Investigating cell communication between bone modulating cells via gap junction connexin proteins.

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Bone remodelling is a coordinated dynamic process between bone resorbing and bone formation by osteoclasts and osteoblasts respectively. The process is regulated by the recruitment, proliferation and differentiation of these bone modulating cells with accompanying circulating growth factors, cytokines, hormones and cell signals.

Gap junctions are membrane forming channels that enable the passage of ions and signalling molecules of appropriate size between adjacent cells. The gap junction, composed of two hemichannels, each comprising six connexions, mediates in part, intercellular communication. The predominant connexion in osteoblasts and osteocytes is connexin43 (Cx43) which regulates osteoblast, osteocyte and osteoclast differentiation and function. Studies have shown the interplay between CX43 and other connexions such as CX 45, which play a role in restoring intercellular communication in CX43-deficient mice[1]. In another study, osteocytes lacking Cx43 were stimulated to respond to mechanical stimulation and can cause bone formation by a mechanism that might involve accumulation of β-catenin[2]. Hence cell communication appears to play an important role in bone mineralisation and may be used to prevent the onset of bone disorders.

This study aims to formulate an in-situ gel containing anti-sense connexin to explore the role of connexion 43 and 45 on bone cell recruitment, differentiation and bone formation in the presence of loading. This understanding will aid the development of novel therapeutic targets for disorders of bone metabolism.

References

1 .Chaible LM, et al, (2011), Toxicol Pathology, 9(7):1046-55.
2. Bivi N, et al, (2013) R. J Orthop Research, 31(7): 1075–1081.