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Targeting Neuropeptides to Bone Fractures for Accelerated Healing

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ABSTRACT

In patients over the age of 65 especially, bone fractures represent a significant disease burden. Non-invasive drug therapies are not available for bone fractures which represents a problem for this population. Vasoactive intestinal peptide (VIP) and Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP), two neuromodulator peptides in the glucagon superfamily, have demonstrated positive regulation of osteoblast proliferation and activity. Using acidic oligopeptides, we have developed ligands that target to and accumulate at fracture sites. These targeting ligands can be synthesized in sequence with bone anabolic peptides to minimize off target effects and increase potency at the fracture site to create safer and more efficacious therapeutic molecules. The conjugation of PACAP and VIP to acidic oligopeptide targeting ligands results in compounds that demonstrate significant improvements in regeneration of bone at fracture site *in vivo* in terms of strength and mineralization of fracture callus.

KEYWORDS

Neuropeptides, Pituitary Adenylate Cyclase-Activating Polypeptide, PACAP, Vasoactive intestinal peptide, VIP, bone, anabolic, targeted therapeutics, bone fracture