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The role of microRNA-138 in extracorporeal shockwave stimulated osteogenesis of mesenchymal stem cells

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Extracorporeal shockwave (ESW) has been shown of great potential in promoting the osteogenesis of bone marrow mesenchymal stem cells (BMSCs), but it is unknown whether this osteogenic promotion effect can also be achieved in other MSCs (i.e., tendon-derived stem cells (TDSCs) and adipose-derived stem cells (ADSCs)). In the current study, we aimed not only to compare the osteogenic effects of BMSCs induced by ESW to those of TDSCs and ADSCs; but also to investigate the underlying mechanisms. We show here that ESW (0.16 mj/mm^2) significantly promoted the osteogenic differentiation in all the tested types of MSCs, accompanied with the down-regulation of miR-138 but the activation of FAK, ERK1/2 and RUNX2. The enhancement of osteogenesis in these MSCs was consistently abolished when the cells were pretreated with one of the following conditions: Overexpression of miR-138, FAK knockdown using specific siRNA and U0126, implying that all of these elements are indispensable for mediating the effect of ESW. In addition, our study provides converging genetic and molecular evidence that the miR-138-FAK-ERK1/2-RUNX2 machinery can be generally activated in ESW-preconditioned MSCs. More importantly, this machinery has also been confirmed by our *in vivo* experiments including nude mice spontaneous implantation model and rat femur close fracture model. All these findings suggest that ESW may be a promising therapeutic strategy for the enhancement of osteogenesis of MSCs, regardless of their origins.

Biography

Jun Hu has completed his MD from Xiangya Medical College of Zhongnan University and Postdoctoral studies from South China Normal University. He is the Director of the Department of Orthopaedics in Shantou University Medical College. His research team is interested in the development of innovative approaches for enhancing bone fracture healing and cartilage repair. He has published a number of original papers in reputed journals including *Nanomedicine, the Journal of Biological Chemistry, Scientific Reports* and *Journal of Biomedical Optics*. He also serves as a nominated Reviewer for NSFC proposals in China.

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