ML 32-19 (04/11/2019)

Int J Mol Sci. 2019 Oct 29;20(21). pii: E5386. doi: 10.3390/ijms20215386.

Substantial Overview on Mesenchymal Stem Cell Biological and Physical Properties as an Opportunity in Translational Medicine.

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Abstract

Mesenchymal stem cells (MSC) have piqued worldwide interest for their extensive potential to treat a large array of clinical indications, their unique and controversial immunogenic and immune modulatory properties allowing ample discussions and debates for their possible applications. Emerging data demonstrating that the interaction of biomaterials and physical cues with MSC can guide their differentiation into specific cell lineages also provide new interesting insights for further MSC manipulation in different clinical applications. Moreover, recent discoveries of some regulatory molecules and signaling pathways in MSC niche that may regulate cell fate to distinct lineage herald breakthroughs in regenerative medicine. Although the advancement and success in the MSC field had led to an enormous increase in the amount of ongoing clinical trials, we still lack defined clinical therapeutic protocols. This review will explore the exciting opportunities offered by human and animal MSC, describing relevant biological properties of these cells in the light of the novel emerging evidence mentioned above while addressing the limitations and challenges MSC are still facing.

Curr Gene Ther. 2019 Oct 27. doi: 10.2174/1566523219666191028103703. [Epub ahead of print]

Suicide Gene Therapy Against Malignant Gliomas by the Local Delivery of Genetically Engineered Umbilical Cord Mesenchymal Stem Cells as Cellular Vehicles.

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Abstract

BACKGROUND:

Glioblastoma (GBM) is a malignant tumor that is difficult to eliminate, and new therapies are thus strongly desired. Mesenchymal stem cells (MSCs) have the ability to locate to injured tissues, inflammation sites and tumors and are thus good candidates for carrying antitumor genes for the treatment of tumors. Treating GBM with MSCs that have been transduced with the herpes simplex virus thymidine kinase (HSV-TK) gene has brought significant advances because MSCs can exert a bystander effect on tumor cells upon treatment with the prodrug ganciclovir (GCV).

OBJECTIVE:

In this study, we aimed to determine whether HSV-TK-expressing umbilical cord mesenchymal stem cells (MSCTKs) together with prodrug GCV treatment could exert a bystander killing effect on GBM.

METHODS AND RESULTS:

Compared with MSCTK :U87 ratio at 1:10,1:100 and 1:100, GCV concentration at 2.5μM or 250μM, when MSCTKs were cocultured with U87 cells at a ratio of 1:1, 25 μM GCV exerted a more stable killing effect. Higher amounts of MSCTKs cocultured with U87 cells were correlated with a better bystander effect exerted by the MSCTK/GCV system. We built U87-driven subcutaneous tumor models and brain intracranial tumor models to evaluate the efficiency of the MSCTK/GCV system on subcutaneous and intracranial tumors and found that MSCTK/GCV was effective in both models. The ratio of MSCTKs and tumor cells played a critical role in this therapeutic effect, with a higher MSCTK/U87 ratio exerting a better effect.

CONCLUSION:

This research suggested that the MSCTK/GCV system exerts a strong bystander effect on GBM tumor cells, and this system may be a promising assistant method for GBM postoperative therapy.

J Forensic Leg Med. 2019 Oct 16;69:101875. doi: 10.1016/j.jflm.2019.101875. [Epub ahead of print]

Isolation and culture of human adipose-derived mesenchymal stromal/stem cells harvested from postmortem adipose tissues.

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Abstract

Many cell types maintain their function short-term after death. Stem cells isolated from postmortem tissues have been successfully applied in transplantation studies. However, stem cell viability and stemness are reported to decline with increased time after death. Although postmortem stem cells may be useful for regenerative therapy and forensic diagnostics, their characteristic remain to be better understood. Adipose-derived mesenchymal stromal/stem cells (ASCs) have the capacity to differentiate through several cell lineages and are able to survive in an ischemic environment for a prolonged time. This study aimed to confirm whether human postmortem ASCs can be collected and culture-expanded from cadavers. Axilla subcutaneous adipose tissues were harvested during forensic autopsy and enzymatically digested to obtain a heterogeneous cell mixture, including the ASCs population. The mixture was seeded onto collagen-coated cell culture dishes and spindle-shaped adhesive and proliferative ASCs were confirmed. Senescent cells were also present, visualized as large and flattened cells. When maintained in a cool environment, ASCs were able to survive in the postmortem tissues for up to 7 days after death. We conclude that postmortem ASCs can be readily isolated and culture-expanded from adipose tissues

Stem Cells Dev. 2019 Oct 25. doi: 10.1089/scd.2019.0154. [Epub ahead of print]

Mesenchymal stem cell-platelet aggregates increased in the peripheral blood of patients with acute myocardial infarction and might depend on the CXCR4/SDF-1 axis.

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Abstract

Bone marrow mesenchymal stem cells (BM-MSCs) are a rare subset of non-hematopoietic progenitor cells and are appealing biomaterial for multiple tissue damage repairs. Transplantation of MSCs are proved to improve heart function after myocardial ischemia. However, the limitations of MSCs injection approaches are equally obvious. As a multiple-function cell, Platelets (PLTs) are also known playing important roles in cardiac recovery after myocardial infarction. In this study, we analyzed circulating MSC-PLT aggregates numbers in acute myocardial infarction (AMI) patients by flow cytometry. we found more MSC-PLT aggregates in patients with AMI than in healthy controls, and the patients with higher MSC-PLT aggregates had better prognosis. When stromal cell-derived factor 1 (SDF-1) binds to its receptor CXC chemokine receptor 4 (CXCR4), they play an important role in MSCs migration and engraftment. We explored SDF-1 and CXCR4 expression on PLT surface by flow cytometry, and found relative mean fluorescence intensity (RMFI) of PLT CXCR4 and the number of MSC-PLT aggregates showed a significant correlation. Meanwhile, in vitro experiments demonstrated that SDF-1/CXCR4 was crucial in MSC-PLT aggregate formation, which might suggest a novel mechanism that SDF-1/CXCR4 involved in MSCs homing and myocardial repair after AMI. There may be another strategy to encourage myocardial repair in AMI patients by increasing the expression of SDF-1 on MSCs and promoting the formation of MSC-PLT aggregates.