Introducing a Peptide enhanced bone graft with a unique mechanism of action

Current Solutions in Spine Surgery,
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Faculty Disclosure

I am President and COO of Cerapedics.

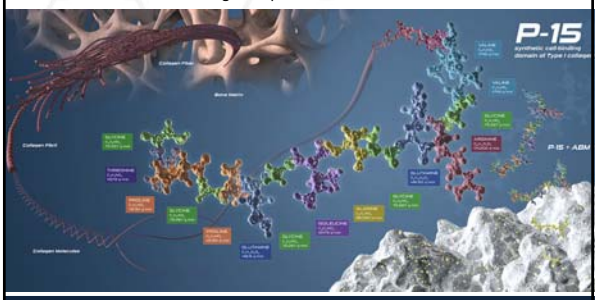
i-FACTOR peptide enhanced bone graft

A clinically proven, advanced **drug-device combination bone graft**

- PMA approved, backed by Level 1 Human clinical data
- Statistical superiority to autograft
- Improved safety & cost effectiveness vs. BMP's

Synthetic Collagen Fragment (P-15)

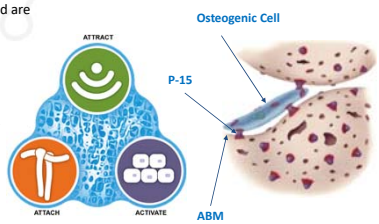
- Synthetic peptide of a 15 Amino Acid sequence from type 1 Collagen
- Functional domain of collagen responsible for the attachment of cells



i-FACTOR™ Peptide Enhanced Bone Graft

- Osteogenic cells in the surrounding tissues have an affinity for and are naturally ***attracted*** to P-15
- Osteogenic cells ***attached*** via cellular surface receptors to the P-15
- Osteogenic cells are naturally attachment ***activated***

Mechanism of Action:
"Attract - Attach - Activate"



P-15 has been shown to enhance bone formation by facilitating cellular attraction and attachment which activates natural signaling, creating a micro-environment conducive to new bone formation

Mechanism of Action

- i-FACTOR attracts osteogenic precursor cells by making an abundance of P-15 binding sites available for cellular adhesion
- Cell binding between P-15 integrins activates natural mechanical and chemical signalling pathways within the cell stimulating the release of specific growth factors, cytokines and Bone Morphogenic Proteins (BMPs)
- The cascade of events leads to cell proliferation and natural bone healing

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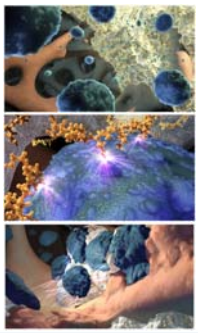
ATTACH

ACTIVATE



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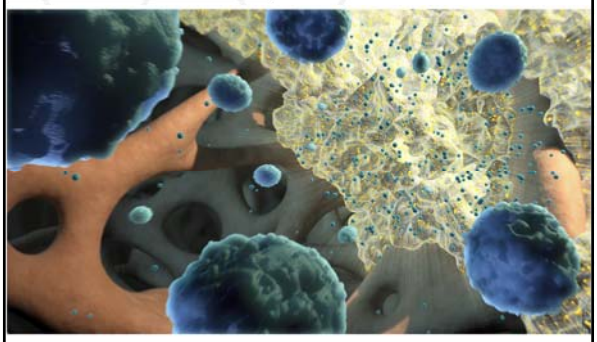
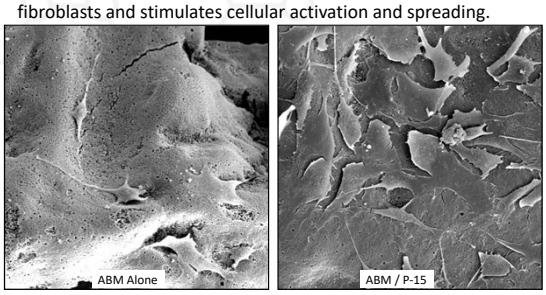


Enhances Cell Attraction & Attachment

P15 bound to ABM increases the number of bound human fibroblasts and stimulates cellular activation and spreading.



Qian JJ., Bhatnager RS., JBMR (1996) 31:545

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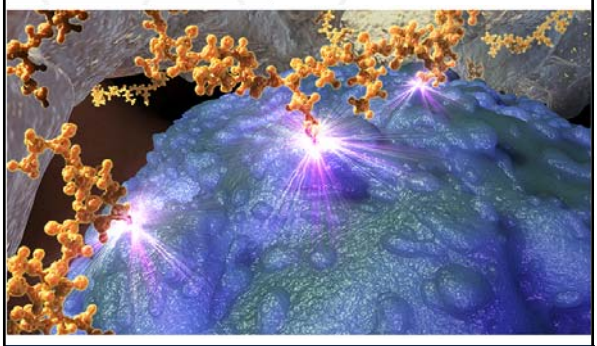
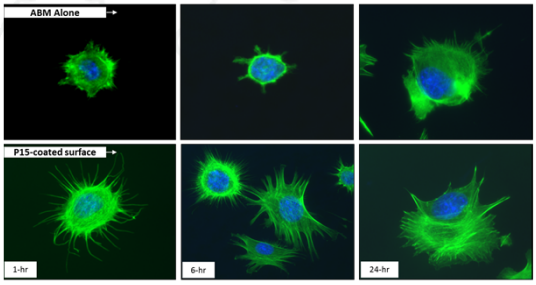


Proven to Enhance Cell Proliferation

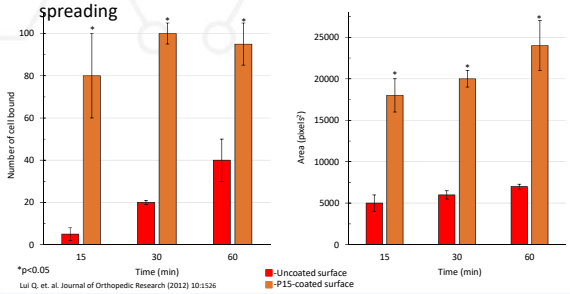
P15 bound to surface increases the number of bound pre-osteoblastic cells and stimulates cellular activity



Lui Q., Lemthongkul W., et. al. Journal of Orthopedic Research (2012) 10:1526

Cell Attachment & Activation

P15 bound to surface increases the number of bound pre-osteoblastic cells and stimulates cellular activation and spreading



*p<0.05

Lui Q, et. al. Journal of Orthopedic Research (2012) 10:1526

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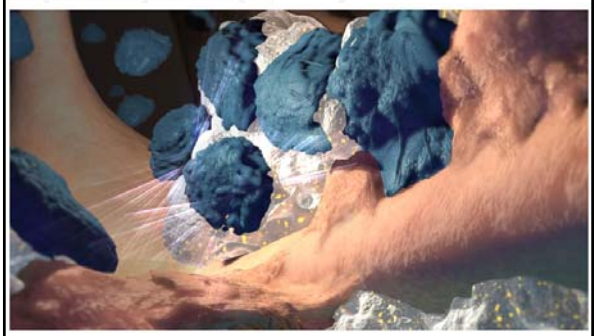
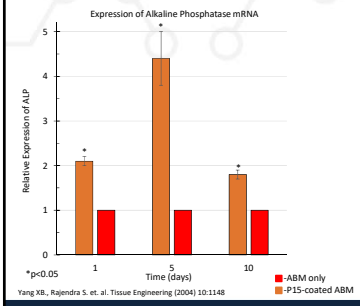
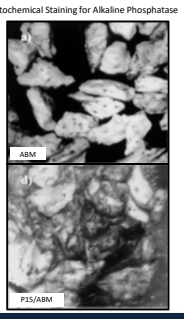


Cell Activation: Gene Expression

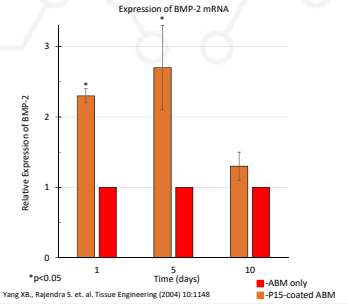
P15 bound to ABM stimulates upregulation of Alkaline Phosphatase at the gene expression and protein synthesis levels

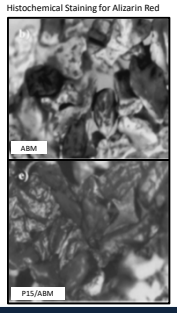




Cell Activation: Gene Expression

P15 bound to ABM stimulates upregulation of BMP-2 at the gene level and onset of calcification





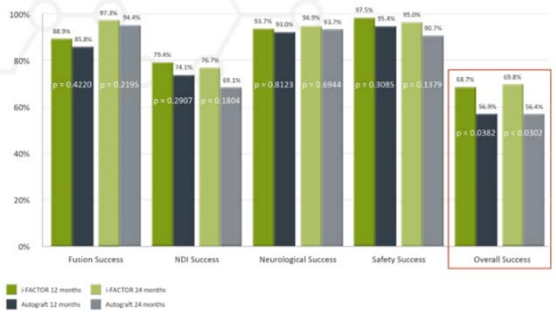
i-FACTOR Bone Graft: Clinical Track Record

- CE Mark / TGA approved since 2008
  - Putty & Strip form factors
  - No special handling requirements
  - Over 25,000 cases performed
  - Multiple studies / peer-reviewed (PLIF, ALIF)
- i-FACTOR Putty: U.S. PMA approval Nov'15

i-FACTOR Cervical Study - FDA IDE Trial

Procedure	Single-level Anterior Cervical Discectomy & Fusion (ACDF) Allograft ring with anterior plate
Patients	319 patients enrolled at 24 clinical sites in US and Canada
Study arms	1:1 randomization i-FACTOR P-15 Putty versus Autograft
Endpoints	**Primary**: Efficacy (Fusion, NDI, Neurological Outcomes) and Safety (Complications) at 12 months. Non-inferiority statistical plan. **Secondary**: Pain, Kyphosis, SF-36, Modified Odom's Criteria
Extended study Follow-Up	18, 24, 36, 48 and 60 months

Overall Success Outcomes

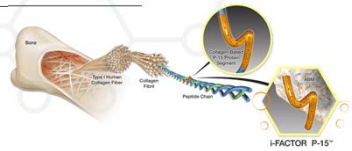


Overview

- In Level-I IDE study, **i-FACTOR** demonstrated superior to autograft in overall clinical success
- ***Accelerates & enhances*** bone growth
- Only second PMA approved drug-device combination product in $2.5B U.S. Spine market, and first & only bone graft approved for U.S. Cervical Spine
- > 40,000 procedures with multiple Peer-reviewed publications
- Very positive clinician response and rapid commercial uptake
- Preparing to initiate IDE trial in TLIF with next-generation version of the product

Thank You!

Mechanism of Action Evidence



- **Increases the number of cells available** – Bhatnagar *et al*, Design of Biomimetic Habitats for Tissue Engineering with P-15……., Tissue Engineering, Vol 5, Number 1, 1999
- **Leads to cell differentiation** – Qian & Bhatnagar, Enhanced Cell Attachment to anorganic bone……., J of Biomedical Materials Research, Vol. 31, 1996
- **Produces increases in BMP2 and ALP** – Yang, Bhatnagar, *et al.*, Biomimetic Collagen Scaffolds for Human Bone Cell Growth and Differentiation, Tissue Engineering, Vol. 10, 2004
- **Early bone laid down (& increased ALP, BMP2 and BMP7)** – Thorwarth, *et al*, Bioactivation of anorganic bone Matrix by P-15 peptide for promotion of early bone formation, Biomaterials, Vol. 26, 2005
- **Enhances cell viability (& increased cells on surface)** – Hanks and Atkinson, Comparison of cell viability on aBM with or without P-15 cell binding peptide, Biomaterials, Vol. 25, 2004