth factor- $\beta$ 1 in human fibroblasts induced with bacterial toxins. *J Korean Assoc Oral Maxillofac Surg* 2000;26:345-54.
- Park KL. Insulin-like growth factor-II in MC3T3 osteoblasts. *J Korean Assoc Oral Maxillofac Surg* 2007;33:617-24.
- Kim JM, Lee JH, Park IS. New bone formation using fibrin rich block with concentrated growth factors in maxillary sinus augmentation. *J Korean Assoc Oral Maxillofac Surg* 2011;37:278-86.
- Kim UK, Choi YS, Jung JS. The effect of growth factors on osteogenic differentiation of adipose tissue-derived stromal cells. *J Korean Assoc Oral Maxillofac Surg* 2006;32:327-33.
- Choi BH, Huh JY, Park DJ, Kim BY, Lee SHR, Park SY. Differentiation of adult canine bone marrow stem cells into neurons. *J Korean Assoc Oral Maxillofac Surg* 2003;29:1-4.
- Kim DH, Yun JY, Lee JH, Myoung H, Kim SM. Cancer stem cell theory and update in oral squamous cell carcinoma. *J Korean Assoc Oral Maxillofac Surg* 2011;37:97-108.
- Lee JK, Lee JH. A study on differentiation potency of adult stem cells from pulp, periodontal ligament, and dental follicle to osteoblast. *J Korean Assoc Oral Maxillofac Surg* 2010;36:7-15.
- Kim CH, Park CH, Lee IK, Pyo SW. Osteogenesis by BMP-2 in adult stem cell derived from buccal fat pad. *J Korean Assoc Oral Maxillofac Surg* 2008;34:412-8.
- Byun JH, Kang EJ, Maeng GH, Rho GJ, Kang DH, Lee JS, et al. Maxillary sinus floor elevation using autogenous skin-derived mesenchymal stem cells in miniature pigs. *J Korean Assoc Oral Maxillofac Surg* 2010;36:87-93.
- Song JH, Park BW, Byun JH, Kang EJ, Rho GJ, Shin SH, et al. Isolation and characterization of human dental tissue-derived stem cells in the impacted wisdom teeth: comparison of dental follicle, dental pulp, and root apical papilla-derived cells. *J Korean Assoc Oral Maxillofac Surg* 2010;36:186-96.
- Kim ES, Kim HO. Endothelial progenitor cells and mesenchymal stem cells from human cord blood. *J Korean Assoc Oral Maxillofac Surg* 2005;31:39-45.
- Lee J, Sung DH, Choi JY, Choi SR, Cha SR, Jang JD, et al. The effects of Bio-Oss, as a scaffolds during sinus bone graft using mesenchymal stem cells in rabbit. *J Korean Assoc Oral Maxillofac Surg* 2007;33:405-18.
- Kim JH, Choi JY. Study on thermosensitivity of chitosan scaffold and on its effects on fibroblast proliferation in cell therapy for soft tissue augmentation. *J Korean Assoc Oral Maxillofac Surg* 2009;35:146-52.
- Lee J, Min H, Jung J, Kang N. Effect of different sterilization methods on the surface morphology of PPDO-hybrid-PLGA nanofiber scaffold and attachments of PC12 cell. *J Korean Assoc Oral Maxillofac Surg* 2008;34:635-9.
- Kim YK, Kim SG, Oh JS, Jin SC, Son JS, Kim SY, et al. Analysis of the inorganic component of autogenous tooth bone graft material. *J Nanosci Nanotechnol* 2011;11:7442-5.
- Kim YK, Kim SG, Byeon JH, Lee HJ, Um IU, Lim SC, et al. Development of a novel bone grafting material using autogenous teeth. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010;109:496-503.
- Jeong HR, Hwang JH, Lee JK. Effectiveness of autogenous tooth bone used as a graft material for regeneration of bone in miniature pig. *J Korean Assoc Oral Maxillofac Surg* 2011;37:375-9.
- Kim GW, Yeo IS, Kim SG, Um IW, Kim YK. Analysis of crystalline structure of autogenous tooth bone graft material: X-Ray diffraction analysis. *J Korean Assoc Oral Maxillofac Surg* 2011;37:225-8.