Impaired of a non-DNA dependent methylation status decides the fat decision of bone marrow-derived C3H10T1/2 stem cell

ABSTRACT

A decrease in the lineage commitment of multipotent Mesenchymal stem cells (MSC) to the bone forming osteoblast lineage and an increase in the commitment to the fat forming adipocyte lineage is more common in bone marrow of elderly persons. A link between methylation status and MSC differentiation remains unclear. Therefore, we hypothesize that hypomethylation may decide the fate decisions of MSC. In the current study, murine bone marrow derived-C3H10T1/2 stem cell was used to examine the role of methylation mechanism on the differentiation potential of stem cells into osteoblasts or adipocytes. C3H10T1/2 cells were treated with Periodate oxidized adenosine (Adox), an inhibitor of S-adenosylhomocysteine-dependent hydrolase (SAHH), which in turn block the non-DNA methylation pathway. The effect of hypomethylation on C3H10T1/2 stem cell differentiation was determined by measuring the alkaline phosphates activity and the degree of mineralization as well as Oil-red O staining and lipid content. The ratio of S-adenosylmethionine (SAM) and S-adenosylhomocysteine (SAH) was determined as a metabolic indicator of cellular methylation potential. It was clearly observed that hypomethylation significantly ($P < 0.05$) reduces SAM: SAH ratio, alkaline phosphates activity, calcification and thereby, osteoblast differentiation. Conversely, adipocyte differentiation was stimulated by hypomethylation. Altogether, our data suggest that non-DNA hypomethylation changes the differentiation potential of C3H10T1/2 stem cells for less osteogenic and more adipogenic.

Keyword: Methylation mechanism; C3H10T1/2 stem cell; S-adenosylmethionine; S-adenosylhomo-cysteine; Osteablast; Adipocyte