

Understanding Osteoblast Bioenergetics: Lessons for Engineering Bone Biomimetics

The emergence of the endochondral skeleton in terrestrial animals enabled ambulation against increased gravitational forces and provided a storage site for scarce minerals essential for life. This skeletal upgrade increased overall fuel requirements and altered global energy balance, prompting the evolution of endocrine networks to coordinate energy expenditure. Bone-forming osteoblasts require a large and constant supply of energy substrates to fuel bone matrix production and mineralization. When fuel demands are unmet, bone quality and strength are compromised. Studies in genetically altered mice have confirmed a link between bone cells and global metabolism and have led to the identification of hormonal interactions between the skeleton and other tissues. These observations have prompted examination of the nature of the mechanisms of fuel sensing and processing in the osteoblast and their contribution to overall energy utilization and homeostasis. This work has led to the notion that key developmental signaling pathways (e.g. Wnt) are coupled to bioenergetic programs (e.g. anaerobic glycolysis) to accommodate changes in energy requirements at different stages in the osteoblast lifecycle. Other studies have identified mechanisms whereby citrate produced during the TCA cycle or transported from blood accumulates in bone mineral at very high concentrations where it is postulated to function in hydroxyapatite crystal integrity. Together, such findings are reshaping our understanding of the role of the osteoblast in healthy and diseased bone and should inspire strategies for the design of novel bone biomimetics.