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Adipose-derived mesenchymal stem cells differentiate into pancreatic cancer-associated fibroblasts in vitro

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Free article

Abstract

Cancer-associated fibroblasts (CAFs) are key components of the dense, proliferating stroma observed in pancreatic ductal adenocarcinoma (PDAC), and CAF subpopulations drive tumor heterogeneity and play a major role in PDAC progression and drug resistance. CAFs consist of heterogenous subpopulations such as myoblastic CAF (myCAF) and inflammatory CAF (iCAF), and each has distinct essential roles. However, it is not clear how CAF subpopulations are formed in PDAC. Adipose-derived MSCs (AD-MSCs), which possess a high multilineage potential and self-renewal capacity, are reported to be one of the in vivo CAF sources. Here, we aimed to investigate whether AD-MSCs can act as precursors for CAFs in vitro. We recorded morphological features and collected omics data from two in vitro co-culture models for recapitulating clinical PDAC. Additionally, we tested the advantages of the co-culture model in terms of accurately modelling morphology and CAF heterogeneity. We showed that AD-MSCs differentiate into two distinct CAF subpopulations: direct contact co-culture with PDAC cell line Capan-1 induced differentiation into myCAFs and iCAFs, while indirect co-culture induced differentiation into only iCAFs. Using these co-culture systems, we also identified novel CAF markers that may be helpful for elucidating the mechanisms of CAFs in the tumor microenvironment. In conclusion, AD-MSCs can differentiate into distinct CAF subtypes depending on the different co-culture conditions in vitro, and the identification of potential CAF markers may

aid in future investigations of the mechanisms underlying the role of CAFs in the tumor microenvironment.

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Periodontal Regeneration using a Xenogeneic Bone Substitute seeded with Autologous Periodontal Ligament derived Mesenchymal Stem Cells: a 12-month quasi-randomized controlled pilot clinical trial

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Abstract

Aim: To evaluate the safety and efficacy of autologous periodontal ligament-derived mesenchymal stem cells (PDL-MSCs) embedded in a xenogeneic bone substitute (XBS) for the regenerative treatment of intra-bony periodontal defects.

Material and methods: This quasi-randomized controlled pilot phase II clinical trial included patients requiring a tooth extraction and presence of one intra-bony lesion (1-2 walls). Patients were allocated to either the experimental (XBS + $10x10^6$ PDL-MSCs/100mg) or the control group (XBS). Clinical and radiographical parameters were recorded at baseline, 6, 9 and 12 months. The presence of adverse events was also evaluated. Chi-square, Student`s t-test, U-Mann Whitney, repeated-measures ANOVA and regression models were used.

Results: Twenty patients were included. No serious adverse events were reported. Patients in the experimental group (n=9) showed greater clinical attachment level (CAL) gain [1.44, standard deviation (SD)=1.87] and probing pocket depth (PPD) reduction (2.33, SD=1.32) than the control group (n=10; CAL gain=0.88, SD=1.68, and PPD reduction=2.10, SD=2.46), without statistically significant differences.

Conclusion: The application of PDL-MSCs to XBS for the treatment of one-two wall intra-bony lesions was safe and resulted in low postoperative morbidity and appropriate healing, although its additional benefit, when compared with the XBS alone, was not demonstrated.

Cancers (Basel)

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Mesenchymal Stromal-Like Cells in the Glioma Microenvironment: What Are These Cells?

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Free article

Abstract

The glioma microenvironment is a critical regulator of tumor progression. It contains different cellular components such as blood vessels, immune cells, and neuroglial cells. It also contains non-cellular components, such as the extracellular matrix, extracellular vesicles, and cytokines, and has certain physicochemical properties, such as low pH, hypoxia, elevated interstitial pressure, and impaired perfusion. This review focuses on a particular type of cells recently identified in the glioma microenvironment: glioma-associated stromal cells (GASCs). This is just one of a number of names given to these mesenchymal stromal-like cells, which have phenotypic and functional properties similar to those of mesenchymal stem cells and cancer-associated fibroblasts. Their close proximity to blood vessels may provide a permissive environment, facilitating angiogenesis, invasion,

and tumor growth. Additional studies are required to characterize these cells further and to analyze their role in tumor resistance and recurrence.

Biochem J

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Hurdles to uptake of mesenchymal stem cells and their progenitors in therapeutic products

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Abstract

Twenty-five years have passed since the first clinical trial utilising mesenchymal stomal/stem cells (MSCs) in 1995. In this time academic research has grown our understanding of MSC biochemistry and our ability to manipulate these cells in vitro using chemical, biomaterial, and mechanical methods. Research has been emboldened by the promise that MSCs can treat illness and repair damaged tissues through their capacity for immunomodulation and differentiation. Since 1995, 31 therapeutic products containing MSCs and/or progenitors have reached the market with the level of in vitro manipulation varying significantly. In this review, we summarise existing therapeutic products containing MSCs or mesenchymal progenitor cells and examine the challenges faced when developing new therapeutic products. Successful progression to clinical trial, and ultimately market, requires a thorough understanding of these hurdles at the earliest stages of in vitro pre-clinical development. It is beneficial to understand the health economic benefit for a new product and the reimbursement potential within various healthcare systems. Pre-clinical studies should be selected to demonstrate efficacy and safety for the specific clinical indication in humans, to avoid duplication of effort and minimise animal usage. Early consideration should also be given to manufacturing: how cell manipulation methods will integrate into highly controlled workflows and how they will be scaled up to produce clinically relevant quantities of cells. Finally, we summarise the main regulatory pathways for these clinical products, which can help shape early therapeutic design and testing.

Stem Cell Res

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Strategies for scalable manufacturing and translation of MSC-derived extracellular vesicles

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Abstract

Mesenchymal Stem/Stromal Cells (MSCs) are a well-studied cellular therapy with many clinical trials over the last few decades to treat a range of therapeutic indications. Recently, extracellular vesicles secreted by MSCs (MSC-EVs) have been shown to recapitulate many of the therapeutic effects of the MSCs themselves. While research in MSC-EVs has exploded, it is still early in their development towards a clinical therapy. One of the main challenges in cellular therapy, which will clearly also be a challenge in MSC-EV manufacturing, is developing a scalable, cGMP-compatible manufacturing paradigm. Therefore, the focus of this review is to identify some key MSC-EV manufacturing considerations such as the selection of critical raw materials, manufacturing platforms, and critical quality attribute assays. Addressing these issues early in research and development will accelerate clinical product development, clinical trials, and commercial therapies of MSC-EVs.