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ERK1 and ERK2 involvement in human Mesenchymal Stem Cells adipogenic differentiation

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Aims In order to develop therapeutic strategies to control obesity and the related pathologies, it is very important to deepen the knowledge of adipocytes biology and the mechanisms that control adipogenesis. In the present work we have studied the molecular mechanisms at the basis of the adipocytes differentiation using the human Mesenchymal Stem Cells (hMSCs), undifferentiated stem cells present in the bone marrow that are the physiological precursors of adipocytes in the organism. In particular we have focused our attention on the MAPKinases ERK1 and ERK2, that are involved in many biological and cellular processes.

Methods hMSCs, obtained from iliac crest bone marrow, were induced to adipogenic differentiation by treatment with Adipogenic Induction Medium for 10 days (determination phase), then replaced with Adipogenic Maintenance Medium until the end of treatment at day 28 (terminal differentiation phase). hMSC adipogenic differentiation was evaluated by morphological and molecular techniques. Control cells were represented by hMSCs cultured in absence of adipogenic supplements. ERK1 and ERK2 expression and phosphorylation were evaluated by immunoblotting experiments. The specific ERK inhibitor U0126 was added to the adipogenic medium at different times during the adipogenic differentiation protocol.

Results hMSC treated with adipogenic differentiation protocol showed lipid droplets that increased in number and size during the whole differentiation period. In treated hMSC both ERK1 and ERK2 phosphorylation was reduced in comparison to control hMSCs, but time and intensity of these reductions were different for the two isoforms. A decrease of the total amount of ERK1 was also observed. The presence of U0126 during the whole differentiation period hampered the adipogenic differentiation of hMSCs, as very few hMSCs showed the appearance of lipid droplets that were reduced both in number and size. When U0126 was administered only during the determination phase the number of hMSCs recruited in the differentiation program was reduced, while when U0126 was administered only in the terminal differentiation phase, hMSCs did not acquired a mature adipocytic phenotype.

Conclusion In this work we demonstrate that ERK1 and ERK2 are important for hMSC adipogenic differentiation. Our results suggest that ERK1 and ERK2 play a key role in determining how many cells enter into the adipogenic differentiation program and acquire the phenotipycal and molecular characteristics of mature adipocytes.

Key words

ERK, Mesenchymal Stem Cells, Adipogenic Differentiation, Adipocytes Biology, U0126