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The mechanisms of fibroblast growth factor-2 and glucose regulating the chondrogenic potential of pre-differentiation human mesenchymal stem cells

Wan-Ju Li[1,2], Andrew M. Handorf[1,2], Tsung-Lin Tsai[1,2] and Matthew W. Squire[1]

[1]Department of Orthopedics and Rehabilitation, University of Wisconsin-Madison, USA
[2]Department of Biomedical Engineering, University of Wisconsin-Madison, USA

Multipotent human mesenchymal stem cells (hMSCs) capable of differentiating into chondrocytes are considered a promising cell source for cartilage tissue engineering. While many studies have reported that chondrogenesis (CG) is regulated by biochemical molecules during hMSC differentiation, few have shown that treating pre-differentiation hMSCs with molecules, such as growth factors, affects subsequent CG. In this study, we investigated the molecular mechanisms by which fibroblast growth factor-2 (FGF-2) and glucose regulate the chondrogenic potential of pre-differentiation of hMSCs. Our results showed that FGF-2 pretreatment primed hMSCs for enhanced CG by reducing the expression of pluripotency genes and increasing Sox9 protein levels. Further, we showed that FGF-2 increased Sox9 protein levels in both proliferating and non-proliferating hMSCs, with proliferating hMSCs elevating Sox9 protein levels more dramatically. In addition, we demonstrated that glucose concentration in pre-differentiation culture affected the chondrogenic potential of hMSCs and subsequent CG by regulating the expression of phosphorylated PKC (pPKC) and type II TGF-β receptor (TGFβRII) of the cells. High-glucose maintained hMSCs were less responsive to chondrogenic induction than low-glucose maintained cells due to the lower level of TGFβRII. By inhibiting the PKC activity of high-glucose maintained cells in pre-differentiation culture, TGFβRII of chondrogenic pellets was upregulated to enhance chondrogenesis. Taken together, our findings provide new insights into the mechanism by which FGF-2 and glucose regulate pre-differentiation hMSCs to undergo enhanced CG.

Biography

Wan-Ju Li is the principal investigator leading the Laboratory of Musculoskeletal Biology and Regenerative Medicine at the University of Wisconsin-Madison. He is an assistant professor in the Department of Orthopedics and Rehabilitation and the Department of Biomedical Engineering, and a faculty member in the Stem Cell and Regenerative Medicine Center and the Cellular and Molecular Biology Program. Dr. Li received his Ph.D. in Cell and Tissue Engineering from Thomas Jefferson University in 2004. He has received research awards from National Institutes of Health and North American Spine Society. Dr. Li has published more than 30 papers, including several highly cited papers, in the field of stem cell and cartilage tissue engineering.