The roles of HDAC9c and p38 MAPK in modulation of osteogenesis

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Mesenchymal stem cells (MSCs) have multipotency to differentiate into distinct lineages including adipocytes and osteoblasts. The differentiation of adipogenic and osteogenic lineages is mutually exclusive. Previously we have demonstrated that EZH2, a histone lysine methyltransferase, binds to the HDAC9c (also called myocyte enhancer factor-2 interacting transcriptional repressor, MITR) promoter and inhibits HDAC9c expression in adipocytes but not in osteoblasts. Expression of HDAC9c promotes MSC osteogenesis while attenuates MSCs adipogenesis through inactivating the transcriptional activity of PPARγ-2. In addition, knockingdown HDAC9c inhibits osteogenesis and enhances adipogenesis. To further investigate how HDAC9c regulates the osteogenesis while inactivates PPARγ-2, we found that phosphorylation of p38 MAPK was increased in osteoblasts compared with undifferentiated MSCs using antibody array assays. Blocking of p38 MAPK using p38 MAPK kinase inhibitor or shRNA repressed the differentiation of MSC into osteoblasts. In addition, knockdown of HDAC9c resulted in inhibition of p38 MAPK expression. However, knockdown of p38 MAPK didn't affect HDAC9c expression, suggesting HDAC9c might act at upstream of p38 MAPK. The roles of HDAC9c and p38 MAPK in modulation of osteogenesis will be investigated further (supported by grants NSC101-2321-B-039-002, NSC102-2325-B-039-002 and NSC99-2632-B-039-001-MY3).