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MiR-542-3p suppresses osteoblast cell proliferation and differentiation, targets BMP-7 signaling and inhibits bone formation

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MicroRNAs (miRNAs) are short non-coding RNAs that interfere with translation of specific target mRNAs and thereby regulate diverse biological processes. Recent studies have suggested that miRNAs might play a role in osteoblast differentiation and bone formation. Here, we show that miR-542-3p, a well characterized tumor suppressor whose down-regulation is tightly associated with tumor progression via C-src related oncogenic pathways, inhibits osteoblast proliferation and differentiation. miRNA array profiling in Medicarpin (a pterocarpan with proven bone forming effects) induced mice calvarial osteoblast cells and further validation by quantitative RT-PCR (qRT-PCR) revealed that miR-542-3p was down-regulated during osteoblast differentiation. Over-expression of miR-542-3p inhibited osteoblast differentiation, whereas inhibition of miR-542-3p function by anti-miR-542-3p promoted expression of osteoblast-specific genes, alkaline phosphatase (ALP) activity, and matrix mineralization. Target prediction analysis tools and experimental validation by luciferase 3′ UTR reporter assay identified BMP-7 (bone morphogenetic protein-7) as a direct target of miR-542-3p. It was seen that over-expression of miR-542-3p leads to repression of BMP-7 and inhibition of BMP-7/PI3K-survivin signalling. This strongly suggests that miR-542-3p suppresses osteogenic differentiation and promotes osteoblast apoptosis by repressing BMP-7 and its downstream signaling. Furthermore, silencing of miR-542-3p led to increased bone formation, bone strength and improved trabecular micro architecture in sham and ovariectomized mice. Although miR-542-3p is known to be a tumor repressor, our studies identified a second complementary function of miR-542-3p where it inhibits BMP-7-mediated osteogenesis. Our findings suggest that pharmacological inhibition of miR-542-3p by anti-miR-542-3p could represent a therapeutic strategy for enhancing bone formation *in vivo*.

Biography

Divya Singh has completed her PhD at the age of 29 years from Jawaharlal Nehru University, New Delhi. Subsequently, she joined as a Scientist at the Division of Endocrinology, Central Drug Research Institute. She has published more than 25 papers in peer reviewed journals. Her main research interests include osteoimmunology, microRNAs in regulation of osteoblast function and identification of novel anabolic agents and their mode of action.

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