ML 03-20 (14/01/2020)

J Orthop Res. 2020 Jan 10. doi: 10.1002/jor.24583. [Epub ahead of print]

Orbital seeding of mesenchymal stromal cells increases osteogenic differentiation and bone-like tissue formation.

Melke J[1,2], Zhao F[1,2], Ito K[1,2,3], Hofmann S[1,2].
Author information

Abstract

In bone tissue engineering, an efficient seeding and homogenous distribution of cells is needed to avoid cell loss and damage as well as to facilitate tissue development. Dynamic seeding methods seem to be superior to the static ones because they tend to result in a more homogeneous cell distribution by using kinetic forces. However, most dynamic seeding techniques are elaborate or require special equipment and its influence on the final bone tissue engineered construct is not clear. In this study, we applied a simple, dynamic seeding method using an orbital shaker to seed human bone marrow derived mesenchymal stromal cells (hBMSCs) on silk fibroin scaffolds. Significantly higher cell numbers with a more homogenous cell distribution, increased osteogenic differentiation and mineral deposition were observed using the dynamic approach both for 4 and 6 h as compared to the static seeding method. The positive influence of dynamic seeding could be attributed to both cell density and distribution but also nutrient supply during seeding and shear stresses (0.0 - 3.0 mPa) as determined by computational simulations. The influence of relevant mechanical stimuli during seeding should be investigated in the future, especially regarding the importance of mechanical cues for bone tissue engineering applications. Our results highlight the importance of adequate choice of seeding method and its impact on developing tissue engineered constructs. The application of this simple seeding technique is not only recommended for bone tissue engineering but can be used for seeding similar porous scaffolds with hBMSCs in other tissue engineering fields

Adv Exp Med Biol. 2020 Jan 9. doi: 10.1007/5584_2019_464. [Epub ahead of print]

Adipose-Derived Mesenchymal Stem Cells Promote Growth and Migration of Lung Adenocarcinoma Cancer Cells.

Zakaria N[1], Yahaya BH[2].

Author information

Abstract

INTRODUCTION:

Mesenchymal stem cells (MSCs) have been used in cancer therapy as vehicles to deliver therapeutic materials such as drugs, apoptosis inducers and cytokines due to their ability to migrate and home at the tumour site. Furthermore, MSCs have been genetically engineered to produce anticancer molecules such as TRAIL that can induce apoptosis of cancer cells. However, MSCs' presence in the tumour microenvironment has shown to be involved in promoting tumour growth and progression. Therefore, the roles of MSCs either promoting or suppressing tumorigenesis need to be investigated.

METHODS:

Human adipose-derived MSCs (Ad-MSCs) and A549 cells are co-cultured together in indirect co-culture system using Transwell insert. Following co-culture, both cells were analysed in terms of growth rate, migration ability, apoptosis and gene expression for genes involved in migration and stemness characteristics.

RESULTS:

The result shows that Ad-MSCs promoted the growth of A549 cells when indirectly co-cultured for 48 and 72 h. Furthermore, Ad-MSCs significantly enhanced the migration rate of A549 cells. The increased in migration rate was in parallel with the significant increase of MMP9. There are no significant changes observed in the expression of TWIST2, CDH2 and CDH1, genes involved in the epithelial-to-mesenchymal transition (EMT). Ad-MSCs also protect A549 cancer cells from undergoing apoptosis and increase the survival of cancer cells.

CONCLUSION:

Secretion of soluble factors from Ad-MSCs has been shown to promote the growth and metastatic characteristics of A549 cancer cells. Therefore, the use of Ad-MSCs in cancer therapy needs to be carefully evaluated in the long-term aspect.

Adv Exp Med Biol. 2020 Jan 9. doi: 10.1007/5584_2019_464. [Epub ahead of print]

Adipose-Derived Mesenchymal Stem Cells Promote Growth and Migration of Lung Adenocarcinoma Cancer Cells.

Zakaria N[1], Yahaya BH[2].

Author information

Abstract

INTRODUCTION:

Mesenchymal stem cells (MSCs) have been used in cancer therapy as vehicles to deliver therapeutic materials such as drugs, apoptosis inducers and cytokines due to their ability to migrate and home at the tumour site. Furthermore, MSCs have been genetically engineered to produce anticancer molecules such as TRAIL that can induce apoptosis of cancer cells. However, MSCs' presence in the tumour microenvironment has shown to be involved in promoting tumour growth and progression. Therefore, the roles of MSCs either promoting or suppressing tumorigenesis need to be investigated.

METHODS:

Human adipose-derived MSCs (Ad-MSCs) and A549 cells are co-cultured together in indirect co-culture system using Transwell insert. Following co-culture, both cells were analysed in terms of growth rate, migration ability, apoptosis and gene expression for genes involved in migration and stemness characteristics.

RESULTS:

The result shows that Ad-MSCs promoted the growth of A549 cells when indirectly co-cultured for 48 and 72 h. Furthermore, Ad-MSCs significantly enhanced the migration rate of A549 cells. The increased in migration rate was in parallel with the significant increase of MMP9. There are no significant changes observed in the expression of TWIST2, CDH2 and CDH1, genes involved in the epithelial-to-mesenchymal transition (EMT). Ad-MSCs also protect A549 cancer cells from undergoing apoptosis and increase the survival of cancer cells.

CONCLUSION:

Secretion of soluble factors from Ad-MSCs has been shown to promote the growth and metastatic characteristics of A549 cancer cells. Therefore, the use of Ad-MSCs in cancer therapy needs to be carefully evaluated in the long-term aspect.

J Exp Clin Cancer Res. 2020 Jan 8;39(1):2. doi: 10.1186/s13046-019-1505-4.

A pre-existing population of ZEB2^{+} quiescent cells with stemness and mesenchymal features dictate chemoresistance in colorectal cancer.

Francescangeli F[1], Contavalli P[1], De Angelis ML[1], Careccia S[2], Signore M[3], Haas TL[2,4], Salaris F[1], Baiocchi M[1], Boe A[5], Giuliani A[6], Tcheremenskaia O[6], Pagliuca A[1], Guardiola O[7], Minchiotti G[7], Colace L[8], Ciardi A[9], D'Andrea V[8], La Torre F[10], Medema J[11], De Maria R[12,13], Zeuner A[14].

Author information

Abstract

BACKGROUND:

Quiescent/slow cycling cells have been identified in several tumors and correlated with therapy resistance. However, the features of chemoresistant populations and the molecular factors linking quiescence to chemoresistance are largely unknown.

METHODS:

A population of chemoresistant quiescent/slow cycling cells was isolated through PKH26 staining (which allows to separate cells on the basis of their proliferation rate) from colorectal cancer (CRC) xenografts and subjected to global gene expression and pathway activation analyses. Factors expressed by the quiescent/slow cycling population were analyzed through lentiviral overexpression approaches for their ability to induce a dormant chemoresistant state both in vitro and in mouse xenografts. The correlation between quiescence-associated factors, CRC consensus molecular subtype and cancer prognosis was analyzed in large patient datasets.

RESULTS:

Untreated colorectal tumors contain a population of quiescent/slow cycling cells with stem cell features (quiescent cancer stem cells, QCSCs) characterized by a predetermined mesenchymal-like chemoresistant phenotype. QCSCs expressed increased levels of ZEB2, a transcription factor involved in stem cell plasticity and epithelial-mesenchymal transition (EMT), and of antiapototic factors pCRAF

and pASK1. ZEB2 overexpression upregulated pCRAF/pASK1 levels resulting in increased chemoresistance, enrichment of cells with stemness/EMT traits and proliferative slowdown of tumor xenografts. In parallel, chemotherapy treatment of tumor xenografts induced the prevalence of QCSCs with a stemness/EMT phenotype and activation of the ZEB2/pCRAF/pASK1 axis, resulting in a chemotherapy-unresponsive state. In CRC patients, increased ZEB2 levels correlated with worse relapse-free survival and were strongly associated to the consensus molecular subtype 4 (CMS4) characterized by dismal prognosis, decreased proliferative rates and upregulation of EMT genes.

CONCLUSIONS:

These results show that chemotherapy-naive tumors contain a cell population characterized by a coordinated program of chemoresistance, quiescence, stemness and EMT. Such population becomes prevalent upon drug treatment and is responsible for chemotherapy resistance, thus representing a key target for more effective therapeutic approaches.