



Cellumed Co., Ltd. aims to become a top musculoskeletal biotechnology company through research in the field of orthobiologics, medical device, bio-similar, and cell therapy.

Cellumed is committed to the improvement of human health and the quality of life. We will continue to strive toward our goal of putting smiles on our patients' faces as they recover their health and look forward better life.

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The Innovative Technology for Bone Formation
The Innovator in Biosimilars & Biotechnology

Rafugen™ **BMP2**

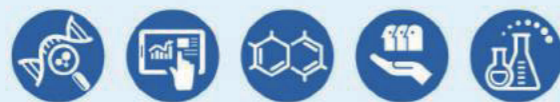
ZENITON 

World-leading enterprise in the biotech industry
Rafugen™ BMP2

Bone morphogenetic protein 2 (BMP2) is a member of the BMP subgroup of the TGF-β superfamily. It plays a dominant role in embryonic dorsal-ventral patterning, organogenesis, limb bud formation, and bone formation and regeneration. Human BMP2 is synthesized as a 396 amino acid (aa) proform that contains 23 aa signal sequence, 259 aa prosegment, and 114 aa mature region. Proteolytic removal of the propeptide enables mature BMP2 to form active disulfide linked homodimers and heterodimers with BMP7. Mature monomer BMP2 is an 18kDa glycosylated peptide with seven conserved cysteines that form a cystine knot structure. Mature human BMP2 shares 100% aa sequence identity with mouse and rat BMP2. It shares 85% aa sequences identity with human BMP4 and less than 51% with other BMPs.

RELIABILITY

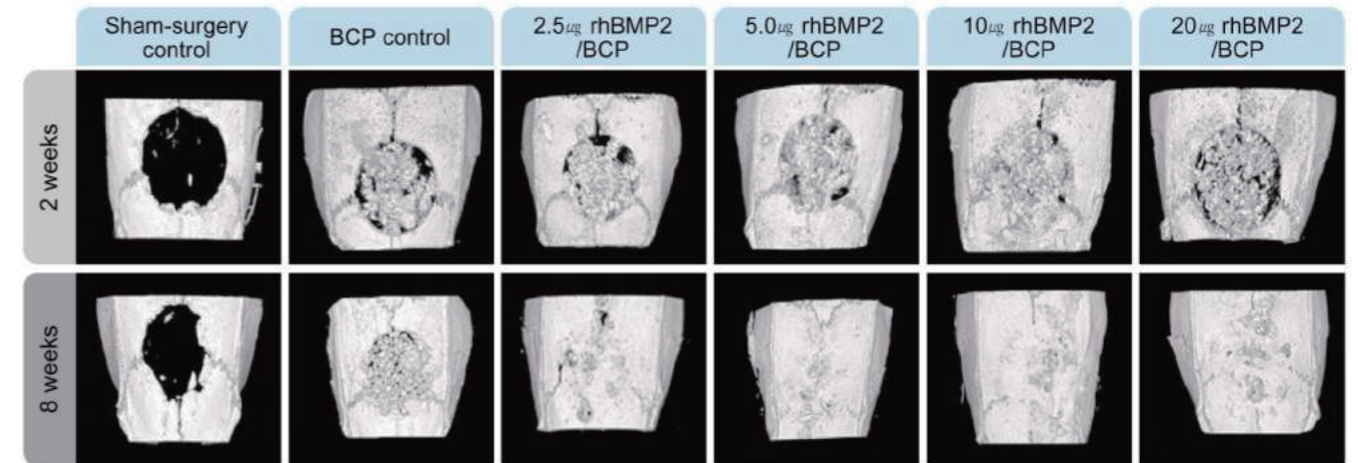
- Validation of specifications and QC testing to ensure consistent quality
- Low endotoxin levels are essential when proteins are used in biological systems that are sensitive to its effect.
- Recombinant proteins are typically over 95% pure.
- Minimal lot-to-lot variability



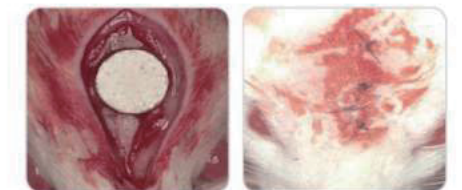
WORLD-LEADING ENTERPRISE
 IN THE BIOTECH INDUSTRY

Efficacy of BCP-rhBMP2 Complex, Implantation Test in Rat Calvarium Defect Model

Activity test of Osteoinductivity

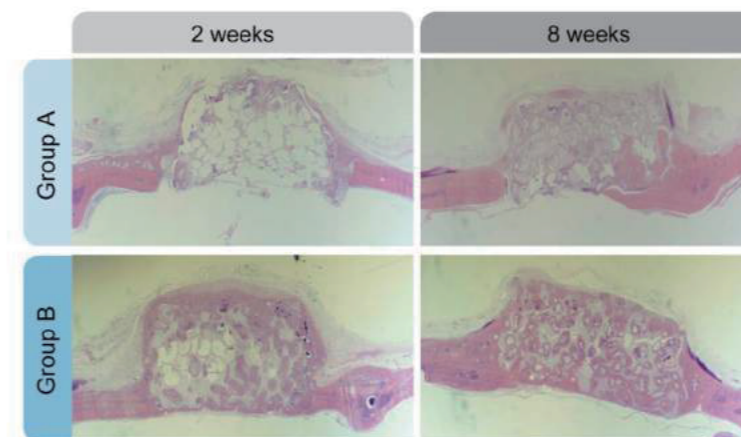


The test of osteoinductive activity of biphasic calcium phosphate with different rhBMP2 dose in rats : In the results of micro-CT analysis of defect sites, the percentages of new bone after 2 and 8 weeks of healing were significantly greater in the rhBMP2 treated groups (at all doses) than in the control groups.



(Reference : JW Jang, JH Yun, KI Lee, JW Jang, UW Jang, CS Kim, SH Choi, KS Choi "Osteoinductive activity of biphasic calcium phosphate with different rhBMP2 doses in rats." Oral Surg Oral Med Oral Pathol Oral Radiol 2012;Vol. 113, pp 480-487.)

Efficacy of MBCP-rhBMP2 Complex, Implantation Test in Rat Calvarium Defect Model



- Group A MBCP Block alone
- Group B MBCP Block + rhBMP2

Study group : Prof. Cho in Yonsei University, Dental College

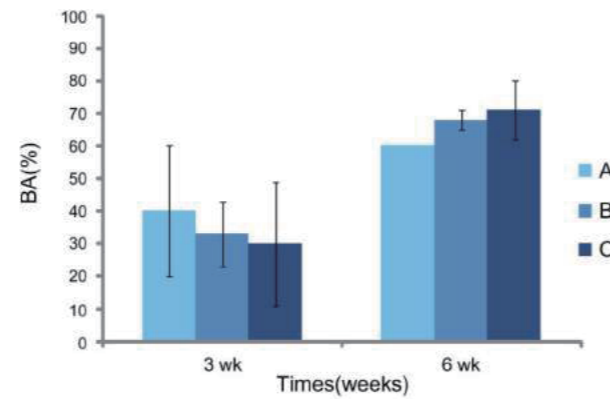
H-E staining

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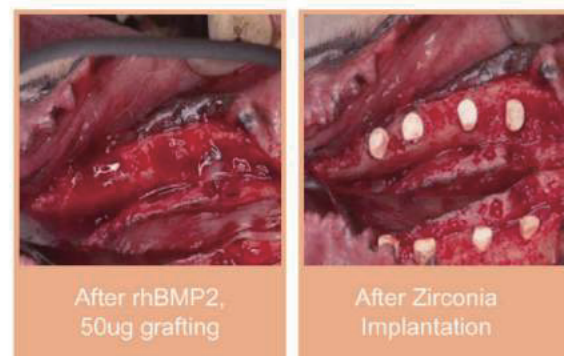
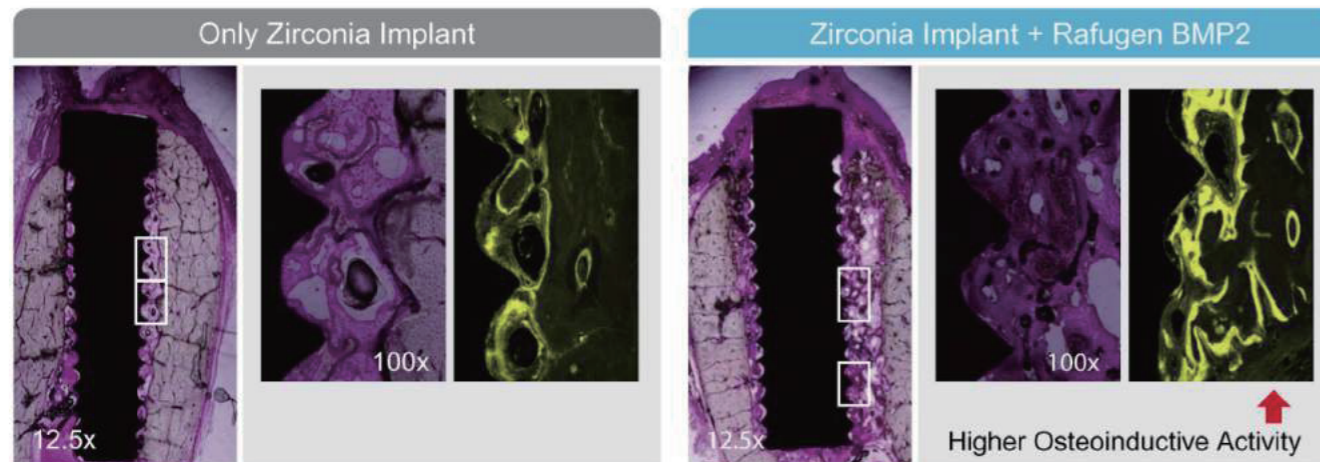
Efficacy of Rafugen BMP2, Dental Implantation Test in Lower Jawbone of Beagle Dog

According to the test of dental implantation in lower jawbone of beagle dog, Rafugen BMP2 shows the highest bone formation ratio after 6 weeks.

- Group A : Only Implant
- Group B : Implant + DBM Gel
- Group C : Implant + Rafugen BMP2



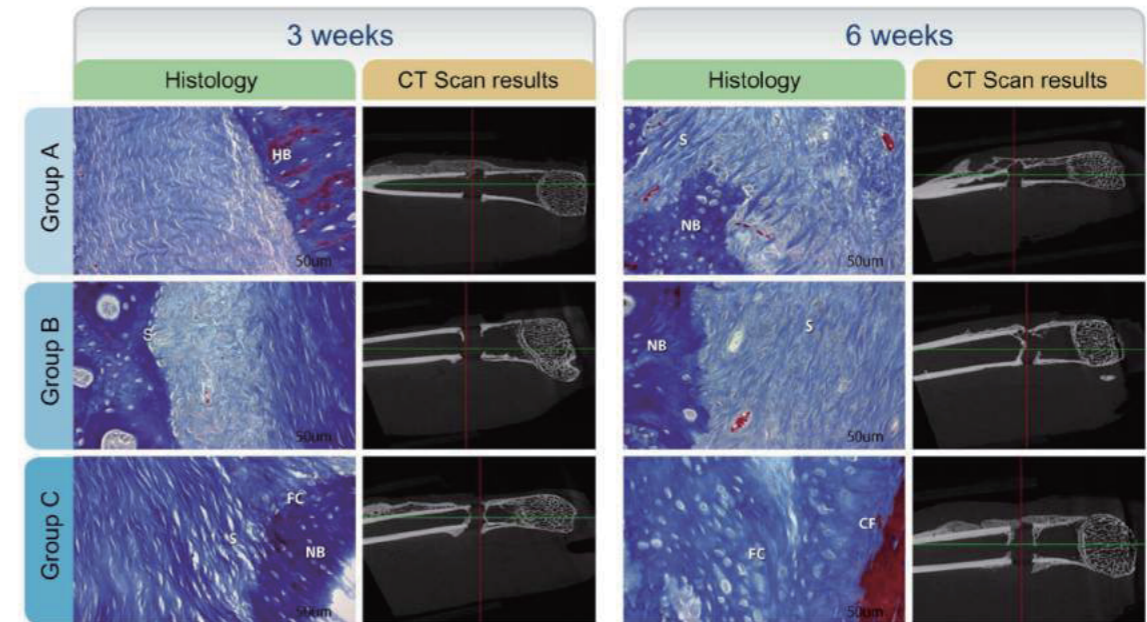
Efficacy of Rafugen BMP2, Dental Implantation Test in Lower Jawbone of Beagle Dog



Animal : Beagle dogs
Method : Lower jawbone implantation for 3 weeks

Study group : Prof. Han in Seoul National University, Dental College

Efficacy of rhBMP2, Ligament Implantation Test in Proximal Tibia of Rabbit



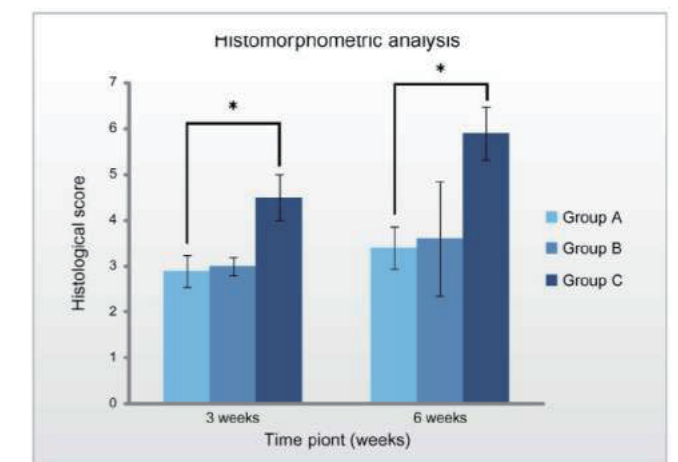
Representative masson's trichrome stained histological images and CT image of the enthesis generated by transfer of the ligament or rhBMP2(+, -) bone complex to the proximal tibia; Group A (Control), Group B (Collagen without rhBMP2), Group C (collagen with rhBMP2) at 3 & 6 weeks after surgery showing the matrix components of the tendon-to-bone interface. T, tendon; HB, host bone; NB new bone; FC, fibrocartilage; CF, collagen fibers; S, Sharpey-like fibers. Original magnification: 400x

- Group A Ligament implantation
- Group B Ligament + collagen
- Group C Ligament + collagen + rhBMP2

Efficacy of rhBMP2, Toe Flexor Implantation Test in Proximal Tibia of Rabbit

Characteristics	Points (total of 9)
Fibrocartilage formation	
Abundant	3
Moderate	2
Slight	1
None	0
New bone formation	
Abundant	3
Moderate	2
Slight	1
None	0
Tendon allograft bonding to adjacent tissue	
75% to 100%	3
50% to 75%	2
25% to 50%	1
0% to 25%	0

Histomorphometric analysis system for assessign healing of the tendon grafts within the bone tunnel. A full score would be nine points



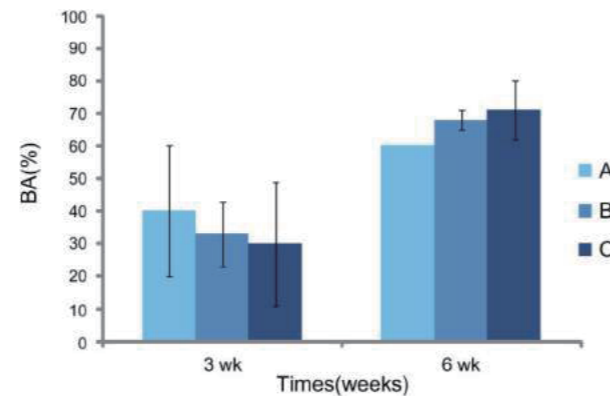
Histological score of the enthesis generated by transfer of the toe flexor or rhBMP2 (+, -) bone complex to the proximal tibia at 3, 6 weeks

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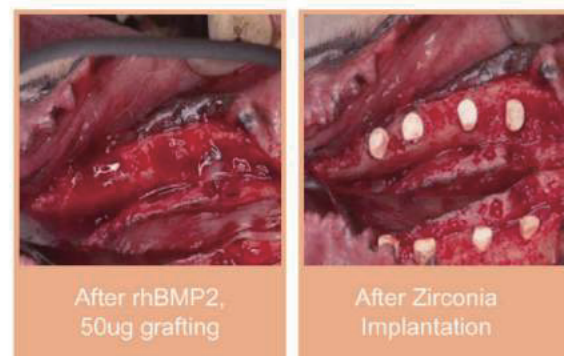
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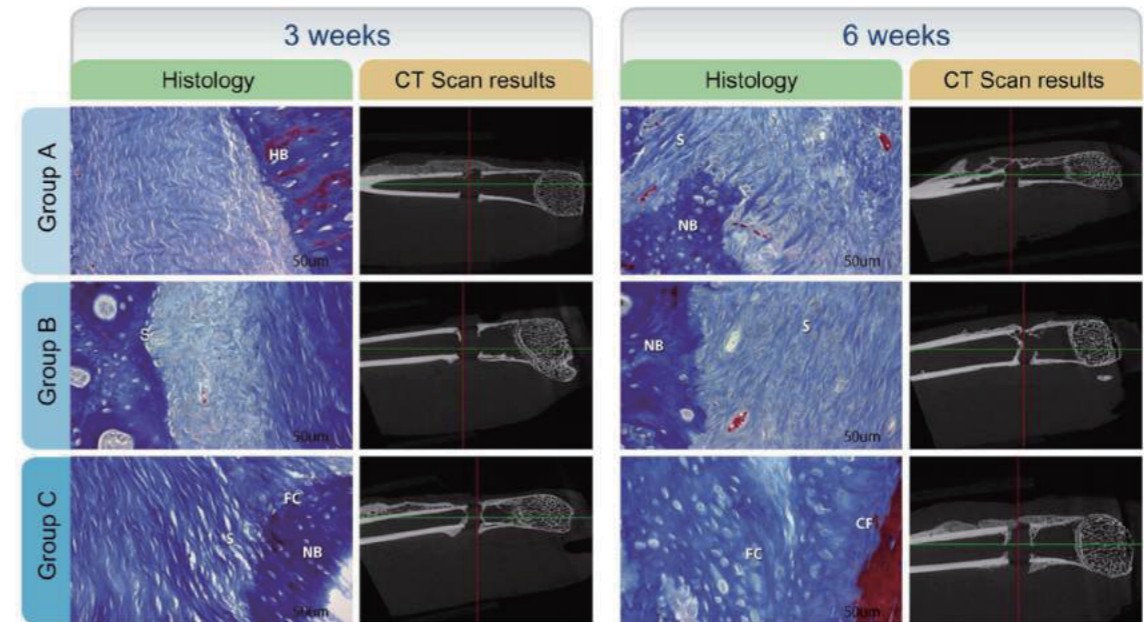
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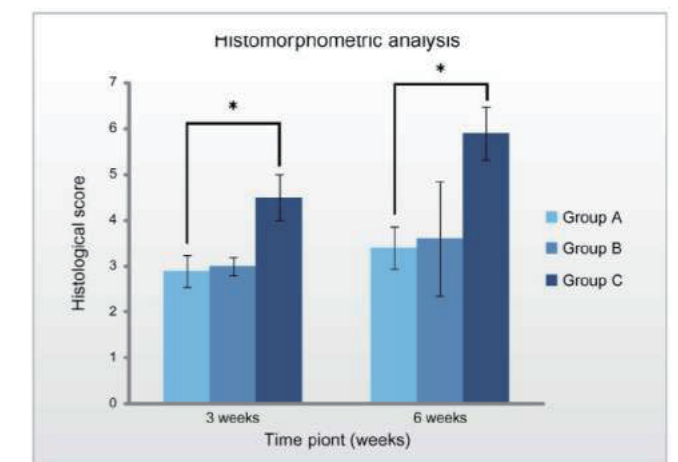
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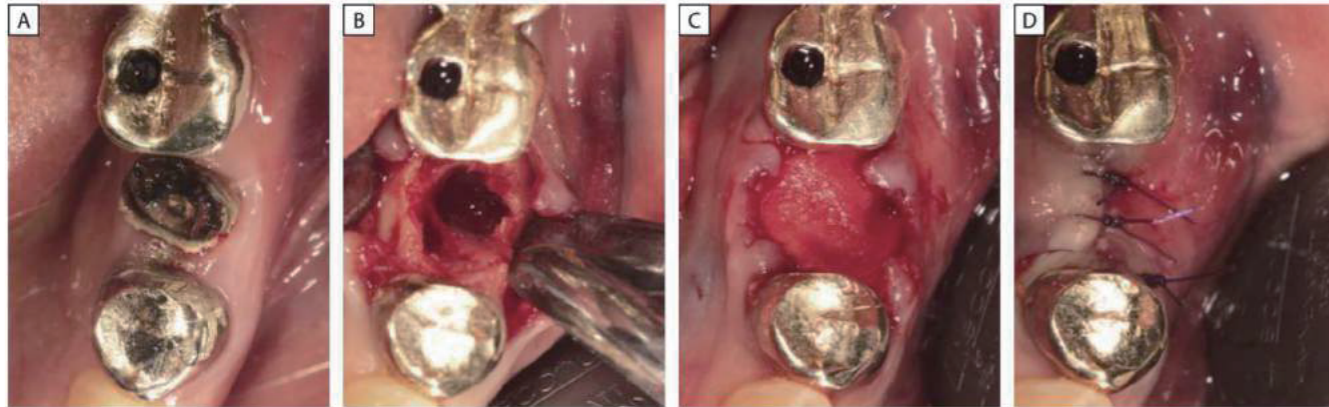
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Histological score of the enthesis generated by transfer of the toe flexor or rhBMP2 (+, -) bone complex to the proximal tibia at 3, 6 weeks

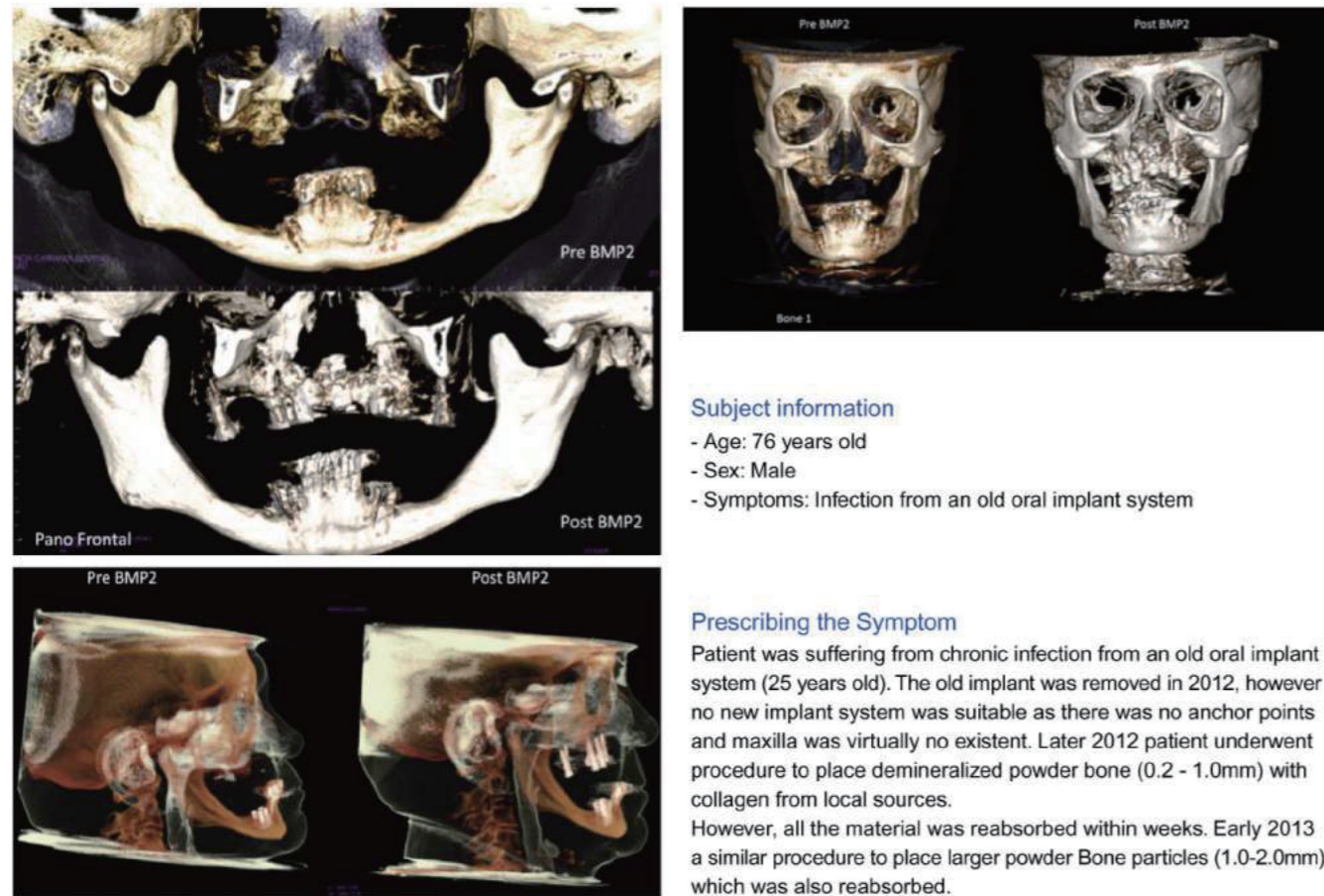
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Rafugen™ BMP2

Clinical Results of rhBMP2



Clinical photographs of the surgical procedure. A, Residual root of the mandibular second premolar. B, Extraction site after atraumatic exodontia. C, Placement of recombinant human bone morphogenetic protein-2/demineralized bone matrix into the socket (which was ultimately covered with a collagen membrane). D, Primary coverage was achieved.

Kim et al. Effect of rhBMP-2/DBM Gel in Alveolar Ridge Preservation, J Oral Maxillofac Surg 2014.



Subject information

- Age: 76 years old
- Sex: Male
- Symptoms: Infection from an old oral implant system

Prescribing the Symptom

Patient was suffering from chronic infection from an old oral implant system (25 years old). The old implant was removed in 2012, however no new implant system was suitable as there was no anchor points and maxilla was virtually no existent. Later 2012 patient underwent procedure to place demineralized powder bone (0.2 - 1.0mm) with collagen from local sources. However, all the material was reabsorbed within weeks. Early 2013 a similar procedure to place larger powder Bone particles (1.0-2.0mm) which was also reabsorbed.

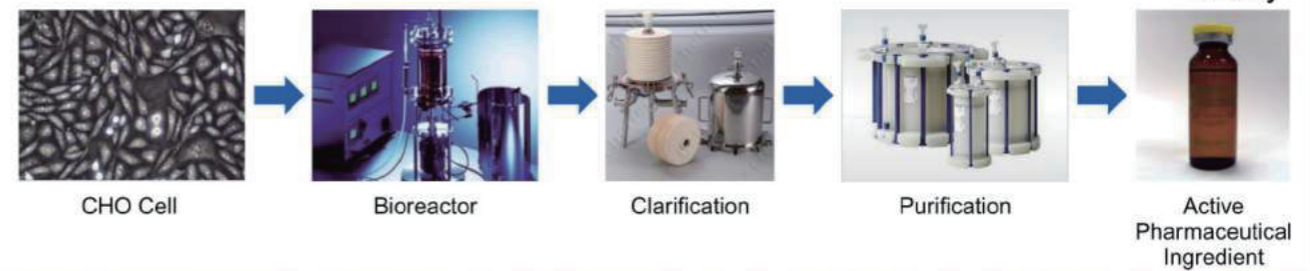
Clinic Method

On March 2014 Dr. Fernando G. Ortega treated patient Mr. Eleuterio V. Carranza age 76 in Hospital Century 2000 in the City of Guadalajara Mexico. The operation included a thin bone graft from the patient rib 2.5cm and 9cc of Rafugen BMP2 kept in place with membranes. After the operation it was noticed that the new Maxilla seems solid and later was corroborated by X-rays and CT scan. On May 2014 Dr. Ortega commenced standard oral implantology scheduled to complete on November 2014.

Clinical Results of rhBMP2

- Unlike the E.Coli derived competition products, animal (CHO) cell derived glycosylated BMP2 is structurally identical to human protein.
- Animal Cell derived BMP2 is most identical to Human BMP2 and vitality is 5~25 times more superior. (ED50 of CHO cell expressed BMP2 concentration is 40-200ng/ml while ED50 of E.Coli expressed BMP2 showed concentration of 0.3-1µg/ml)
- Consistently induce bone regeneration because of its similarity to Human BMP2 and its low catabolic rate.
- It is most identical to Human BMP2, there is no immune response in the body and is thereby safe.

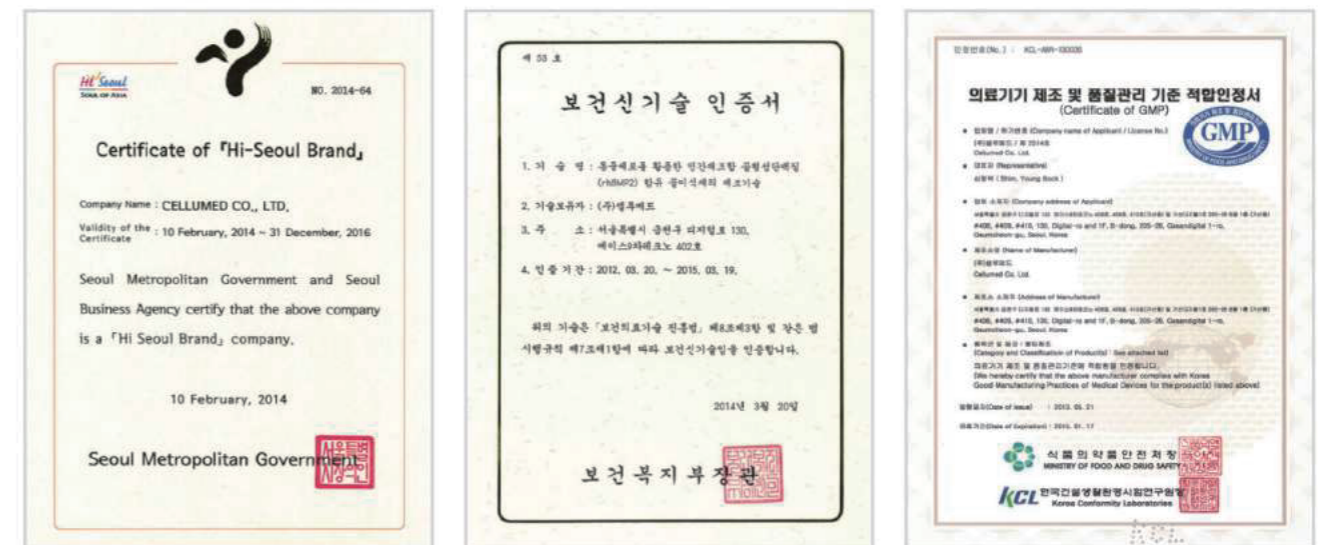
CHO Cell



Characteristics	E. coli	CHO Cell
Cell growth	7days	30days
Cost of growth medium	Low	High
Glycosylation	Non-Glycosylation (Low similarity)	Glycosylation (High similarity)
Stability	Low	High
Immune response	High	Very Low
Activity	-	5~25 times higher than E-coli
Global Trend	Under 5%	Over 95%
FDA Approved	No	Yes

* CHO Cell is recognized as more effective BMP2 production than E.coli by global market.

Clinical Results of rhBMP2



Hi Seoul Brand Certificate

NET (New Excellent Technology) Certificate

GMP Certificate