Effect of Anandamide and R(+)-Methanandamide on Adipocyte Differentiation Process

S.Karaliota, C.Gontinou, A.Gountopoulou, A.Siafaka-Kapadai, M.Mavri-Vavayanni,
Laboratory of Biochemistry, Department of Chemistry, University of Athens, Zografou, 15771 Athens, Greece

The ability of adipose tissue to increase its mass during adulthood through the differentiation of preadipocytes to adipocytes has stimulated scientific interest. Free fatty acids such as oleic and arachidonic have been found to induce this differentiation although the effect of AA is still ambiguous. Arachidonoylethanolamine, which is commonly known as anandamide (AEA), was the first endogenous compound identified to act through cannabinoid 1 (CB1R) and 2 (CB2R) receptors. AEA regulates body weight, mainly through feeding modulation and exhibits a lipolytic effect on adipocytes but not via CB1R and CB2R. In addition, AEA has been recently shown to induce 3T3-L1 preadipocyte differentiation, through transcriptional activation of PPARγ.

In the present work, the differentiation of adipocytes was studied by a flow cytometry method based on the change of cell internal complexity and on the increase of cell size during the accumulation of lipid droplets. This method is simple, easy and cheap and offers high precision and accuracy. Confluent primary preadipocytes from rat epididymal adipose tissue were incubated in the presence or absence of AEA, R(+)-methanandamide (R(+)-mAEA), a stable to hydrolysis AEA derivative, and indomethacin, a COX inhibitor, in order to investigate their effect on the differentiation process. In parallel, we studied the effect of AEA, R(+)-mAEA and indomethacin on PPARγ gene expression and on CBRs expression in an effort to investigate the mechanism of AEA action. According to our results, adipocyte differentiation degree was increased by AEA and R(+)-mAEA in a dose-dependent manner. AEA and R(+)-mAEA also induced PPARγ gene expression suggesting that adipocyte differentiation is accomplished through this transcriptional factor. Interestingly, indomethacin decreased the differentiation degree caused by AEA showing that the effect of AEA on the differentiation is probably mediated by its metabolites produced by COX. Finally, the differentiation process seems to alter CBRs expression levels.

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