Yin Yang 1 is Required for PHD Finger Protein 20-mediated Myogenic Differentiation *in vitro* and *in vivo*

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The development of skeletal muscle requires progression of a highly ordered cascade of events comprising myogenic lineage commitment, myoblast proliferation, and terminal differentiation. The process of myogenesis is controlled by several myogenic transcription factors that act as terminal effectors of signaling cascades and produce appropriate developmental stage-specific transcripts. PHD finger protein 20 (PHF20) is a multidomain protein and subunit of a lysine acetyltransferase complex that acetylates histone H4 and p53, but its function is unclear. Notably, it has been reported that PHF20 knockout mice die shortly after birth and display a wide variety of phenotypes within the skeletal and hematopoietic systems. Therefore, the putative role of PHF20 in myogenic differentiation was further investigated. In the present study, we found that protein and mRNA expression levels of PHF20 were decreased during myogenic differentiation in C_2C_{12} cells. At the same time, Yin Yang 1 (YY1) was also decreased during myogenic differentiation. PHF20 overexpression increased YY1 expression during myogenic differentiation, together with a delay in MyoD expression. PHF20 expression enhanced the transcriptional activity of YY1 while shRNA-mediated depletion of PHF20 resulted in the reduction of YY1 promoter activity in C_2C_{12} cells. In addition, PHF20 directly bound to the YY1 promoter in C_2C_{12} cells. In a similar manner, YY1 expression was elevated while myosin heavy chain expression was decreased in PHF20 transgenic (TG) mice. Histological analysis revealed abnormalities in the shape and length of muscles in PHF20-TG mice. Furthermore, PHF20-TG muscles slowly regenerated after cardiotoxin injection, indicating that PHF20 affected muscle differentiation and regeneration after injury *in vivo*. Taken together, these results suggested that PHF20 plays an important role in myogenic differentiation by regulating YY1.

Keyword: PHF20, YY1, myogenic differentiation, muscle, transcription factor