

Mirna Expression Profile is Different in Human Amniotic Mesenchymal Stem Cells Isolated from Obese Respect to Normal Weight Women

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Abstract : Maternal obesity and nutrient excess in utero increase the risk of future metabolic diseases in the adult life. The mechanisms underlying this process are probably based on genetic, epigenetic alterations and changes in foetal nutrient supply. In mammals, the placenta is the main interface between foetus and mother, it regulates intrauterine development, modulates adaptive responses to sub optimal in uterus conditions and it is also an important source of human amniotic mesenchymal stem cells (hA-MSCs). We previously highlighted a specific microRNA (miRNA) profiling in amnion from obese (Ob) pregnant women, here we compared the miRNA expression profile of hA-MSCs isolated from (Ob) and control (Co) women, aimed to search for any alterations in metabolic pathways that could predispose the new-born to the obese phenotype. Methods: We isolated, at delivery, hA-MSCs from amnion of 16 Ob- and 7 Co-women with pre-pregnancy body mass index (mean/SEM) 40.3/1.8 and 22.4/1.0 kg/m², respectively. hA-MSCs were phenotyped by flow cytometry. Globally, 384 miRNAs were evaluated by the TaqMan Array Human MicroRNA Panel v 1.0 (Applied Biosystems). By the TargetScan program we selected the target genes of the miRNAs differently expressed in Ob- vs Co-hA-MSCs; further, by KEGG database, we selected the statistical significant biological pathways. Results: The immunophenotype characterization confirmed the mesenchymal origin of the isolated hA-MSCs. A large percentage of the tested miRNAs, about 61.4% (232/378), was expressed in hA-MSCs, whereas 38.6% (146/378) was not. Most of the expressed miRNAs (89.2%, 207/232) did not differ between Ob- and Co-hA-MSCs and were not further investigated. Conversely, 4.8% of miRNAs (11/232) was higher and 6.0% (14/232) was lower in Ob- vs Co-hA-MSCs. Interestingly, 7/232 miRNAs were obesity-specific, being expressed only in hA-MSCs isolated from obese women. Bioinformatics showed that these miRNAs significantly regulated (P<0.001) genes belonging to several metabolic pathways, i.e. MAPK signalling, actin cytoskeleton, focal adhesion, axon guidance, insulin signaling, etc. Conclusions: Our preliminary data highlight an altered miRNA profile in Ob- vs Co-hA-MSCs and suggest that an epigenetic miRNA-based mechanism of gene regulation could affect pathways involved in placental growth and function, thereby potentially increasing the newborn's risk of metabolic diseases in the adult life.

Keywords : hA-MSCs, obesity, miRNA, biosystem

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