Commentary

iMedPub Journals
www.imedpub.com

Medical Case Reports
ISSN 2471-8041

2023
Vol.9 No.2:277

Extracellular Vesicles are Biomimetically Blended and Enhanced for Bone Healing

Qian Zhang*

Department of Orthopedics, Chongqing Medical University Chongqing, PR China

Corresponding author: Qian Zhang, Department of Orthopedics, Chongqing Medical University Chongqing, PR China, E-mail: Zhang_q@stonybrook.edu

Received date: January 27, 2023, Manuscript No. IPMCRS-23-16565; **Editor assigned date:** January 30, 2023, PreQC No. IPMCRS -22-16565 (PQ); **Reviewed date:** February 10, 2023, QC No. IPMCRS-22-16565; **Revised date:** February 20, 2023, Manuscript No. IPMCRS-22-16565 (R); **Published date:** February 27, 2023, DOI: 10.36648/2471-8041.9.2.279

Citation: Zhang Q (2023) Extracellular Vesicles are Biomimetically Blended and Enhanced for Bone Healing. Med Case Rep Vol.9 No.2:279.

Introduction

Craniofacial bone is a complex arrangement of numerous skeletons that mainly consists of the facial and calvaria bones. Bone formation in the craniofacial bone is either by intramembranous or endochondral ossification. Unlike the appendicular or other axial bones, the majority of the craniofacial bones is formed *via* intramembranous ossification, where the mesenchymal stem cells condense and differentiate to form osteoid and then mineralized bone. In contrast, a few bones are produced similar to the long bones through endochondral ossification (for example, cranial base). Several factors have been demonstrated which control the overall craniofacial bone development, and metabolism. The nervous system has been recognized as one of the regulators of bone development, metabolism, homeostasis, and remodeling. Two types of peripheral nervous systems are detected in the bone, the sensory and autonomic nervous systems (further classified as sympathetic and parasympathetic nerves).

Craniofacial Bone Development

In developing calvaria, peripherin and CGRP-positive nerve fibers have been identified traversing periosteum, endosteum, sutures, and the trabecular bone in an unorganized manner. Contrary to the pups, the trabecular bone of the adult calvaria is devoid of sensory nerve fibers, whereas the sutures are appeared to be densely innervated and serve the main route for the nerve fibers between the dura and periosteum. Moreover, sensory nerve fibers are detected in the temporomandibular joint. Sympathetic innervation has also been noticed in the developing calvaria that originates from the dura but is not found in the calvaria sagittal, coronal, and metopic sutures. Inconsistent with those studies, sensory nerve fibers, positive for CGRP and SP, and sympathetic nerve fibers positive for VIP, NPY, and dopamine beta-hydroxylase have also been observed in adult's calvarial and mandibular periosteum.

Trauma, infection, tumors, or inherent genetic disorders may cause craniofacial bone defects, which are a major challenge in clinical practices. There is evidence that nerve fibers target the bone and play a critical role in bone repair and regeneration. Nerve fiber sprouting has been visualized during the regeneration of calvarial bone defects. The majority of those nerve fibers are sensory nerve fibers expanding from adjacent sutures, periosteum, and endosteum. However, a small portion represents tyrosine hydroxylase-positive sympathetic nerve fibers. Experimental studies have also provided that loss of the sensory nerves results in a decrease of the new bone quality during the mandibular Distraction Osteogenesis (DO). In contrast, sympathetic innervation loss improves mandibular DO and new bone formation, which implies that the sympathetic nervous system might negatively regulate the process of DO. An independent study has also shown that intact innervation of bone is required for the normal fracture healing process. In vitro studies have demonstrated that Dorsal Root Ganglion (DRG) of sensory neurons maintains the stemness of Bone Marrow Mesenchymal Stem Cells (BMSCs) by enhancing autophagy through the AMPK/mTOR pathway in the coculture system. Moreover, the direct interaction of DRG neurons with BMSCs also promotes the proliferation and osteoblast differentiation potential of BMSCs. The osteogenic effect of DRG neurons on BMSCs is mediated by activating the canonical/β-catenin Wnt signaling pathway.

Bone Metabolism

The evidence mentioned above confirms that the peripheral nervous system plays a crucial role in craniofacial bone development and regeneration processes. Notably, those nerves interact with the bone through neuron-derived factors and which is mediated by a receptor-based mechanism since bone cells produce receptors for various signaling molecules of neuronal origin. Therefore, this review explicitly addresses neuron-derived factor SEMA3A, SP, CGRP, NPY, VIP, SN, and SPX role in craniofacial bone metabolism, remodeling and regeneration. SEMA3A is a membrane-associated and secreted protein that belongs to the semaphorin family. It is ubiquitously expressed in various tissues, including the brain, heart, lungs, and bone. Studies have demonstrated that SEMA3A acts via its receptor, Neuropilin-1(NP1) and plexin A complex. It possesses chemorepellent activity, inhibiting axonal outgrowth or chemoattractant activity and stimulating the growth of apical dendrites. SEMA3A has also been shown to regulate neurogenesis, angiogenesis, vascularization, and the immune system. Furthermore, it has been involved in bone formation, growth, remodeling, and regeneration.

The expression of Sema3a in bone increases during osteoblast differentiation, whereas it decreases during osteoclast

differentiation. SEMA3A has been shown to stimulate osteoblast differentiation through the canonical Wnt/β-catenin signaling pathway. In addition, overexpression of Sema3a promotes proliferation and osteogenic differentiation of alveolar mesenchymal stem cells. It has also been revealed that SEMA3A induces osteocytes maturation via increasing dendrite elongation. However, SEMA3A treatment inhibits receptor activator of nuclear factor-kB ligand (RANKL)-induced osteoclast differentiation by inhibiting the Immunoreceptor Tyrosine-Based Activation Motif (ITAM) and Ras homolog family member A (RhoA) signaling pathways. In vivo studies have shown that osteoblast-specific Sema3a deficient mice display normal bone formation and bone mass. In contrast, neuron-specific Sema3a deficient mice have a low bone mass similar to Sema3a global knockout mice due to decreased bone formation without overt bone resorption changes. Based on these results, it is suggested that neuronally-derived SEMA3A influences bone formation and bone metabolism. Moreover, it has been demonstrated that the local and systemic administration of SEMA3A to bone fracture increases bone formation in ovariectomized mice. In craniofacial studies, a decreased expression of SEMA3A has been observed as the apical periodontitis progresses by inhibiting osteoblasts and activating osteoclasts. Interestingly, local administration of SEMA3A prevents bone resorption by inhibiting osteoclasts and increasing new bone formation by inducing osteoblasts in a rat calvarial bone defect model. Similarly, it has also been shown to promote calvarial bone regeneration in diabetic rats. These results imply SEMA3A implication in osteoprotective activity and suggest that SEMA3A may be used as a therapeutic agent for bone defects. The overall effect of SEMA3A in bone metabolism is illustrated. However, the detailed mechanism of action SEMA3A in craniofacial regeneration remains elusive.