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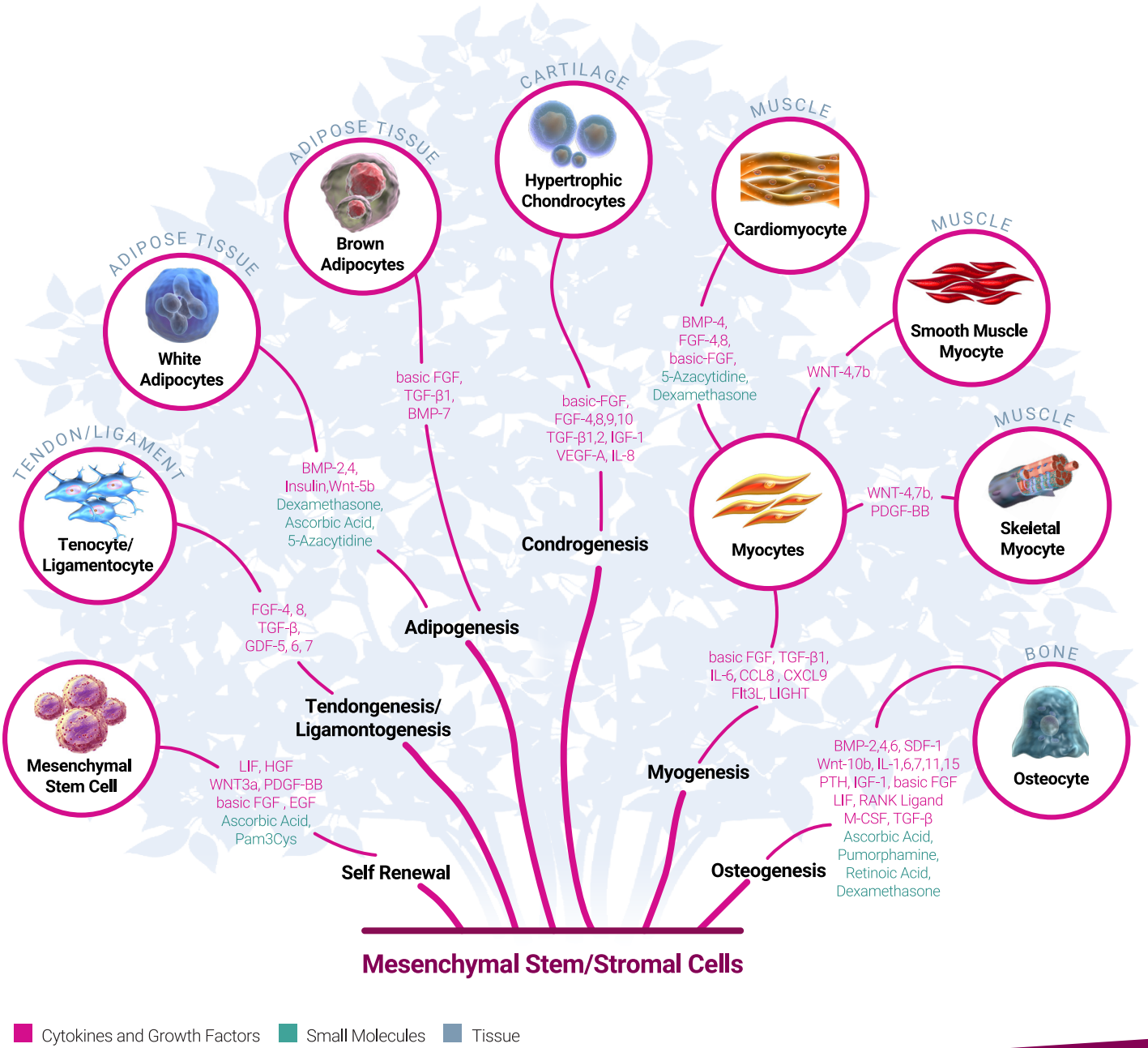
Mesenchymal Stem/Stromal Cells

Mesenchymal stem cells (MSCs), also known as mesenchymal stromal cells, are currently defined as self-renewing, multipotent cells, which can differentiate *in-vitro* into adipocytes, chondrocytes, and osteocytes. They must express the surface markers CD105, CD73, and CD90, while at the same time lack the expression of CD45, CD34, CD14, CD11b, CD79α CD19, or HLA-DR.

MSCs can be isolated from a variety of sources, including amniotic fluid, placenta, umbilical cord blood, dental pulp, synovial fluid, and urine; however, bone marrow- and adipose tissue-derived MSCs have been the most extensively studied. Wharton's Jelly, which is found in the umbilical cord extracellular matrix, has recently been identified as a new source of MSCs. In light of some special features these cells possess, they hold great promise for regenerative purposes.



Mesenchymal Stem/Stromal Cells (continued)

Although they share some common features, MSCs retain a wide variability in terms of differentiation and regenerative capabilities depending on the tissue of origin. Recent studies suggest that MSCs are not of a uniform lineage, but are instead tissue-specific stem/progenitor cells.

Originally MSCs were hypothesized to migrate to inflamed tissues where they have since become engrafted and differentiate to eventually regenerate damaged cells. However, numerous studies demonstrated that duration, and number of cells engrafted do not sufficiently explain the significant regenerative effects observed; suggesting the involvement of other mechanisms.

The present notion is that, in addition to replacing damaged cells at sites of injury, MSCs also act to repair damaged tissues by rescuing dying cells through cell fusion, secreting cytokines and growth factors, transferring mitochondria through tunneling nanotubes, and transferring mRNA and miRNA via extracellular vesicles, such as exosomes or microvesicles. In different settings certain mechanisms tend to be more relevant than others.

MSCs possess several characteristics that make them an attractive tool for cell and regenerative therapy: including, the ability to differentiate into various cell types; an enhanced proliferation rate; the ability to escape immune recognition and to modulate immune functions; the ability to secret a wide array of soluble factors; and the capacity to migrate to injured sites. In addition, they do not raise the ethical and safety concerns generally associated with embryonic stem cells and induced pluripotent stem cells.

Currently, there are over 800 MSC-based clinical trials underway that focus on evaluating the therapeutic potential of MSCs in a variety of diseases, including Graft Versus Host Disease (GVHD), bone, cartilage, cardiovascular, lung, liver, neurological, hematological and inflammatory. These ongoing clinical trials, along with future research support the promise of MSC therapy. However, before MSC therapy can become an accepted therapeutic procedure, issues such as donor heterogeneity, *ex vivo* expansion, immunogenicity and cryopreservation, as well as determining the precise mechanisms of action, would need to be addressed.

References:

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