Chuanyue Wu et al., Madridge J Cancer Stud Res. 2018
http://dx.doi.org/10.18689/2640-5180.a3.006

A Critical Role of Kindlin-2 in Regulation of Mesenchymal Stem Cell Differentiation

Chuanyue Wu[3]*, Ling Guo[1], Ting Cai[1], Keng Chen[1], Rong Wang[1], Jiaxin Wang[1], Chunhong Cui[1], Jifan Yuan[1], Kuo Zhang[1], Zhongzhen Liu[1], Yi Deng[1] and **Guozhi Xiao[1,2]**
[1]Department of Biology, Southern University of Science and Technology, China
[2]Department of Biochemistry, Rush University Medical Center, USA
[3]Department of Pathology, University of Pittsburgh School of Medicine, USA

Precise control of mesenchymal stem cell (MSC) differentiation is critical for tissue development and regeneration. Our recent studies have shown that kindlin-2 is a key determinant of MSC fate decision. Depletion of kindlin-2 in MSCs is sufficient to induce adipogenesis and inhibit osteogenesis *in vitro* and *in vivo*. Mechanistically, kindlin-2 regulates MSC differentiation through controlling YAP1/TAZ at both the transcript and protein levels. Kindlin-2 physically associates with myosin light chain kinase (MLCK) in response to mechanical cues of cell microenvironment and intracellular signaling events and promotes myosin light chain phosphorylation. Loss of kindlin-2 inhibits RhoA activation and reduces myosin light chain phosphorylation, stress fiber formation and focal adhesion assembly, resulting in increased Ser127 phosphorylation, nuclear exclusion and ubiquitin ligase atrophin-1 interacting protein (AIP)4-mediated degradation of YAP1/TAZ. Our findings reveal a novel kindlin-2 signaling axis that senses the mechanical cues of cell microenvironment and controls MSC fate decision, and suggest a new strategy to regulate MSC differentiation, tissue repair and regeneration.

Biography:

Dr. Chuanyue Wu is a professor and the Lombardi and Shinozuka Experimental Pathology Research Chair in the Department of Pathology, the University of Pittsburgh School of Medicine, USA. His research focuses on the molecular basis and functions of cell-extracellular matrix adhesion in regulation of cell behavior including cell differentiation, migration, proliferation and survival. He holds a B.S. and a M.S. from the East China University of Science and Technology in Shanghai, China and a Ph.D. from the University of Pittsburgh, Pittsburgh, PA, USA.