MCB, vol.16, supplemental 2, pp.119, 2019

Identification of Btg2 As A Mechanosensitive Gene by Functional Screening Integrative Analyses

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Abstract: Osteoarthritis (OA), with its high disability and mortality rate, is the most common arthritis throughout the world [1]. Exposure of articular cartilage to excessive mechanical stress is deeply involved in the pathogenesis of osteoarthritis (OA) [2,3]. However, the mechanism of how mechanical stress causes cartilage degradation is not clear yet. Here we report that bioinformatics-based integrative analyses can assist in the study of mechanisms modulated by mechanical stress within OA pathology, and we reveal that B-cell Translocation Gene 2 (BTG2) can be a mechanosensitive gene involved in OA development. We obtained OA-associated differentially expressed genes from human and rat datasets through a series of comparisons between OA and normal cartilage. In addition, a similar procedure was followed to gain mechano-associated differentially expressed genes under various mechanical conditions. Thus, we identified BTG2 as a potential mechanosensitive gene which responds to mechanical stimulation in OA cartilage. On this foundation, we employed *in vitro* and *in vivo* models in order to validate the functions of BTG2. In two-dimensional *in vitro* cell loading experiments, BTG2 expression of human chondrocytes was elevated when exposed to low cyclic tensile strain. Additionally, IL-1β was used to simulate the inflammatory microenvironment in human articular chondrocytes whose BTG2 expression was upregulated after IL-1β induction. These results reveal that BTG2 expression is regulated by mechanical stimulation and closely related to an inflammatory environment. Therefore, we hypothesize that BTG2 is an instantaneous early response gene regulating mechano-transduction cascade signaling [4,5] and takes part in the early OA development as well. In conclusion, we identify BTG2 as a mechanosensitive gene that should be considered as an appropriate diagnostic and therapeutic biomarker for OA.

Keywords: Orthopaedic Biomechanics; mechanobiology; mechanosensitive genes; osteoarthritis; BTG2.

Acknowledgement: This work was supported by National Natural Science Foundation of China (31270990, 11532004) and Innovation and Attracting Talents Program for College and University (‘‘111’’ Project) (B06023).

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