Inhibition of Human Mesenchymal Stem Cell Deacetylation via C-11 Novel Compound Enhanced Adipocytic Differentiation

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According to 2014 World Health Organization figures, more than 600 million adults were obese and approximately 2.8 million people die each year as a result of obesity, presenting health and financial burden. The capability of Human mesenchymal stem cells (hMSCs) differentiation into adipocytes make them linked to fat metabolism and thus have an effect in obesity. hMSCs differentiation is regulated at the epigenetic level which involve histone modification. The aim of this study is to investigate the effect of the novel compound C-11 Histone Deacetylase Inhibitor (HDACi) on regulation of hMSC differentiation into adipocytes at the cellular and molecular levels. Adipocytic differentiation was assessed using Oil Red O and Nile Red staining. Gene expression regulated during hMSC differentiation was assessed using qRT-PCR. HDAC activity was measured using HDAC-Glo I//11 assay and western blot. The data showed significant (P = 0.001) increase (~ 2.5 fold) in hMSC differentiation into adipocytes when treated with C-11 and qRT-PCR demonstrated significant (P = 0.001) increase (~ 3 fold) in main adipocytic genes. Genome-wide microarray analysis revealed significant up-regulation of genes involved in adipocytic differentiation in cells treated with C-11. hMSCs treated with C-11 exhibited significant (P = 0.001) decrease (~ 10 fold) in HDAC activity and marked increase in acetylation, suggesting histone modifications as potential mechanisms that promote adipogenesis. The data revealed a novel role for the C-11 HDACi in regulating and promoting adipocytic differentiation of hMSCs. Manipulating such pathways may have significant impact in regenerative medicine application and treatment of obesity.

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