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Expert Opinion

What's in a Name?

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Dear Editor:

In the late 1980s, I coined the name "mesenchymal stem cell" (MSC) to provocatively emphasize that multi-lineage progenitor cells could be isolated and culture-expanded from human adult bone marrow.[1,2] The studies from our lab and others provided the basis for the hypothesis diagram pictured in Figure 1.[2,3] The appropriate acronym, MSC, was generally accepted, and the use of this term eventually resulted in a consensus paper that further strengthened the use of MSC for this class of cells.[4]

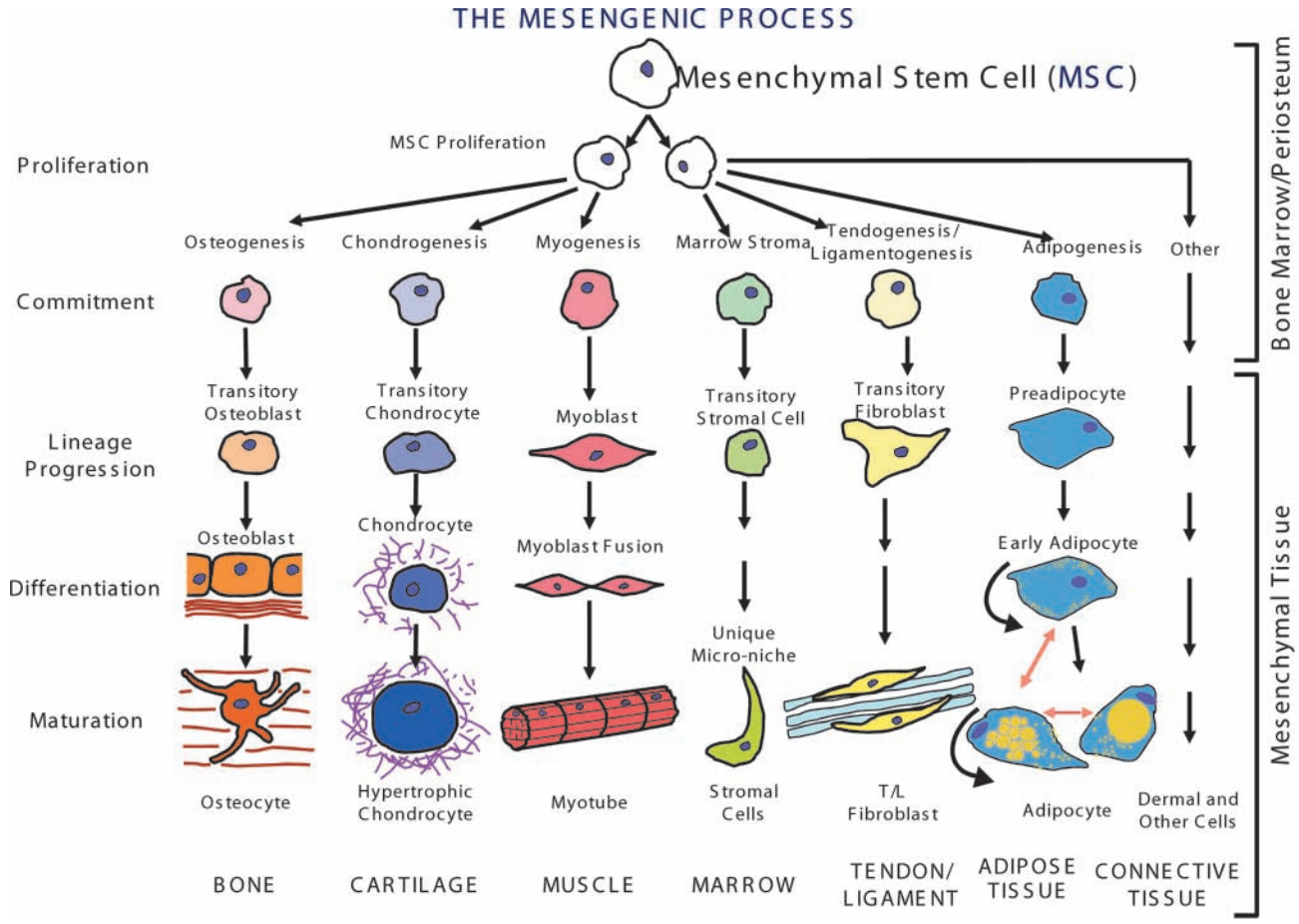

FIG. 1. Mesengenic process: This diagram was originally structured after the hematopoietic lineage diagrams available in the late 1980s, although the original diagrams were based on concepts developed in the 1960s. The MSCs can be induced to enter various mesenchymal lineage pathways to eventually differentiate into end-stage cell types that fabricate various tissues such as bone and cartilage. The Mesengenic process diagram was originally constructed from left to right based on our detailed understanding of the osteogenic lineage and the least information on the right (although the new diagram pictured here integrates newer information into the diagram). Clearly, the lineages are important for tissue engineering uses of MSCs, while the regenerative medicine uses involve the MSCs themselves. MSCs, mesenchymal stem cells.

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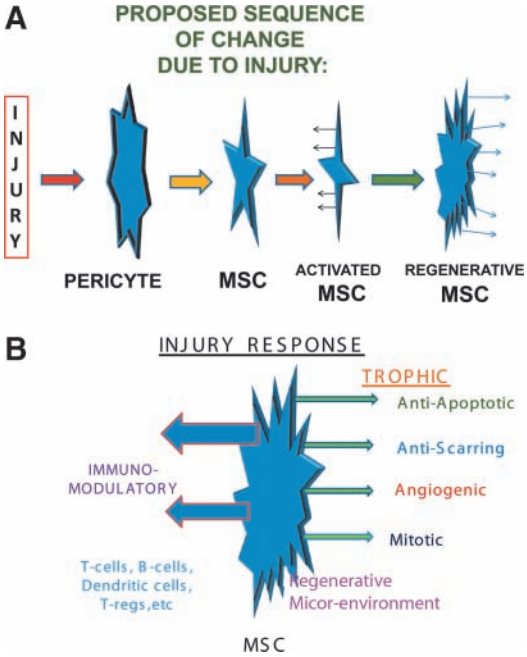

FIG. 2. Injury response: (**A**) Pericytes that reside on the ablumenal surface of blood vessels are released upon vessel damage or inflammation to provide activated MSCs. (**B**) The activated MSC secretes bioactive molecules[12] that are immunomodulation[10,14] and serve to protect ischemic or injury sites from immunosurveillance and thus provide a barrier for protecting against the invitation of autoimmune reactions. Also, the MSCs secrete agents that are trophic[11] which contribute to establishing a regenerative microenvironment.

Two important recent pieces of information strongly argue that I should rename the MSC. First is the realization that this class of cells can be isolated from almost every tissue in the human body. The central connecting aspect to explain this fact is that all of these tissues are vascularized and that every blood vessel in the body has mesenchymal cells in abluminal locations. These perivascular cells can be summarily called pericytes, and, indeed, when cells are fluorescent activated cell sorting (FACS) analyzed for pericyte markers (e.g., CD146) these co-localize with MSC markers (e.g., CD105).[5,6] This led me to suggest that "all MSCs are pericytes."[7] The opposite is not correct, that all pericytes are MSCs, since some pericytes exhibit highly specialized characteristics and do not exhibit MSC multipotency properties.

The second issue is that MSCs are being used therapeutically because they home to sites of inflammation or tissue injury[8] and they secrete massive levels of bioactive agents[9] that are both immunomodulatory[10] and trophic[11] as depicted in Figure 2.[12] Indeed, these powerful therapeutic capacities have absolutely nothing to do with the fact that MSCs are able to differentiate in a lineage sequence into several different end-stage mesenchymal cell types as pictured in Figure 1. The use of human MSCs in both xenogeneic[13] and allogeneic infusions (e.g., see Osiris Therapeutics, Inc., Web site for results from clinical trials, www.osiristx.com/.) to cure various disease states or injury situations has been clearly documented.[12–15] In this regard, I would suggest that MSCs are powerful site-regulated DRUG STORES or dispensing sites that may serve as modulatory or curative agents for a variety of human maladies.

Since the multipotency of MSCs is not the key aspect for their current therapeutic use, I herein propose a name change:

MSCs = Medicinal Signaling Cells

This clearly separates these cells from the stem cell category and focuses their name on their current therapeutic use. I point out for the sake of completeness that neural stem cells and hematopoietic stem cells are also immunomodulatory and trophic in ways similar to, but distinct from, MSCs.

What's in a name: both knowledge and ignorance in that we now appreciate the strong therapeutic potential of MSCs (knowledge) and I now confess my previous ignorance about their immunomodulatory and trophic potentials. The new name is sensitive to the old literature and history and is more descriptive of the current use and our meager understanding of how MSCs function at sites of tissue inflammation, disease, or injury. The multipotency of MSCs is still an important aspect of tissue engineering strategies, although the powerful immunomodulatory and trophic functions of MSCs must be more comprehensively considered.[15]

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