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Gene amplification in mesenchymal stem cells and during differentiation towards adipocytes or osteoblasts.

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Abstract

Gene amplifications are an attribute of tumor cells and have for long time been overlooked in normal cells. A growing number of investigations describe gene amplifications in normal mammalian cells during development and differentiation. Possibly, tumor cells have rescued the gene amplification mechanism as a physiological attribute of stem cells. Here, we investigated human mesenchymal stem cells (hMSCs) for gene amplification using array-CGH, single cell fluorescence *in situ* hybridization and qPCR. Gene amplifications were detected in mesenchymal stem cells and in mesenchymal stem cells during differentiation towards adipocytes and osteoblasts. Undifferentiated hMSCs harbor 12 amplified chromosomal regions, hMSCs that differentiated towards adipocytes 18 amplified chromosome regions, and hMSCs that differentiate towards osteoblasts 19 amplified regions. Specifically, hMSCs that differentiated towards adipocytes or osteoblasts harbor *CDK4* and *MDM2* amplifications both of which frequently occur in osteosarcoma and liposarcoma that are both of same cell origin. Beside the amplifications, we identified 36 under-replicated regions in undifferentiated and in differentiating hMSC cells.

J Extracell Vesicles. 2018 Jan 21;7(1):1422674. doi: 10.1080/20013078.2017.1422674. eCollection 2018.

Efficient ultrafiltration-based protocol to deplete extracellular vesicles from fetal bovine serum.

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Abstract

Fetal bovine serum (FBS) is the most commonly used supplement in studies involving cell-culture experiments. However, FBS contains large numbers of bovine extracellular vesicles (EVs), which hamper the analyses of secreted EVs from the cell type of preference and, thus, also the downstream analyses. Therefore, a prior elimination of EVs from FBS is crucial. However, the current methods of EV depletion by ultracentrifugation are cumbersome and the commercial alternatives expensive. In this study, our aim was to develop a protocol to completely deplete EVs from FBS, which may have wide applicability in cell-culture applications. We investigated different EV-depleted FBS prepared by our novel ultrafiltration-based protocol, by conventionally used overnight ultracentrifugation, or commercially available depleted FBS, and compared them with regular FBS. All sera were characterized by nanoparticle tracking analysis, electron microscopy, Western blotting and RNA quantification. Next, adipose-tissue mesenchymal stem cells (AT-MSCs) and cancer cells were grown in the media

supplemented with the three different EV-depleted FBS and compared with cells grown in regular FBS media to assess the effects on cell proliferation, stress, differentiation and EV production. The novel ultrafiltration-based protocol depleted EVs from FBS clearly more efficiently than ultracentrifugation and commercial methods. Cell proliferation, stress, differentiation and EV production of AT-MSCs and cancer cell lines were similarly maintained in all three EV-depleted FBS media up to 96 h. In summary, our ultrafiltration protocol efficiently depletes EVs, is easy to use and maintains cell growth and metabolism. Since the method is also cost-effective and easy to standardize, it could be used in a wide range of cell-culture applications helping to increase comparability of EV research results between laboratories.

Stem Cells Int. 2017;2017:6305295. doi: 10.1155/2017/6305295. Epub 2017 Dec 19.

Focus on Mesenchymal Stem Cell-Derived Exosomes: Opportunities and Challenges in Cell-Free Therapy.

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Abstract

Mesenchymal stem cells have been at the forefront of regenerative medicine for many years. Exosomes, which are nanovesicles involved in intercellular communication and the transportation of genetic material transportation that can be released by mesenchymal stem cells, have been recently reported to play a role in cell-free therapy of many diseases, including myocardial infarction, drug addiction, and status epilepticus. They are also thought to help ameliorate inflammation-induced preterm brain injury, liver injury, and various types of cancer. This review highlights recent advances in the exploration of mesenchymal stem cell-derived exosomes in therapeutic applications. The natural contents, drug delivery potency, modification methods, and drug loading methods of exosomes are also discussed.