Bone Morphogenetic Proteins—An Update

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ABSTRACT

Bone Morphogenetic Proteins (BMPs) are a group of growth factors and cytokines known for their ability to induce the formation of bone and cartilage. Originally seven such proteins were discovered. Of these six (BMP2 to BMP7) belong to TGF-B superfamily of proteins. BMP1 is a metalloprotease. Since then thirteen more BMPs have been discovered bringing the total to twenty. Marshall Urist proposed the name ‘BONE MORPHOGENETIC PROTEIN’ in the scientific literature in 1971. BMPs interact with specific receptors on the cell surface referred to as bone morphogenetic protein receptors (BMPRs). BMPs are now produced using recombinant DNA technology. BMP is the most promising osteoinductive protein for bone induction and regeneration. Recombinant human BMP (rhBMP) stimulates osteoblast differentiation in various cells in vitro and induces ectopic bone formation in vivo. These formulations have found applications in many disciplines of medicine and dentistry. Orthopaedic and Oral surgery have benefitted greatly from commercially available BMP formulations in the last few years.

Key words: Bone Morphogenetic Proteins, Growth factors, Osteoinduction, Reconstruction.

INTRODUCTION

Bone Morphogenetic Proteins (BMPs) are a group of growth factors and cytokines which induces formation of bone and cartilage. Growth factor is a naturally occurring protein or steroid hormone capable of stimulating cellular growth, cellular differentiation and proliferation. They act as signaling molecules between cells that binds to specific receptors on the target cells. They promote cell differentiation and maturation which varies between growth factors. For example, Bone morphogenetic proteins stimulate bone cell differentiation while fibroblast growth factors and vascular endothelial growth factors stimulate blood vessel differentiation. Recombinant human BMPs (rhBMPs) are widely used in several tissue-engineering products that might serve for the complete regeneration of bone or cartilage.

Discovery of BMP

Senn, a surgeon from Chicago, described the utility of antiseptic decalcified bone implants in the treatment of osteomyelitis and certain bone deformities. Pierre Lacroix proposed, that in bone, osteogenin, that might initiate bone growth. Marshall R. Urist made the key discovery that demineralised lyophilised segments of bone induced new bone formation. Also proposed the name “Bone Morphogenetic Protein”. Bone induction is a multistep cascade. The key steps are chemotaxis, mitosis and differentiation. Hari Reddi indicated morphogens were present in bone matrix, upon which a systematic study was undertaken to isolate and purify putative bone morphogenetic proteins. Reddi laboratory brought out the final purification of bone morphogenetic proteins. John Wozney & colleagues at Genetics Institute enabled the cloning of BMPs. Originally seven such proteins were discovered BMP1 is a metalloprotease. BMP2 to BMP7 belong to Transforming growth factor beta superfamily of proteins. Thirteen more BMP’s have also been added to this group.
Bone Morphogenetic Proteins help in differentiation of cells and also in matrix production and vascularisation.

**DISCUSSION**

**Functions and applications of BMPs**

Bone Morphogenetic Proteins interact with specific receptors on the cell surfaces known as BMP receptors (BMPRs). The signal transduction through BMPRs result in mobilisation of members of SMAD family of Proteins. The signaling pathways involving BMPs, BMPRs and SMADs are important in the development of heart, CNS and cartilage, as well as post-natal bone development. They play an important role during embryonic development on the embryonic patterning and early skeletal formation. BMP4 and its inhibitors noggin and...
Bone Morphogenetic proteins have various applications in Oral and Maxillofacial Surgery. It has been used to reconstruct complete or partially resected mandible. It is used in facial clefts, cleft palate cases, alveolar ridge augmentation, cartilage repair in TMJ and in oral implants. Bone morphogenetic proteins produce osteo induction which helps in inducing osteoblasts to produce native bone or cartilage.

Since the evolution of reconstruction, maxillofacial surgeons could bring back the form and function of the bone resected due to pathologies...
Various forms of reconstruction has since then been practised. From simple reconstruction plates to non vascularised bone grafts to vascularised free flaps, maxillofacial surgeons had options to choose which depended on their skills and the conditions warranted during those surgeries. Post surgical resection, bone resorption is inevitable which happens with varying degrees except in case of vascularised free flaps. When it comes to free flaps, the technique sensitivity and surgeon's skill play a key role. In such cases, preventing resorption and inducing bone formation was an able substitute to the technique sensitive free flaps. Bone morphogenetic proteins which are a group of growth factors help in osteoinduction that is inducing bone producing osteoblasts to deposit bone at the native site. BMPs help in bone induction, differentiation and regeneration which can either form bone or cartilage. BMP2 to BMP7 belongs to Transforming growth factor beta superfamily of proteins. Thus BMPs prove to be a boon for reconstruction.

**CONCLUSION**

Resection of diseased bone and replacement of lost structure to bring back form and function has been practised for many years since the evolution of reconstruction. Formation of new bone and cartilage was not possible with the preliminary form of reconstruction. Nonvascularised bone grafts undergo resorption at the recipient site and replacement leading to decreased amount of bone deposition. Vascularised free flaps are technique sensitive and require good surgical acumen which also has its own complications such as flap necrosis. In order to bring back the native bone with the same form and function, osteoinduction, differentiation, maturation and regeneration of the recipient bone by Bone morphogenetic proteins play a vital role in reconstruction and are time-tested till date.

**REFERENCES**


