A New Regenerative Therapy Of Elastic Cartilage Grafting For Craniofacial Deformities

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Background : Craniofacial injuries and abnormalities such as deviated nose and microtia etc., are often treated by self-cartilage grafting. For autologous tissue grafting, limitations include the collectable volume, donor site morbidity, and tissue absorption; more importantly, the long-term clinical outcomes remain quite poor due to tissue maintenance failures

We recently identified a promising regenerative method based on the xenotransplantation of human cartilage progenitor cells in immunodeficient animals(1) and autotransplantation of monkey cartilage progenitors cells (2) to reconstruct self-renewing elastic cartilage. The aim of this study was to control the volume and shape of self-renewing elastic cartilage by two another methods as a pre-clinical study.

Methods : Three monkeys (*Macaca fascicularis*) were used. First, we identified the progenitor population from the monkey ear perichondrium. Progenitor cells were expanded and differentiated extensively into chondrocytes *in vitro*. First group(Two-stage grafting(3)) was atuotransplanted the differentiated progenitor cells into monkeys abdominal lesions, after 6 month collect reconstructive tissue ,process them and re-autotransplanted craniofacial area. Second group(Using rotating wall vessel bioreactor(4)) was added cutured the differentiated progenitor cells using rotating wall vessel bioreactor(RWV) in vitro 3 weeks, then autotransplanted craniofacial area. This autotransplantated tissue regeneration was monitored using non-invasive magnetic resonance imaging (MRI). The transplanted cells were retrieved three months later. Histological assessment and glycosaminoglycan (GAG) levels of reconstructed tissue were assessed.The experimental animal protocols were approved by the Animal Welfare and Animal Care Committee of the National Institute of Biomedical Innovation (Osaka, Japan)(approval ID: DS25-32).

Results : Remarkable formation change was detected in both of 2 groups clinically. We also detected density difference in the MRI T1/T2 images. Elastic cartilage was detected in histological assessment, GAG levels were nearby original auricular cartilage. No complication such as inflammation and tumorigenesis were observed in any of the experiments.

Conclusion : These 2 methods will be a highly promising to treat craniofacial deformities. We conclude that to use properly these methods will be needed for patient condition.

REFERENCES:

1. Kobayashi, S.; Takebe, T.; Inui, M.; Iwai, S.; Kan, H.; Zheng, Y. W.; Maegawa, J.; Taniguchi, H. Reconstruction of human elastic cartilage by a CD44+ CD90+ stem cell in the ear perichondrium. Proc. Natl. Acad. Sci. USA. 2011;108(35):14479-14484

2. Shintaro,K.; Takebe,T.; Kobayashi,S.; Yabuki,Y.; Hori,A.; Hirotomi,K.; Mikami, T.; Uemura,T.; Maegawa,J.; Taniguchi,H. Autotransplantation of monkey ear perichondrium-derived progenitor cells for cartilage reconstruction. Cell Transplant.2016; 25(5):951-62

3. Yanaga, H.; Imai, K.; Fujimoto, T.; Yanaga, K. Generating ears from cultured autologous auricular chondrocytes by using two-stage implantation in treatment of microtia. Plast. Reconstr. Surg. 2009;124(3):817-825

4. Takebe,T.; Kobayashi,S.; Kan,H.; Suzuki,H.; Yabuki,Y.; Mizuno,M.; Adegawa,T.; Yoshioka,T.; Tanaka,J.; Maegawa,J.; Taniguchi,H. Human Elastic Cartilage Engineering from Cartilage Progenitor Cells Using Rotating Wall Vessel Bioreactor. Transplant. Proceed. 2012;44(4):1158-1161