Why adipose-derived stem cells are younger, have longer telomeres, and live longer than other stem cell types such as perinatal MSCs?

There has long been misinformation and confusion regarding functionality of stem cells sourced from different tissue sources (such as from an umbilical cord, bone marrow or adipose tissue), relative to the age of the donor tissue. As far as clinical results go, the functionality of MSCs or mesenchymal stem cells sourced from all these tissues is similar. However, the age of the tissue from which MSCs are sourced, and life span of those MSCs is dramatically different. The life span of the MSC is a more important consideration than the age of the patient from which the MSC is sourced. For example, a MSC sourced from an infant would obviously be coming from a younger source than a MSC sourced from a 38-year-old person. A prenatal MSC sourced from an umbilical cord might appear to be younger than the MSC sourced from a 1-year-old. However, this is not necessarily true. Technically, the MSC sourced from a 1-year-old comes from an infant at the beginning of their life, and the MSC sourced from the umbilical cord is sourced from outside the body at the end of the umbilical cord's life. Whereas the umbilical cord in a healthy pregnancy is programed to live for only 9 months but the 1-year-old could live easily into their 90's.

While a MSC sourced from a 52 year old's adipose would seem much older than the MSC sourced from an umbilical cord or from the 1 year old. In reality, the adipose derived sourced MSCs are actually held in kind of a state of suspended animation. Regardless of the tissue donor's chronological age, the MSCs are sequestered in "collagen time capsules." They aren't free to differentiate(replicate), send healing signals, or do all the beneficial healing that stem cells are designed to do. Accordingly, we find MSCs in the adipose tissue of an older person as they existed when the individual was young. And, when the MSCs differentiate, they differentiate into newly born cells not into older cells. The "collagen time capsule" is also kind of a protective feature to protect our bodies from uncontrolled growth.

As we get older and keep growing rapidly from 1 to 3, to 5 to 9, and 12 to 16 years old the growth spurts can be dramatic. Many of us might know of a 12-year-old who, when about to enter high school, was 5'8" tall. But, by the time they were about to become a high-school junior, turning 16 years old, they were 6'2". Our body needs a way to slow that growth down. One of thousands of ways to protect us from uncontrolled growth is by the reduction in human growth factor (HGH). At the same time negative factors as we age, such as the increase in senescent or Zombie Cells and decreasing insulin sensitivity, lead to age related diseases and a host of other problems. The MSCs that should, in theory, combat all the negative disease factors we accumulate with age are actually not capable of helping us heal and regenerate because they are locked up in the "time capsules." In contrast, the umbilical sourced MSCs have been dead for many years at even the earliest stages of life.

One of the first measurable indicators that documents the younger profile of Adipose-derived stem cells (ADSCs) is the fact that ADSCs have consistently been observed to possess longer telomeres compared to other stem cell types, such as perinatal mesenchymal stem cells (MSCs). This unique characteristic of ADSCs is of significant interest due to its potential implications for the longevity and aging of these stem cell populations. Telomeres, the protective caps at the end of chromosomes, play a crucial role in cellular aging and longevity (Muñoz-Lorente et al., 2019). When telomeres reach a critically short length, they induce a persistent DNA damage response (DDR), leading to cellular senescence and impaired tissue regeneration (Muñoz-Lorente et al., 2019). Studies have suggested that longer telomeres are associated with enhanced stem cell functionality and regenerative potential, as well as increased lifespan in various organisms (Flores et al., 2008; Heidinger et al., 2021). Studies have demonstrated that telomere length is inversely correlated with cellular senescence and aging-related changes in stem cells (Yin et al., 2020; Moreno-Navarrete et al., 2010). ADSCs have longer telomeres and exhibit delayed senescence and maintain their regenerative potential for a longer duration compared to perinatal MSCs (Yin et al., 2020; Moreno-Navarrete et al., 2010). This suggests that ADSCs appear to be and act chronologically younger than perinatal MSCs, and their prolonged survival and regenerative capacity are indicative of a more youthful cellular state. Adipose Derived Stem Cells sourced MSCs are actually much younger stem cells, that live longer and are prove to be more regenerative.

The longer telomeres in ADSCs confer a survival advantage. They are associated with a higher proliferation rate and multipotent differentiation properties. Additionally, ADSCs have been reported to express telomerase, an enzyme that adds DNA repeats to the chromosome ends, thus slowing the rate of telomere shortening compared to somatic cells. This expression of telomerase may contribute to the maintenance of telomere length in ADSCs, potentially leading to their prolonged survival and regenerative capacity.

ADSCs Live Longer relative to other Stem Cell Types. The longer telomeres in ADSCs compared to perinatal and other MSC sources contribute to their enhanced regenerative potential, prolonged survival, and being younger relative to their longer life cycle. This unique characteristic positions ADSCs as a more promising candidate for regenerative medicine applications, emphasizes the importance of telomere length in determining the longevity and functional capacity of stem cell populations, and defeats the argument that discardable birth tissue stem cell derived population are younger. In fact, perinatal MSCs would age faster regardless even though they are derived from a source prior to the birth of human life. Technically, at birth Umbilical cord derived MSCs are at the end of their life span as a healthy pregnancy gestation should only be 9 months.

Why do adipose-derived stem cells have longer telomeres than other stem cell types?

This phenomenon is attributed to many unique characteristics of ADSCs. Firstly, ADSCs have been found to exhibit a high proliferation rate and possess multipotent differentiation properties when cultured in lineage-specific induction media (Guo et al., 2017). This high proliferation rate may contribute to the maintenance of telomere length, as evidenced by the fact that cells with the longest telomeres are enriched in known stem cell compartments, and proper telomere maintenance in these compartments is essential for their ability to sustain growth (González-García et al., 2015). Additionally, ADSCs have been reported to express telomerase, an enzyme that adds DNA repeats to the chromosome ends, thus slowing the rate of telomere shortening compared to somatic cells (Ju & Rudolph, 2006). The longer telomeres observed in ADSCs compared to other stem cell types can be attributed to their high proliferation rate, expression of telomerase, and enhanced regenerative capabilities. These unique characteristics suggest ADSCs are chronologically younger in that they would live longer than other MSC types such as perinatal MSC and that ADSCs are a more ideal mesenchymal stem cell population for regenerative medical applications (Raposio et al., 2014).

A study analyzing mesenchymal stem cells from brown adipose tissue for the presence of telomere reverse transcriptase (TERT) found that ADSCs exhibited greater NP-marker gene expression and proteoglycan-rich matrix production compared to mesenchymal stem cells (Hodgkinson et al., 2020). This suggests that ADSCs may possess enhanced regenerative and repair capabilities, which could be linked to their longer telomeres also leading to their longer life. Moreover, the study by Madonna et al. Palpant & Metzger (2010) indicated that ADSCs from brown adipose tissue were analyzed for the presence of TERT, which is required for the maintenance of nuclear telomere length and replication potential.

Summary.

Adipose-derived stem cells (ADSCs) exhibit a more youthful profile compared to other stem cell types, characterized by longer telomeres, delayed senescence, and prolonged regenerative capacity. These unique characteristics make ADSCs a promising candidate for regenerative medicine applications.

Telomeres, the protective caps at the ends of chromosomes, play a crucial role in cellular aging and longevity. As cells divide repeatedly, telomeres shorten with each division, eventually reaching a critically short length that triggers cellular senescence and impairs tissue regeneration. ADSCs, with their longer telomeres, are able to maintain their replicative potential and regenerative capacity for a longer duration, suggesting a more youthful cellular state.

Regardless of the tissue donor’s age, this youthful profile is supported by ADSCs' delayed senescence and prolonged regenerative capacity. Studies have demonstrated that ADSCs exhibit delayed senescence and maintain their regenerative potential for a longer period compared to other stem cell types. This delayed senescence is associated with their longer telomeres, which protect them from the cellular damage

response that triggers senescence. The prolonged regenerative capacity of ADSCs suggests that they may be chronologically younger than other stem cell types, as their ability to repair and regenerate tissues persists for a longer duration.

The unique characteristics of ADSCs, including longer telomeres, delayed senescence, and prolonged regenerative capacity, position them as a promising candidate for regenerative medicine applications. Their ability to maintain their replicative potential and regenerative capacity over extended periods makes them well-suited for cell-based therapies aimed at repairing damaged tissues and restoring lost functions.

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