

Growth Factor Research and Why Growth Factors Have Performed Poorly in Clinical Trials.

BMP-7 (bone morphogenic protein 7)

OP-1(BMP-7) in collagen carrier showed only one out of three sinus augmentations producing enough bone for implant placement after 6 months.

Histomorphometrical analysis of bone formed in human maxillary sinus floor elevations grafted with OP-1 device, demineralized bone matrix or autogenous bone. Comparison with non-grafted sites in a series of case reports.

Groeneveld EH, van den Bergh JP, Holzmann P, ten Bruggenkate CM, Tuinzing DB, Burger EH.

BMP-2 (bone morphogenic protein 2)

BMP-2 produced inferior results for sinus augmentation when compared to other graft materials. 21% of sinus lifts failed and implants could not be placed. Of the implants placed 18% failed within 6 months of loading.

Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. Triplett RG, Nevins M, Marx RE, Spagnoli DB, Oates TW, Moy PK, Boyne PJ

BMP-2 stimulates both osteoblasts and osteoclasts.

Enhanced osteoclastogenesis causes osteopenia in twisted gastrulation-deficient mice through increased BMP signaling. Sotillo Rodriguez JE, Mansky KC, Jensen ED, Carlson AE, Schwarz T, Pham L, MacKenzie B, Prasad H, Rohrer MD, Petryk A, Gopalakrishnan R

PDGF (platelet derived growth factor)

PDGF stimulates mesenchymal stem cell proliferation but does not stimulate mesenchymal stem cells toward osteogenic differentiation and also does not stimulate factors involved in osteogenesis. Platelet-derived growth factor receptor signaling is not involved in osteogenic differentiation of human mesenchymal stem cells. Kumar A, Salimath BP, Stark GB, Finkenzeller G.

PDGF when applied to beta tricalcium phosphate results in no clinical attachment gain over beta tricalcium phosphate alone and equal bone regeneration after 3 years.

Platelet Derived Growth Factor (rhPDGF-BB) Stimulates Bone Fill and Rate of Attachment Level Gain. Results of a Large, Multicenter Randomized Controlled Trial Nevins m, Giannobile WV, McGuire MK, Kao RT, Mellonig JT, Hinrichs JE, McAllister BS, Murphy KS, McClain PK, Nevins ML, Paquette DW, Han TJ, Reddy MS, Lavin PT, Genco RJ, Lynch SE.

Why growth factors perform poorly in clinical trials.

1. Growth factor half-life in intercellular fluid is between seconds to minutes depending on the growth factor.
2. Cell membrane receptors for growth factors are limited, therefore, applying additional growth factor molecules will not increase cell response.
3. Creating a tissue requires a very large number of molecules to be present at a specific time, concentration and sequence to create normal tissue. A single growth factor is a very minor part of a regenerating tissue.
4. Due to immune reaction to the foreign growth factor many growth factors can only be used one time in a patient and cannot be used if pregnant or will become pregnant within one year.