i-FACTOR BIOLOGIC BONE GRAFT

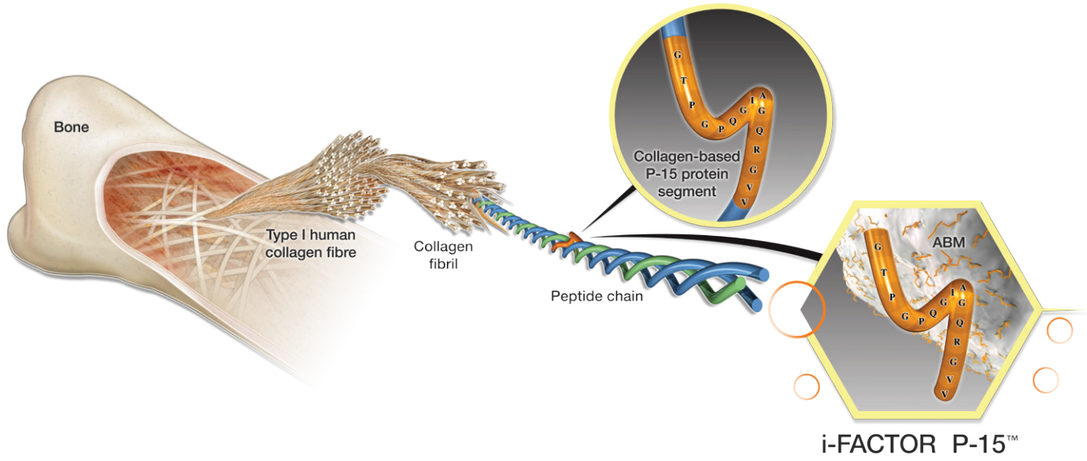
i-FACTOR Biologic Bone Graft is the only bone graft that combines a unique anorganic bone mineral (ABM) and small peptide (P-15) to act as an attachment factor for specific integrins on osteogenic precursor cells. This novel mechanism of action enhances the body's natural bone healing process, resulting in safe, predictable bone formation. P-15/ABM has been in human clinical use for more than 17 years in an estimated 500,000 patients worldwide.

i-FACTOR Putty is ideal for contained areas such as interbody fusion devices

i-FACTOR Flex FR can be cut or shaped to fit the particular dimensions of an osseous defect or interbody fusion device

SYNTHETIC REPLICATE OF P-15

i-FACTOR technology is based on the biological activity of a 15 amino acid peptide naturally found in Type I human collagen. Type I collagen is the primary organic component making up autograft bone. This protein segment (P-15) is responsible for the attachment and proliferation of osteogenic cells. These cells bind to the synthetic P-15 found in i-FACTOR the same way they would bind to Type I collagen. [8]



ANORGANIC BONE MINERAL (ABM)

One component of i-FACTOR Biologic Bone Graft is anorganic bone mineral. ABM particles are a natural form of hydroxyapatite [$Ca_{10}(PO_4)_6OH_2$] that contains crystal lattice defect sites.

ABM provides an ideal scaffold for bone growth because of its:

COMPOSITION
It is composed of natural calcium phosphate bone mineral.

RESORPTION
It is capable of effective cellular mediated resorption properties.[9, 10]

MANUFACTURABILITY
After processing, ABM shows a high affinity and capacity for binding the P-15 protein segment. [11]

SAFE, NATURAL, PREDICTABLE

- i-FACTOR Biologic Bone Graft offers surgeons the efficacy of autograft while avoiding the long-term morbidity issues associated with harvesting iliac bone graft [3, 4, 12]
- i-FACTOR Biologic Bone Graft actively triggers cellular attachment of osteogenic precursor cells, resulting in production of natural amounts of bone morphogenic proteins and growth factors. Unlike growth factor products, i-FACTOR only stimulates bone growth in the presence of bone forming cells [2, 5, 6, 7, 13]

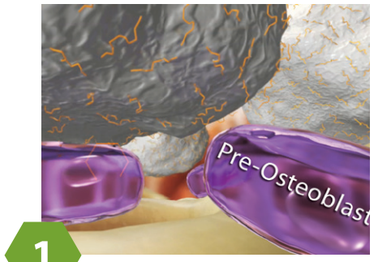
HOW i-FACTOR WORKS

MECHANISM OF ACTION

ATTRACT, ATTACH, ACTIVATE

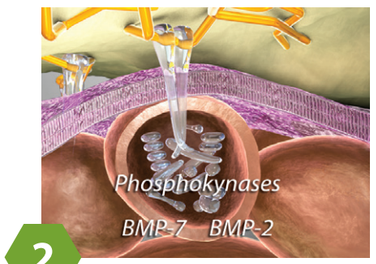
i-FACTOR increases the opportunity for cell binding in the fusion site by making an abundance of P-15 available to osteogenic cells. The ability of P-15 to enhance cell binding hastens the process of new bone formation and closely resembles the natural process of bone regeneration. Once cells attach, to the P-15 immobilised on the ABM substrate, the cascade of events leading to new bone formation commences.

ATTRACT



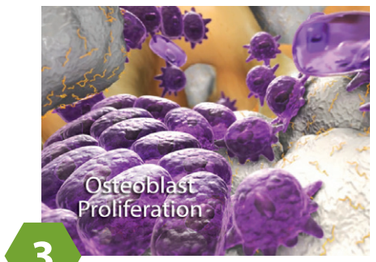
P-15 facilitates and expedites ingrowth of bone by promoting the immigration of reparative cells from the surrounding tissues. [7]

ATTACH



The high affinity between cells and P-15 supports the physiological mechanism in which cells bind to collagen via the domain simulated by P-15 and continue to organize the matrix by tractional forces. Cells attach to and migrate on Type I collagen by haptotactic mechanisms. [8, 14, 15]

ACTIVATE



P-15 enhances bone formation by facilitating cellular attachment with subsequent increase in cell binding, proliferation, and differentiation of cells increasing TGFb-1, BMP-2, and BMP-7 levels that positively influence all processes of new bone formation. [16]

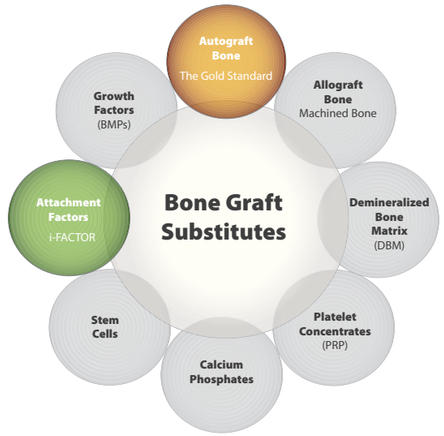
COMPARATIVE METHOD OF ACTION FOR ORTHOBIOLOGICS

AUTOGRAFT is the 'gold standard' of bone grafts because it provides all the necessary elements for bone growth: namely bone mineral, osteogenic precursor cells and biological signals. However, most autograft bone graft originates from the iliac crest, and has variable quality, is limited in availability and causes secondary surgical site morbidity. [12]

GROWTH FACTORS (BMPs) are osteoinductive products, manufactured through recombinant gene technology. These exogenous growth factors are not synthesised by the body's natural mechanism of action for osteogenesis. BMPs direct cells to become bone cells regardless of the cells' lineage, predisposition or early developmental stage. Due to their potent nature, BMPs can also come with complication rates and adverse events, as BMP is a soluble molecule free to migrate to local tissues. [17, 18]

DBM (DEMINERALISED BONE MATRIX) products are derived from human cadaver bone. DBMs are subjected to an acid process to extract mineral, leaving trace amounts of osteoinductive proteins and growth factors. The biologic aspects of DBMs are largely influenced by original donor properties, product processing and storage. The amount of BMPs in DBM products is low and varies between commercial products and even between lots from the same manufacturer. [19]

PLATELET CONCENTRATES (OR PLATELET-RICH PLASMA) use blood harvested from patients to bring cytokines and growth factors to the surgical site, similar to the blood clotting stage of bone repair. Platelet gel preparations vary in quality based upon patient factors and preparation techniques. Platelet concentrates have been shown not to enhance fusion rates, even when added to autograft bone. [20]



STEM CELL-BASED ALLOGRAFTS are marketed as an alternative to autograft and consist of mesenchymal stem cells with cancellous bone or DBM. After six years in the marketplace, no peer-reviewed, randomised, controlled trial exists to support the efficacy of stem cell bone grafts.

ALLOGRAFT BONE, CALCIUM PHOSPHATES and synthetic hydroxyapatites comprise the majority of products in the bone graft substitute market, acting as simple osteoconductive scaffolds that provide a surface that permits bone growth. These bone graft substitutes have little active influence on bone growth, often relying on bone marrow aspirate for biologic activity. [21]

SILICATED CALCIUM PHOSPHATE products have the osteoconductive properties of traditional calcium phosphate bone fillers. These products, marketed as osteostimulatory, rely on the silicate ions and the subsequent negative surface charge of the released Si ions to enhance cellular activity. However, the evidence of this being effective in the clinical setting is lacking at this time. [22]