BIOMINERALIZED MATERIALS AS BONE ECM MIMETICS: FROM UNDERSTANDING MOLECULAR MECHANISMS TO NEW THERAPEUTIC INTERVENTIONS

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Bone extracellular matrix is a heterogeneous composite material consisting, of an inorganic (or mineral) phase, an organic phase and water. In an effort to mimic the mineral environment of bone tissue, we recently employed biomineralization and created mineralized biomaterials (1). Our studies showed that these biomineralized materials induced osteogenic differentiation of stem cells, including human pluripotent stem cells (which includes both embryonic stem cells and induced pluripotent stem cells), even in growth medium devoid of any osteogenic inducing molecules (2,3). By employing these mineralized materials, we have studied the molecular mechanism through which calcium phosphate minerals support osteogenesis with an emphasis on phosphate metabolism (4). Our studies show that extracellular phosphate (resulting from the dissolution of calcium phosphate minerals) uptake through solute carrier family 20 phosphate transporter member 1 (SLC20a1) supports osteogenic differentiation of human mesenchymal stem cells via adenosine, an ATP metabolite, which acts as an autocrine/paracrine signaling molecule through A2b adenosine receptor. Perturbation of SlC20a1 abrogates osteogenic differentiation by decreasing intra-mitochondrial phosphate and ATP synthesis. Our studies further show that the phosphate-ATP-adenosine signaling axis not only promotes osteogenic differentiation of multipotent progenitor cells but also inhibits their adipogenic differentiation (5). When implanted in vivo, these acellular mineralized biomaterials recruited endogenous cells and induced their differentiation to form vascularized bone tissues (6) and also supported donor bone marrow transplantation (7). Leveraging these understandings, we are currently studying the pivotal role of Adenosine A2b receptor, a G-protein coupled receptor on the cell membrane, in regulating bone-specific cells and treating bone metabolic disorders. In this talk, I will discuss these results and the identification of possible drug targets for osteoporosis.

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