

FVIII induced expression in adipose-derived Mesenchymal Stem Cells for Haemophilia A cell therapy

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In the last decades, the use of multipotent adult stem cells has paved way for the identification of new therapeutic approaches for the treatment of acquired or degenerative pathologies. Monogenic diseases such as Haemophilia A are also ideal candidates for the treatment by these emerging therapies, which may success in correcting altered protein expression resulting from genetic mutation. Recently, adipose tissue has proven to serve as an accessible and rich source of adult stem cells with multidifferentiative properties, suitable for regenerative medical applications. Although they have already been studied for these purposes, adipose-derived stem cells are still poorly considered for Haemophilia A cell therapy and few research work have focused on their capacity to produce coagulation factor VIII when properly stimulated. This work has studied the *in vitro* differentiation of an adipose-derived stem cell line towards the endothelial lineage, considered to be responsible for coagulation factor production. At this end, adipose-derived stem cells were cultured into differentiation medium enriched with endothelial growth factors up to 21 days. After the induction treatment, changes in cell morphology, migratory capacity and specific gene/protein expression were evaluated by optical microscopy, transwell migration assay and qPCR/Dot Blot analysis, respectively. Our data highlighted that, already after 7 days of induction treatment, cell cultures showed to change their fibroblastoid morphology, starting to form capillary-like structures. They significantly responded to the chemotactic stimuli of endothelial growth factors, and up-regulated the expression of specific endothelial markers (CD34, PDGFR α , VE-cadherin, CD31, vWF) as the time of induction increased. Most important, we gave the first evidence that adipose stem cells are capable of secreting factor VIII after specific endothelial stimulation and without any need for gene transfection. On the base of that, stem cells from adipose tissue seem to be promising candidate for Haemophila A cell therapy.

Key words

Adipose-derived stem cells, Haemophilia A, coagulation factor VIII, stem cell therapy.