www.cellumed.co.kr

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.

Visit www.cellumed.co.kr to see the innovative products of Cellumed.

[Manufacturer]

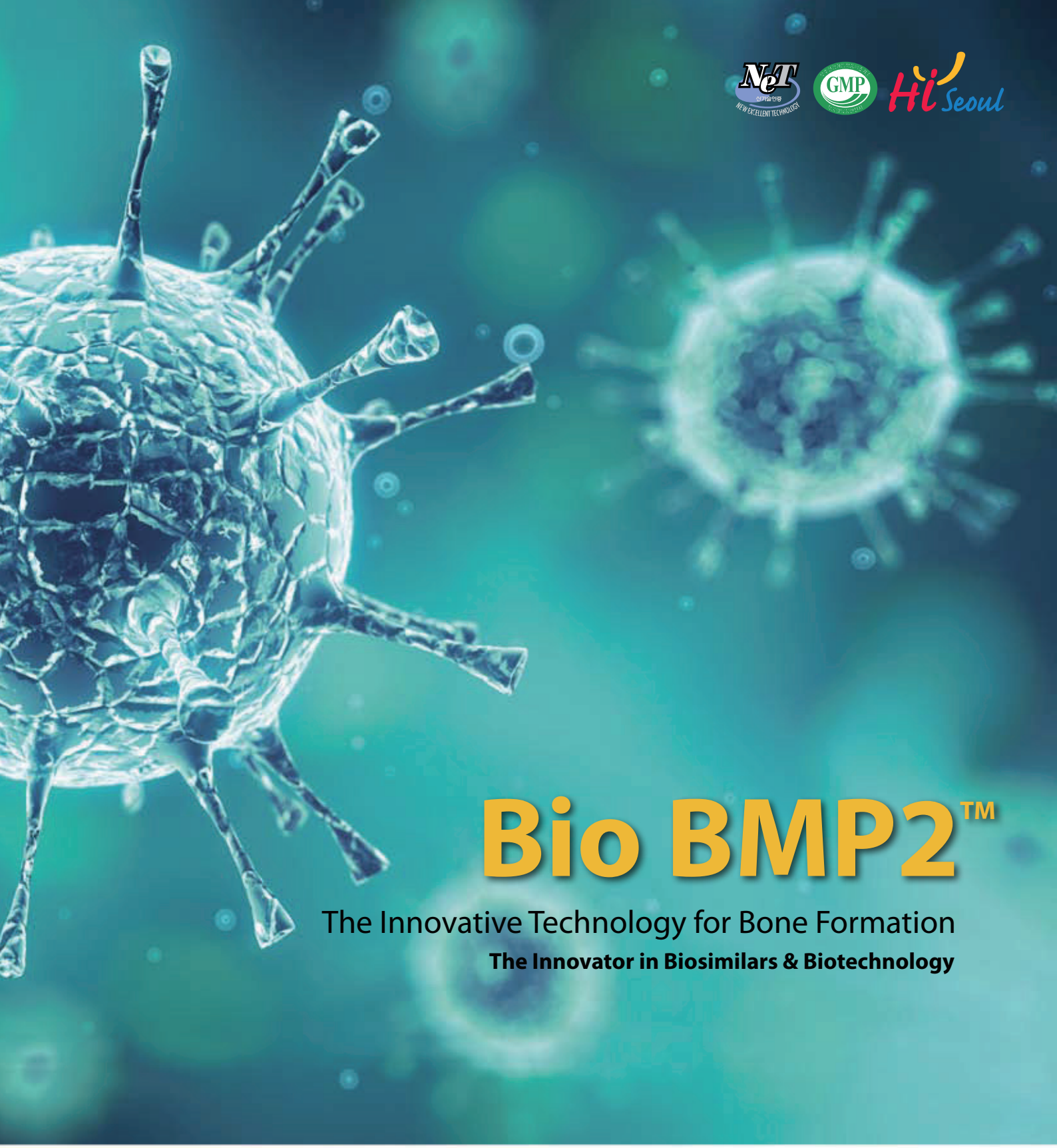
Cellumed Co., Ltd.

#408, #409, #410, 130, Digital-ro and 1F, B-dong, 205-28,
Gasandigital 1-ro, Geumcheon-gu, Seoul, Korea. (Gasan-dong)
TEL : +82-2-2104-0475
FAX : +82-2-2104-0473
E-mail : info@cellumed.co.kr
www.cellumed.co.kr

[Distributor]

STIK Co.,Ltd

#417,417, Guemgang Penterium IT Tower, 282, Hagui-ro,
Dongan-gu, Anyang-si, Gyeonggi-do, 14056, Rep of KOREA
TEL : +82-31-689-3061
FAX : +82-31-463-3061



Bio BMP2™

The Innovative Technology for Bone Formation

The Innovator in Biosimilars & Biotechnology

Cellumed

Bio 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 a 23 aa signal sequence, a 259 aa prosegment, and a 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.

ReLiabi Lity

- **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**

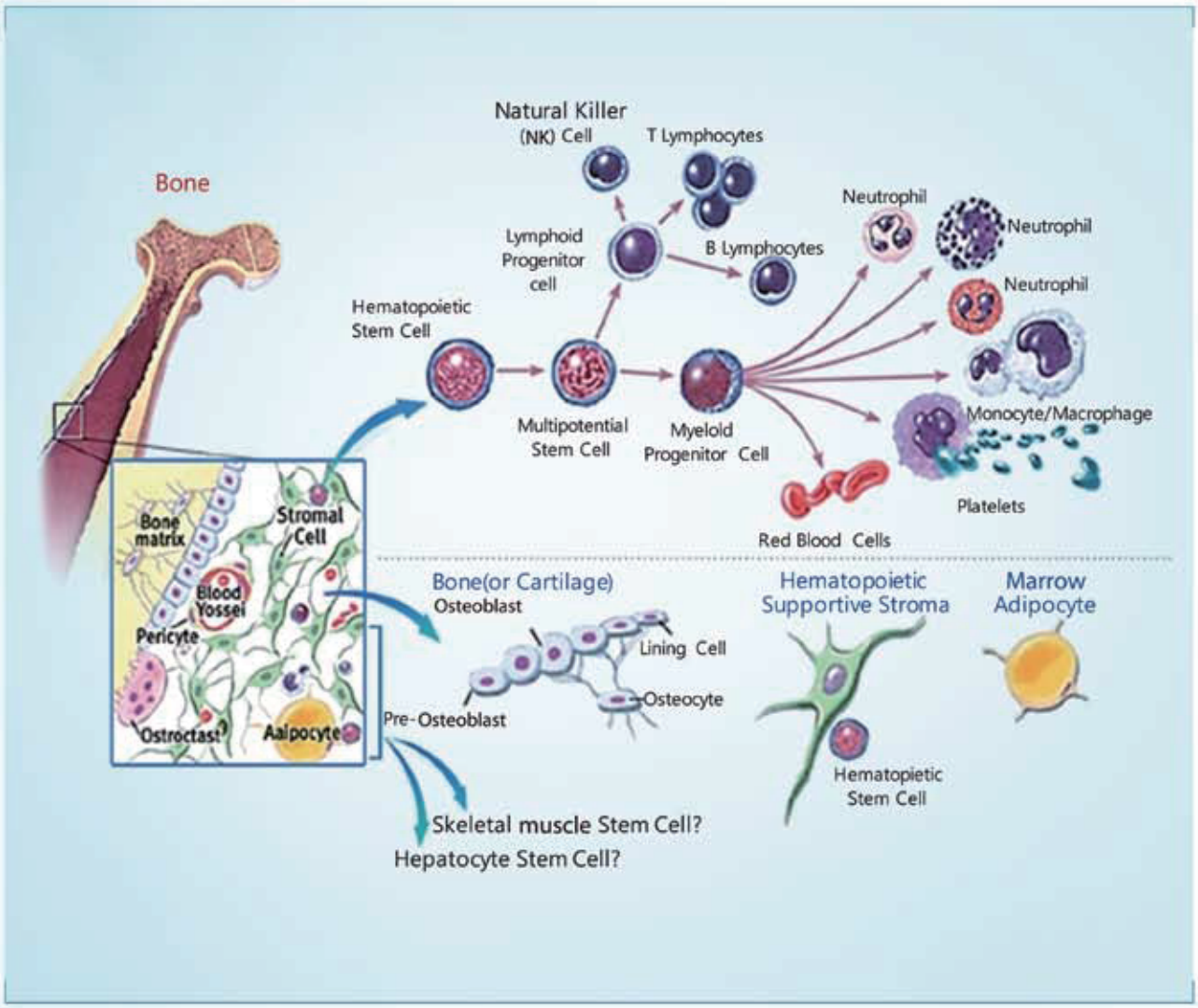
WORLD-LEADING ENTERPRISE
IN THE BIOTECH INDUSTRY

rhbMP2 Reagent

rhBMP2 is a type of recombinant bone morphogenetic protein and this rhBMP2 growth factor induces mesenchymal stem cell(MSC) into osteoblasts and chondrocytes.

Cellumed has succeeded in facilitating mass production system of CHO cell expressed rhBMP2 as the 2nd in the world.

The BMP2 reagent is being sold in domestic and overseas market.



Bio BMP2

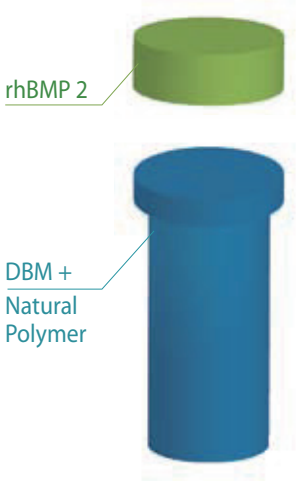
World-leading enterprise in the biotech industry

The Innovative Technology for Bone Formation

Cellumed is dedicated to developing human recombinant protein based on high-level of technology and extent knowledge of Cellumed R&D Center.

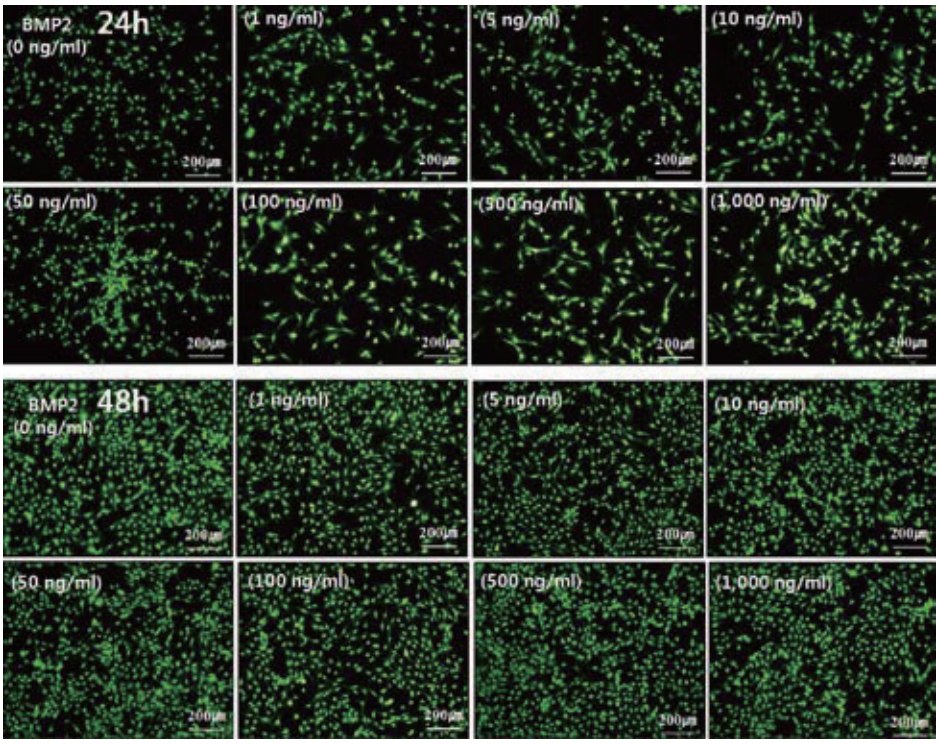
As one of human recombinant protein, rhBMP2 [Bone Morphogenetic Protein 2] plays key role in new bone formation and regeneration.

Bio BMP2 consists of recombinant human BMP2 (rhBMP2) and DBM [Demineralized Bone Matrix], Natural polymer. The human originated rhBMP2 is obtained through CHO [Chinese Hamster Ovary]-cell culture. Cellumed CHO cell derived rhBMP2 is the Asia 1st, world 2nd therapeutic protein.



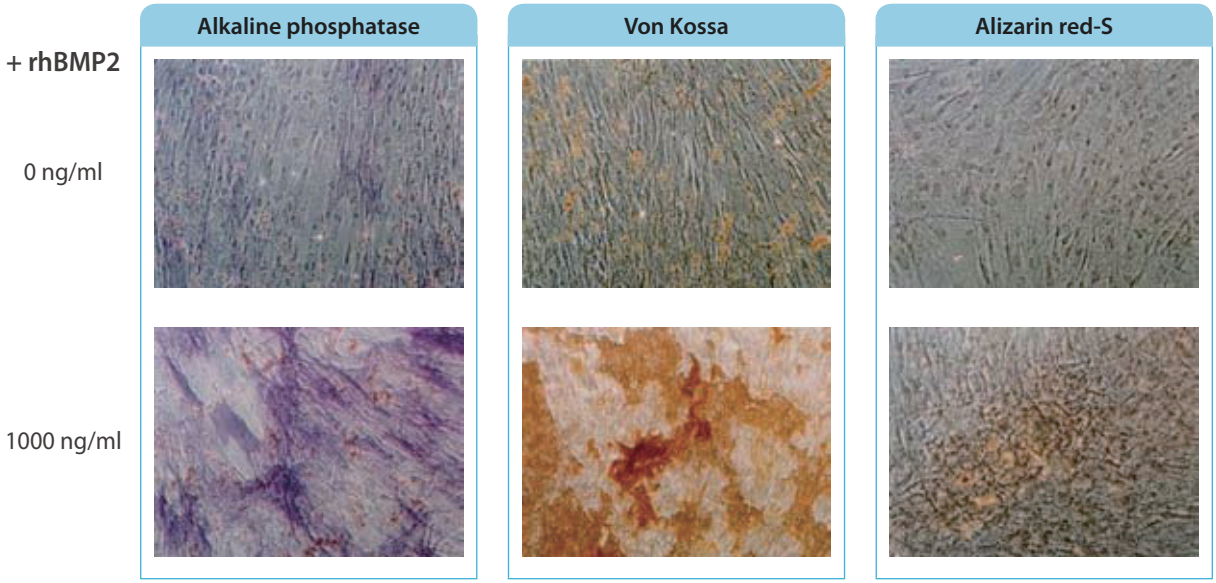
Cytotoxicity by rhBMP2 Dose Dependency

In vitro, live/dead fluorescence staining of rabbit bone marrow stromal cell in response to different concentrations of rhBMP 2 treatment at 24, 48h



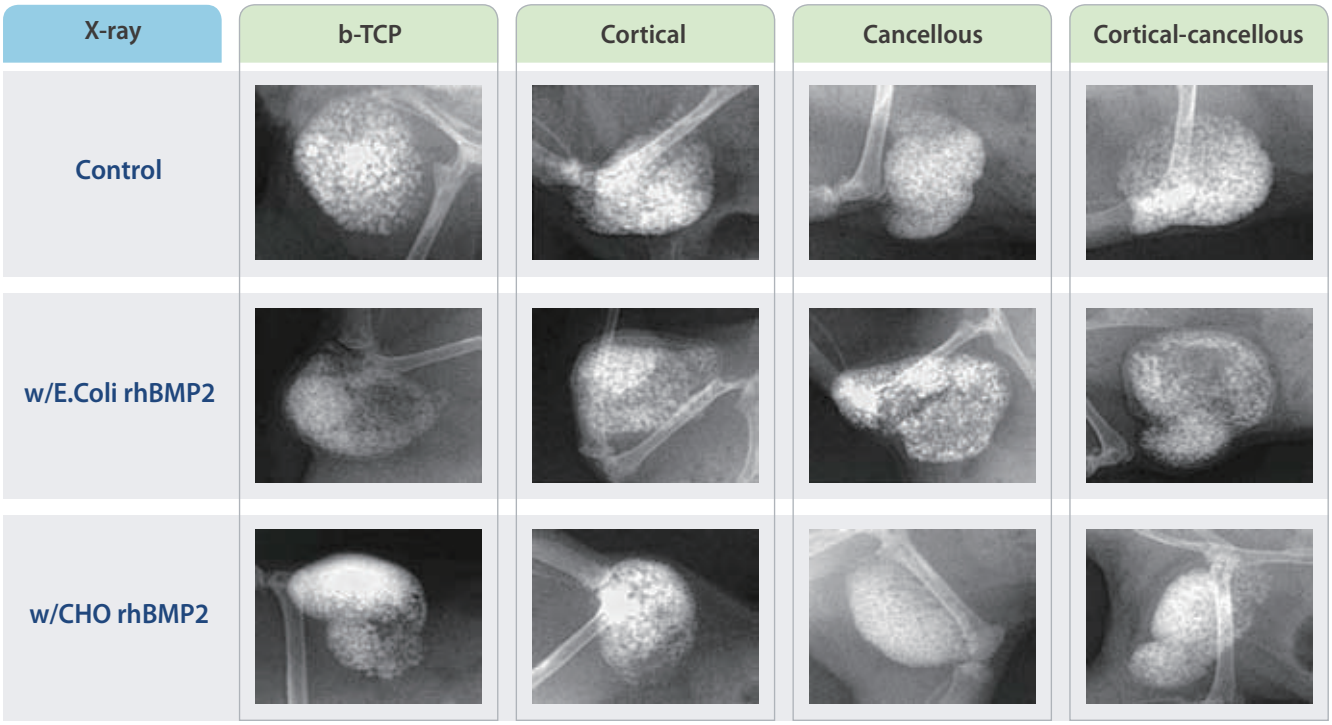
Efficacy of rhBMP2, Osteogenic Differentiation Test of Mesenchymal Stem Cell

Osteogenic marker of human MSC (x100)



Efficacy Implants-rhBMP2, Implantation Test of Nude Mouse Subcutaneous

6W- X-ray



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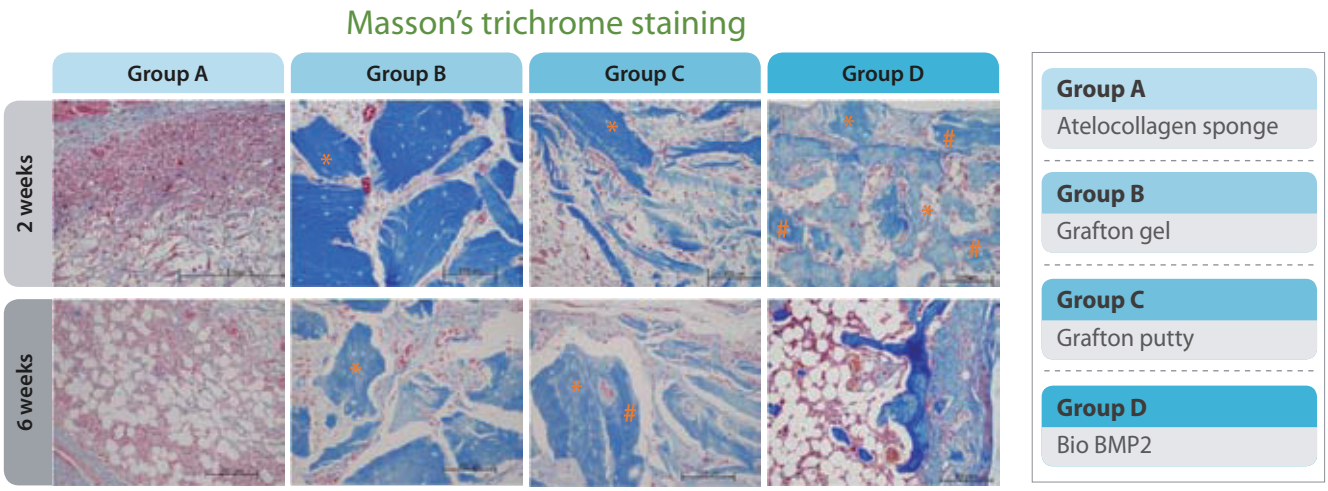
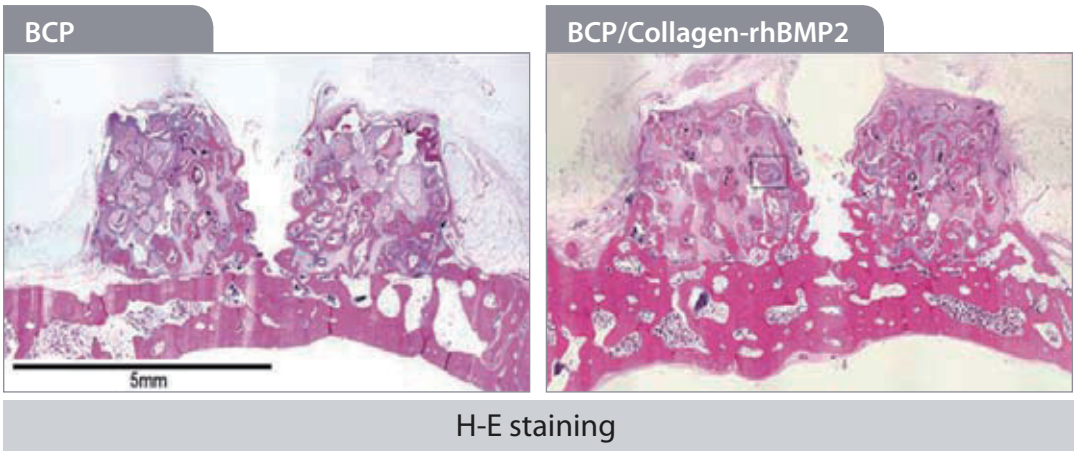
Comparison Study of Ectopic Bone Formation of Bio BMP2 and Other Products, Implantation Test of Rat Subcutaneous

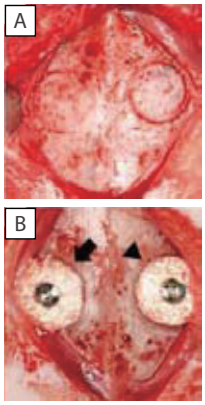


* : DBM / #: Newly synthesized ECM

Study group : Prof. Moon in Yonsei University Medical College

Efficacy of BCP/Collagen-rhBMP2 Complex, Implantation Test in Rabbit Calvarium Defect Model



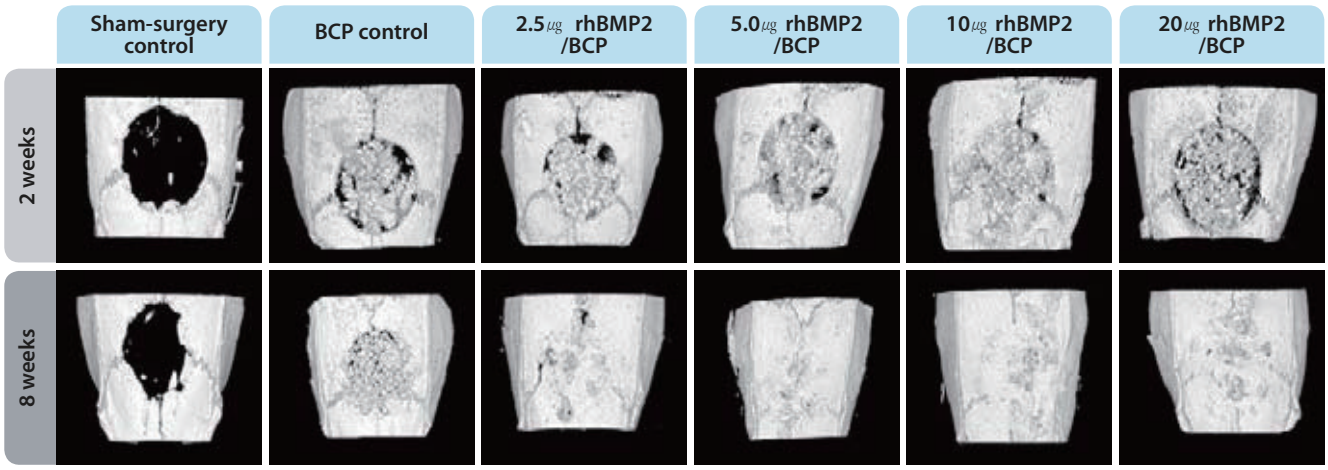


The test of implantation of biphasic calcium phosphate block loaded with rhBMP2 in vertical bone augmentation model of a rabbit calvarium : In the results of H-E staining, The amount of newly formed bone appeared to be considerably higher in groups treated with rhBMP2 than in non-treated groups.
(A: After bone augmentation, B: After implant fixation into augmented area)

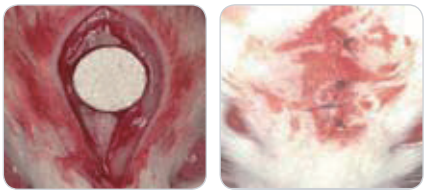
(Reference: JW Kim, IH Jeong, KI Lee, UW Jung, CS Kim, SH Choi, KS Cho, JH Yun. 2012. "Volumetric bone regenerative efficacy of biphasic calcium phosphate-collagen composite block loaded with rhBMP-2 in vertical bone augmentation model of a rabbit calvarium." J Biomed Mater Res Part A. 2012: Vol. 100A:, pp 304–3313.)

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

Activity test of Osteoinductivity

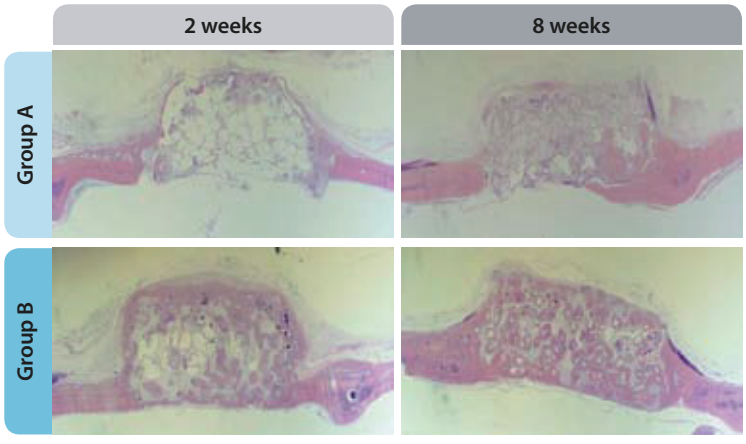


The test of osteoinductive activity of biphasic calcium phosphate with different rhBMP2 dose in rats : In the results of micro-CT analysis of defect sites, The percentages of new bone after 2 and 8 weeks of healing were significantly greater in the rhBMP2 treated groups (at all doses) than in the control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



(Reference: JW Jang, JH Yun, KI Lee, JW Jang, UW Jung, CS Kim, SH Choi, KS Cho. "Osteoinductive activity of biphasic calcium phosphate with different rhBMP-2 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



H-E staining

Group A	MBCP Block alone
Group B	MBCP Block + rhBMP2

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

Bio BMP2

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Efficacy of Bio BMP2, Implantation Test in Pig Ulna Defect Model

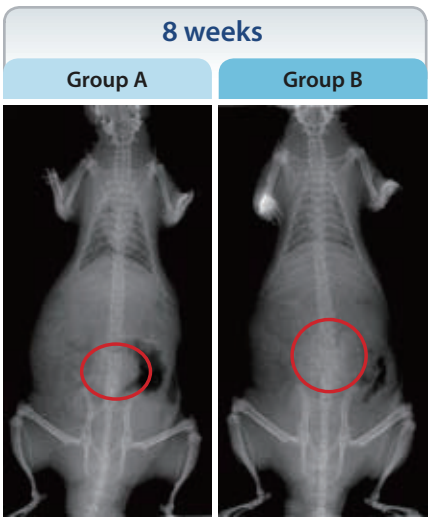
[Synergy effect of DBM and BMP]
The test of bone grafting material implantation in pig ulna defect model

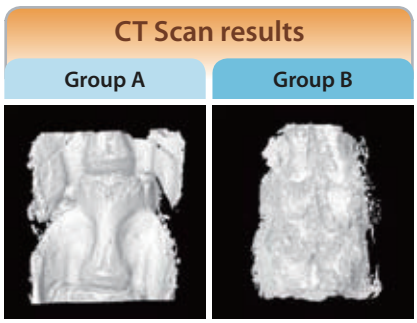
: In the results of X-ray analysis, the group of Bio BMP2 shows the higher bone formation ratio than the DBM gel group after 8 weeks.

Group A	Bio BMP2
Group B	DBM gel

(Reference: DS Kwon, JH Jung, TJ Lee, GW Lee, SH Shin, KH Moon. "Bone Formation Ability of DBM-BMP-2 Complex for Treatment of Bone Defect of Ulna in Pigs." Tissue Engineering and Regenerative Medicine, 2010; Vol. 7, No. 4, pp 432-442.)

Efficacy of Bio BMP2, Implantation Test in Rat Spinal Fusion Model





[Synergy effect of DBM and BMP]
The test of bone grafting material implantation in rat spinal fusion defect model

: In the results of X-ray and Micro-CT analysis, the group of Bio BMP2 shows the higher bone fusion ratio than the DBM gel group after 8 weeks.
This test model shows excellent synergy effect of DBM and BMP2

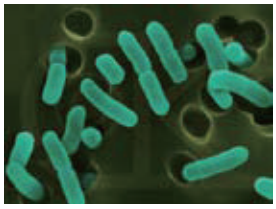
Group A	DBM gel
Group B	Bio BMP2

(Reference: KH Moon, IS Park, MO Lee, HC Park, CO Park, DK Hyun, HS Park, EY Kim, KW Kim, BH Choi, SR Park, DC Rim, SH Yoon. "A Comparative Study of the Osteogenic Potentials of rhBMP-2 in Collagen Sponge or Mixed with Porcine Collagen Gel in a Rat Spinal Fusion Model." Tissue Engineering and Regenerative Medicine, 2009; Vol. 6, No. 4~11, pp 653-658.)

Compare with CHO Cell and E-coli Product System

E-coli

7days


E-coli


Bioreactor


Centrifuge


Ultrasonic Lysis


Recovery insoluble protein

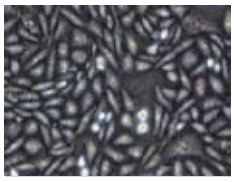

Solubilization


Refolding

Low Activity

CHO Cell

30days


CHO Cell


Bioreactor


Clarification


Purification


Active Pharmaceutical Ingredient

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

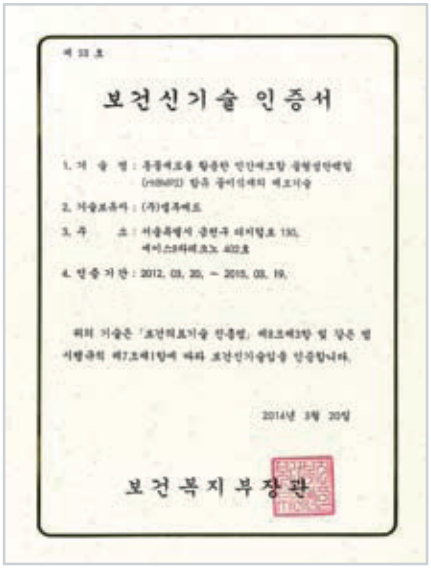
* CHO Cell is recognized as more effective BMP2 production than E.coli by global market.

Bio BMP2

World-leading enterprise in the biotech industry

Bio BMP2 Certificates

Hi Seoul Brand Certificate



NET(New Excellent Technology) Certificate

GMP Certificate

Benefits of Cellumed Bio BMP2

- 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.

FDA approved rhBMP2 is derived from CHO cells.

Specification

CODE	Volume
HHD030001	0.25cc
HHD030002	0.5cc
HHD030003	1.0cc
HHD030004	3.0cc
HHD030005	5.0cc

Application of BMP Family