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Journal of Bone Research

Short Communication

Bone Homeostasis and the Stemness of Bone Marrow Mesenchymal Stem Cells

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DESCRIPTION

Bone is a dynamic organ that gives body structures rigidity, shape, support, and mobility. It constantly remodels and models itself throughout life, transforming in both shape and structure. As illustrated by the changes in bone length and diameter, bone modeling takes place from birth through adulthood and is responsible for accumulating mass and modifying the skeletal structure. Bone remodeling, which directly links bone formation and resorption, functions as a replacement for old tissues by new bones, preserving the strength and equilibrium of the mineral composition. The primary cells involved in bone restructuring are osteoblasts for bone production and osteoclasts for bone resorption; however, osteocytes derived from osteoprogenitors are also essential in this biological process.

According to recent research, the bone is an endocrine organ with an active metabolism, and cell bioenergetics is critical for controlling secondary metabolism. Since coordinated signaling networks help organisms transition between anabolic and catabolic stages effectively, bone cells can survive and expand in situations with varying nutrition sources. Almost all exogenous fuel absorption is necessary for biosynthesis, which can be transformed inside the body into Adenosine 5′-Triphosphate (ATP) hydrolysis to operate all cellular operations [1-3].

Glucose, free fatty acids, and amino acids are efficient substrates for oxidative phosphorylation, which produces ATP in both the cytoplasm and mitochondria. In stages of proliferation, differentiation, and apoptosis, when signal transduction molecules serve as controls for fuel selection, storage, and then use, their consumption and catabolism are automatically changed to match the specific energy demands [4]. Additionally, extrinsic factors like glucocorticoids affect the biological function of bone cells as a result of the fuel metabolism alteration.

Glutamine metabolism

Glutamine is a Nonessential Amino Acid (NEAA) that is primarily produced by the enzyme Glutamine Synthetase (GS) using glutamate and ammonia (NH_3) as sources. Its chemical formula is carbon (41.09%), hydrogen (6.90%), oxygen (32.84%), and nitrogen (19.17%). It makes up around 20% of the total free amino acid pool in blood and 40% to 60% of the total amino acid pool in some tissues, making it the most abundant and adaptable amino acid in the body. Glutaminase (GLS) hydrolyzes glutamine to produce ammonium ions (NH_4) and glutamate, which are then transaminated or deaminated to -Ketoglutarate (-KG) [5].

Glutamine metabolism in BMSCs

Osteoblasts, adipocytes, and chondrocytes can all be transformed into BMSCs, often referred to as nonhemopoietic multipotent mesenchymal cells, to control bone homeostasis. Recent years have seen a continual stream of reports on the energy metabolisms of MSCs, including the metabolism of fatty acids, glucose, and glutamine. Since the early 1960s, it has been recognized that the main nutrient for osteoblasts is glucose, which is a significant source of energy and carbon for mammalian cells. Aerobic glycolysis in osteoblasts may be related to citrate secretion, which is crucial for the synthesis of apatite nanocrystals in bone, instead of operating as an energy source.

Glutamine metabolism in osteoblasts

Osteoblasts, known as the primary bone-forming cells, are in charge of producing the major portion of both collagen-I-rich bone matrix and the ectoenzymes that regulate matrix mineralization. They adhere to predetermined schedules and express particular genes while being guided by prosteogenic pathways. WNT signaling is essential for BMSCs to commit to becoming osteo or chondroprogenitor cells, particularly in the first stages of osteoblast development. It is hypothesised that by enhancing aerobic glycolysis, glutamine catabolism, and fatty acid oxidation in osteoblast lineage cells, WNT transmission directly reprograms cellular metabolism.

Glutamine metabolism in chondrocytes

An essential step during endochondral ossification, in which BMSCs first give rise to immature chondrocytes and cartilage primordia, is the commitment of BMSCs to the chondrogenic lineage. In order to stimulate incremental changes in

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Received: 03-Oct-2022; Manuscript No. BMRJ-22-20231; **Editor assigned:** 05-Oct-2022; PreQC. No. BMRJ-22-20231 (PQ); **Reviewed:** 19-Oct-2022; QC. No. BMRJ-22-20231; **Revised:** 26-Oct-2022; Manuscript No. BMRJ-22-20231 (R); **Published:** 03-Nov-2022, DOI: 10.35248/2572-4916.22.10.192.

Citation: Perng GC (2022) Bone Homeostasis and the Stemness of Bone Marrow Mesenchymal Stem Cells. J Bone Res. 10:192.

endochondral ossification and bone formation, growth factors and elements of the extracellular matrix, including collagen, proteoglycans, Glycosaminoglycans (GAGs), and proteases, interact together to regulate chondrocytes. Glutamine was first demonstrated to assist protein and glycosaminoglycan production as a carbon and nitrogen generator in chondrocyte extracellular matrix metabolism.

Glutamine metabolism in osteoclast

A homeostatic equilibrium between new bone formation and old or damaged bone resorption is essential to preserve skeletal architecture and strength. Osteoclasts of hematopoietic ancestry primarily break down bone matrix and generate calcium and phosphate, eventually demonstrating control over both bone mass and quality. L-glutamine may have a major effect on the early stages of osteoclast formation and maturation, according to researchers. L-glutamine was absorbed by the Na+-dependent transporter SLC1A5 and then transformed by osteoclasts into glutamate, glutamate, and finally α-KG, which was crucial as an anaplerotic substrate in osteoclast differentiation.

CONCLUSION

Recent research has shown that glutamine plays a key role in maintaining the homeostasis of the bones *via* supporting energy production as a substitute carbon source through the TCA cycle and by contributing precursors for the synthesis of nucleic acids and proteins. The bioenergy of bone cells, such as BMSCs, osteoblasts, chondrocytes, and osteoclasts, is mediated by glutamine metabolism at the cellular level. This has an impact on the ability of these cells to proliferate, differentiate, and mineralize. Clinical illnesses like osteoporosis and osteoarthritis are linked to abnormal glutamine metabolism, which is anticipated to offer new therapeutic strategies.

Therefore, the mechanism of glutamine in bone homeostasis is likely multifaceted and additional basic investigation is needed beyond. Although the effects of glutamine metabolism on other cells or tissues are varied, they have not been well understood in bone cells. For example, in embryonic stem cells, it affected cellular development through epigenetic control. Alternately, glutamine supplements have been used in the therapy of various systemic diseases and are anticipated to reverse osteoporosis and osteoarthritis damage. Essentially, less is known about the targets of glutamine in the treatment of bone diseases.

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