

Mesenchymal Stem Cells are Used as a Potential Therapy for Numerous Diseases

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ABSTRACT

Mesenchymal stem cells are a group of multipotent cells separated from human bone marrow and periosteum that hold the capacity to separate into various tissues of mesodermal beginning *in vitro*. They can be separated from nearly all tissues of the human body since they emerge from pericytes and have extra characteristics. *In vivo*, their part is essentially centered on the emission of bioactive components that recognize the location of harm or irritation, intercede the safe reaction, diminish aggravation and advance tissue regeneration.

Keywords: MSCs, BM-MSc, TME, EMT, Health

1. Introduction

Mesenchymal stem cells (MSCs) are considered the key cells in tissue recovery after harm¹. MSCs play a principal part in cancer since they can be enlisted to initiate tumor development and spread. In the final decades, MSCs have illustrated a few molecular characteristics in tissue recovery and cancer advancement: the capacity to elude the resistant framework, actuate tumor angiogenesis and likely confer resistance to cancer from common chemotherapeutic operators. In any case, much remains to be clarified almost their association in the epithelial-mesenchymal transition (EMT) and interaction with cancer stem cells (CSCs), basically due to the complexity of these molecular forms. Other than these perspectives, other modern particles, such as circulating tumor cells (CTCs), appear to emphatically interface with CSCs and MSCs in overseeing pre-metastatic specialty arrangement.

1.1. Adult stem cells

Adult stem cells either have the capacity to separate through the mesodermal lineages, which incorporate myogenic, osteogenic, chondrogenic and adipogenic lines (multipotent) or are unipotent and as it were able to separate into a develop cell sort that is characteristic of the tissue from which it was disconnected². Mesenchymal stem cells (MSCs) are

characteristic multipotent adult stem cells. These cells have been appeared to have immunogenic potential and to discharge cell development, relocation and separation variables through a paracrine instrument. Mesenchymal stem cells can be determined from a few tissue sources counting fat tissue, bone marrow, urine and dental pulp. Bone marrow and adipose-derived MSCs are multipotent and are able to separate into osteogenic, chondrogenic, myogenic and adipogenic cells.

Unipotent stem cells are mindful for tissue development and reaction to damage. These cells are important in the scope of tissue designing and regenerative medication. They speak to cell sorts, which if saddled, may give upgraded cellular fabric and advantageous discharged cytokines that might address the root causes of numerous hopeless ailments. These cells incorporate hepatocyte forebear stem cells, skeletal muscle toady cells, inhabitant cardiac stem cells, endothelial begetter cells and neural stem cells, to title a few. Hepatocyte forebear and inhabitant cardiac stem cells hold guarantee for clinical interpretation but are restricted by confinement and development strategies. Skeletal muscle disciple cells, neural begetter cells and endothelial begetter cells have been more commonly considered in preclinical tests, but are also restricted by the current failure to keep up development and stem cell potential *in vitro*. Due to the restrictions of these cells, most cell treatments

beneath advancement and as of now being utilized in clinical trials include ES (embryonic stem), iPS (induced pluripotent stem) or MSCs.

1.2. BM-MSC

One of the most recognized types of stem cells is the bone marrow-derived mesenchymal stem cell (BM-MSC)³. Mesenchymal stem cells (MSCs) are self-renewing and multipotent cells competent of separating into numerous cells counting osteocytes, chondrocytes, adipocytes, hepatocytes and myocytes, neurons and cardiomyocytes. MSCs reside in the stromal compartment of bone marrow and play an vital part in giving stromal back for hematopoietic stem cells.

One of the downsides of MSCs is that they need tissue particular characteristics, but with the right impact signals they can separate into specialized cells. MSCs can be effortlessly isolated and with the right research facility conditions, they can be extended to exceptionally huge numbers. These cells can be refined in such a way that they do not lose their separation capacities for numerous eras. MSCs have created extraordinary intrigued in the field of tissue designing and regenerative drugs. Different preclinical and clinical trials with MSCs are in advance to recognize and test the helpful esteem of MSCs in different degenerative diseases.

For instance, when treating patients for bone and cartilage malady, adult BM-MSCs are by and large the best treatment choice since these cells have illustrated that they are able to separate from a fundamental marrow cell populace to an whole osteogenic ancestry and hence have been utilized to catalyze repair of bone abandons. These mesenchymal stem cells can be separated from the bone marrow colony-forming unit–fibroblastic (CFUF) and at that point be separated to other osteogenic lineages.

Bone marrow cells are a exceptionally complex blend of cells and in this way require a more characterized beginning cell populace to be disconnected from the blend. Eventually, these cells can be extricated from the marrow and utilized to improve materials like the filler that is utilized for stabilizing fake joints or for joining expansive abandons in bone that would ordinarily be incomprehensible to heal naturally.

1.3. Cancer cells

It is presently caught on that cancer cells do not act alone: They connected with their encompassing stroma, driving to an “activated state” which at that point directs their microenvironment by expanded discharge of pro-inflammatory cytokines and development components, which render the microenvironment conducive to their survival and working¹.

A tumor is in a constant state of irritation and has been portrayed as a “wound that never heals”. This provocative state drives the enlistment of responsive cell sorts, such as macrophages, myeloid-derived silencer cells and mesenchymal stem cells (MSCs). Crosstalk between cancer cells and cells of the encompassing stroma advances tumor movement and makes a energetic extracellular network favorable to the intrusive tumor cells. Be that as it may, characterizing the “tumor stroma” is complicated due to the inconstancy between cancer sorts and tumor heterogeneity. In this setting, it is fundamental to get it what may drive non-cancerous cells toward an actuated state, what that state is and what it implies for tumor cell progression.

MSCs are multipotent stem cells with an exceptional capacity to separate into three lineages: osteoblasts, chondrocytes and adipocytes. They are for the most part confined utilizing particular surface markers, that is, CD73, CD105, CD44 and CD90 and as of late they have been separated into other cell sorts, such as myocytes and neurons. They are determined from bone marrow (BM), fat tissue and dental pulp, in spite of the fact that they are also found in blood and fiery tissues. One of the most energizing perspectives of MSCs, characterized by the logical community, is their capacity to recover different harmed tissues of major organs, such as the heart and lungs and have moved to progressed stages of clinical appraisal. The differences of parts that MSCs are included in based on their science has empowered their utilize in modern viewpoints. They moreover play a vital part in progressing long-term HSC engraftment in HSC-transplanted patients. Be that as it may, in expansion to their kind regenerative characteristics, MSCs can domestic into tumors, contributing to tumor advancement and dispersal. In specific, it has been appeared that these cells are display in a few strong tumors. They may advance cell motility and forcefulness and offer assistance make a metastatic specialty at the auxiliary locus.

1.4. TME

The reasons why MSCs are vital players in the development and advancement of cancers are not well caught on; in any case, credulous MSCs may be actuated through a paracrine cascade, cell-cell contact or introduction to the tumor microenvironment (TME), coming about in an “activated,” tumor-promoting state¹. In this setting, the TME appears to play a imperative part. Be that as it may, the logical community has not however entirely characterized the intuitive among cancer cells, non-malignant cells and the microenvironment, nor what components are basic for the pathophysiology of tumors. In specific, the non-tumoral cells comprising basically of stromal, safe and endothelial cells take part in a bidirectional interaction with cancer cells, which can epigenetically reconstruct the mesenchymal stem/stromal cells. This balance of MSCs is a vigorous pro-tumorigenic handle in which they accept a cancer-promoting phenotype: During this handle, they ended up carcinoma-associated mesenchymal stem/stromal cells (CA-MSCs) that can build up the TME, counting cancer-associated fibroblasts, myofibroblasts and adipocytes. The generation of discharged variables by CA-MSCs actuates angiogenic variables and initiates immunosuppressive myeloid cells, which drive tumor avoidance of the safe system.

MSCs have a vigorous immunosuppressive capacity, as they offer assistance tumor cells elude resistant reconnaissance. MSCs can be enacted in the TME by the pro-inflammatory cytokines tumor corruption factor-alpha (TNF- α), interferon-gamma (IFN- γ) or interleukin (IL)-1 β , which are emitted by macrophages and tumor cells. Noteworthy immunosuppression is along these lines initiated by the emission of solvent components such as indoleamine 2,3-dioxygenase, transforming growth figure beta (TGF- β), TNF- α , IFN- γ , prostaglandin E2, IL-1 β , IL-1 α , IL-4 and IL-6 and through intelligent with T aide cells, T administrative cells, B cells, dendritic cells, NK cells and macrophages. In specific, these discharged variables are dependable for safe resistance of T, B, NK and dendritic cells; apoptosis of lymphocytes and neutrophils; and the enlistment of the inhibitory safe cells myeloid-derived silencer cells. MSCs actuate this recruitment of myeloid-derived silencer cells

through CCL2 signaling. It debilitates the anti-cancer T-cell movement, whereas the hindrance of B-cell expansion is due to cell-cycle capture and galectin-9, which is overexpressed as a result of IFN- γ incitement of MSCs and hinders counter acting agent generation and B-cell expansion. In this way, MSCs show a vigorous inhibitory capacity against versatile safe cells that cancer cells exploit.

1.5. Transformation

The understanding of how typical cells change into tumor cells and advance to intrusive cancer and metastases proceeds to advance⁴. This growing information has motivated amendment of the “hallmarks of cancer” that were set up as the cutting edge establishment for portraying tumor movement. In expansion to procured transformations, genomic precariousness and epigenetic changes that characterize tumor cell change, there is the concept that inside the heterogeneous complex of cells that is named “tumor mass” resides a collection of enrolled have resistant and stromal cells. These cells or maybe than constricting tumor movement, appear to empower tumor development, attack and metastasis. This enrolled “tumor microenvironment” (TME) plays a essential part in the procurement of trademark characteristics and has been the strongly center of current investigate. Total prove has appeared that the components of the microenvironment, counting the extracellular matrix (ECM), fibroblasts, myofibroblasts, leukocytes, endothelial cells, pericytes, smooth muscle cells, dendritic cells, macrophages, lymphocytes, mesenchymal cells and cancer-associated fibroblasts, associated through a complex network of cytokines, mitogens and development components to enact tumor development. As such, the current era of cancer trademarks incorporates the (1) sustainment of proliferative signals, (2) avoidance of development silencers, (3) resistance of cell death, (4) foundation of replicative eternity, (5) acceptance of angiogenesis, (6) enactment of attack and metastasis, (7) reconstructing of vitality digestion system and (8) avoidance of safe destruction.

Recently, epithelial-mesenchymal transition (EMT) has been appeared to be a basic prepare that happens in the TME and drives certain cancer trademark characteristics. EMT is ordinarily a physiologic handle that permits a polarized epithelial cell, which regularly interatomic with storm cellular layer, to experience biochemical and cellular changes that empower it to expect a mesenchymal cell phenotype. These cellular adjustments encourage improved transitory capacity, invasiveness, raised resistance to apoptosis and significantly expanded generation of ECM components. During the last arrange of EMT, the basement membrane is debased and the upgraded mesenchymal characteristics encourage cellular movement absent from the epithelial layer. Expound atomic cascades planning translation calculate enactment, expression of particular cell surface proteins, reorganization and expression of cytoskeletal proteins, production of ECM-degrading chemicals and changes in the expression of particular microRNAs are required to total EMT. Cancer cells experience EMT to attack and metastasize. Critically, cancer cells may embrace mesenchymal characteristics to contrasting degrees, with a few cells holding a few epithelial characteristics whereas others gotten to be completely mesenchymal. The particular instruments that actuate EMT in carcinoma cells stay not completely understood.

1.6. CSCs and CTCs

The scientific community still needs to totally characterize the links between CSCs and circulating tumor cells (CTCs), which attempted to way better characterize these two subpopulations of cells in strong tumors¹. Intrigued in these cells was basically due to the plausibility of focusing on and foreseeing cancer backslide in a few tumor types. In any case, techniques created to utilize CTCs for these purposes have not succeeded. In any case, as of late created advances have opened modern conceivable outcomes with respect to these cell types, as their heterogeneity was confirmed with a next-generation sequencing-based “multiomic” approach. This approach can uncover conceivable associations between CTCs and CSCs, highlighting pathways related to tumor mediate resistance and repeat at two levels, blood and tissue. Fluid biopsy might be an successful and non-invasive approach to characterizing cancer genomic profiles; subsequently, it is vital to get it whether it can supplant tumor biopsy over time. Fluid biopsy with circulating tumor DNA (ctDNA) profiling through next-generation sequencing uncovers the real-time status of the tumor genome and modifications. It guarantees to revolutionize clinical oncology.

The most noteworthy challenge in utilizing CTCs in the clinic is the uncommon recurrence with which they are identified in fringe blood: one cell per ml. Indeed in patients with metastatic illness, as it were a few CTCs are seen. For this reason, a few methods for CTC improvement have been created. Researchers are working difficult to move forward this innovation and endeavoring conceivable ways to abuse the characteristics of tumor cells to distinguish and disconnect CTCs from all ordinary blood cells. Current strategies incorporate attractive globules conjugated with antibodies and columns for sorting EpCAM-positive cells. In any case, EpCAM is a marker of epithelial cells. Other than, the tall changeability in the expression of this surface antigen implies that numerous tumor cells do not express EpCAM, in this way lessening its run of utility. For case, this strategy cannot disconnect neuroendocrine tumors and tumors experiencing EMT. Other advances exhaust all leukocytes through choice based on a CD45 counter acting agent, dispensing with CD45+ cells. It is imperative to note, be that as it may, that there is as of now as it were one FDA-approved stage for CTC capture, to be specific, CELLSEARCH®, a framework from Menarini Silicon Biosystems that is based on attractive partition of CD45-, EpCAM+; and cytokeratin 8+, 18+ and/or 19+ cells in entirety blood. Recognizing these CTCs is related with diminished progression-free survival and by and large survival in patients treated for metastatic breast, colorectal or prostate cancer. There is, in any case, an issue related to the execution time, as 2 hours are required to prepare 8 ml of blood.

The atomic characterization of CTCs employments strategies such as fluorescent in situ hybridization, comparative genomic hybridization and RNA sequencing. These unused approaches may shed light on the oncogenic profile and metastatic potential of CTCs, uncovering data around the hereditary profiles of tumor cells, metastases and typical cells.

1.7. Tissue regeneration

MSCs are broadly dispersed in the body and play fundamental parts in tissue recovery and homeostasis⁵. MSCs can be separated from disposed of tissues, extended in vitro and utilized as therapeutics for immune system diseases and other inveterate

disarranges. MSCs advance tissue recovery and homeostasis by basically acting on resistant cells.

The multipotency property of MSCs has achieved around the world thought since of their colossal potential for immunomodulation and their restorative work in tissue recovery. MSCs can relocate to tissue damage ranges to contribute to resistant balance, emit anti-inflammatory cytokines and cover up themselves from the safe system.

Several clinical trials have detailed that both autologous and allogeneic MSCs are profitable sources for tissue shaping. Especially, autologous MSCs mean the chief sources inspected secure for organization and minimization of immunological danger, in any case of the need of detailed grievances concerning allogeneic MSC-based treatment. Concurring to the thinks about distributed so distant organization of MSCs show up to be more viable and the value of MSC treatment in bone and heart clutters, joint pain, immune system clutters and others has been broadly set up and has brought about to a few endorsements in the past.

Collectively, various considers have surveyed MSC treatments for treating a wide cluster of clutters owing to their powerful immunomodulatory and regenerative properties. Ordinary clinical signs for MSC treatment incorporate musculoskeletal repair, neurological and cardiovascular pathologies (e.g., stroke), cancer treatment, hematological and auto- or allo-immune complications (e.g., GvHD) and more as of late moreover complications related with coronavirus disease 2019 (COVID-19), such as intense respiratory trouble disorder (ARDS) and sepsis. The developing number of clinical ponders with MSCs clearly demonstrate that MSCs will have a incredible guarantee for clinical use.

1.8. Healing effects

A positive regenerative and recuperating impact was apparent after systemic or nearby treatment with MSCs⁶. Confirming the genuine nearness of these cells at the location of damage, in any case, is in some cases troublesome or unfavorably. In reality, a relationship between organization of cells and watched advancement cannot continuously be recognized. Based on this trouble of getting verification of the cells' nearness, it has been hypothesized that it is not MSCs that separate into tissue-specific develop cells, but instep emitted components, more accurately exosomes. Taking after their cell source, the MSC, these discharged exosomes bolster tissue homeostasis and rectify the courses of cell work and recovery, as required. These exercises may approve the restorative capacity of MSCs in a wide assortment of infections. Expanding numbers of MSC inquire about considers have centered on disentangling the MSC secretome, the dissolvable variables or the components discharged in EVs (Extracellular vesicle), such as exosomes and MVs (Microvesicle).

EVs comprise of subgroups (all emitted membrane-enclosed vesicles) that incorporate exosomes, ectosomes, MVs, microparticles, apoptotic bodies and other EV subsets. In a position articulation, the International Society for Extracellular Vesicles announced that there are no particular markers of EVs with which we can build up fundamental measures for distinguishing proof; the organization guessed that this is since EV emission likely changes significantly depending on the environment. In this way distant, there is no strong prove to assert that distinctive classes of EVs speak to unmistakable

organic substances. Morphology and estimate direct us to separate among different exosomes; particularly, nanospheres are composed of a lipid bilayer comparative to a liposome (40-100 nm), MVs or ectosomes are inferred from the shedding of the plasma membrane (100-1000 nm) and apoptotic bodies (1-5 mm) are discharged from the cell membrane as blebs amid apoptosis.

Similar to exosomes in common, MSC exosomes transport a composite stack that contains nucleic acids, proteins and lipids. Special quality items number 857 and more than 150 microRNAs (miRNAs) have been distinguished, in spite of the fact that whether this assorted substance is carried by one select sort of exosome or is part inside diverse sorts of exosomes has however to be determined.

2. Conclusion

Mesenchymal stem cells are utilized in preclinical and clinical inquire about as a potential treatment for various diseases of different organ frameworks, where they appear promising comes about. Mesenchymal stem cells, which can not as it were recover harmed tissues, but also emit various signaling particles. Much obliged to various logical considers, the complex atomic instruments behind the activity of stem cells are progressively caught on. This progressed shape of treatment is based absolutely on this natural insights of cells, i.e. a framework that can recognize harm, communicate with encompassing cells and start the handle of common renewal.

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