**WJ-MSCs mitochondrial transfer: A cure and a risk**

By Kristiane Polido

There has been an increasing body of research regarding the use of Wharton jelly-derived mesenchymal stem cells (WJ-MSCs) to recover from cell injury and tissue degeneration caused by mitochondrial damage. As such, WJ-MSC mitochondrial transfer becomes a pharmaceutical target for tissue repair and cancer therapy. However, this does not come without possible risks, and an important one to note is the potential for growth and proliferation of cancer cells[1].

**Recapturing lost mitochondrial function**

One of the first studies to use WJ-MSCs as mitochondrial donors is by Lin et al. (2015) wherein they identified the novel role of WJ-MSCs in transferring mitochondria to cells with dysfunctional mitochondria[2]. The resulting combination revealed that the recipient cells have replenished mtDNA, expression of mtDNA-encoded proteins, normalized respiratory function, boosted cellular bioenergetics, and OXPHOS-dependent cellular growth and motility. Moreover, the results also demonstrated that mitochondria-related functions remained active after at least 45 passages in 139 days, suggesting that the method used can sustain the therapeutic effect of mitochondrial transfer.

**Potential treatment for stroke and ischemic diseases**

A study by Russo et al. (2020) involving the analysis of metabolic energy profiles[3] of different MSCs (perivascular, cord lining, and Wharton's jelly) showed that the MSCs were able to adapt and survive in a hypoxic and glucose-deprived environment. The study had three major objectives: 1) to establish the energy metabolism profiles of the three MSC populations, 2) to regain the mitochondrial function, and 3) to observe the survival capability in both normal and ischemic conditions. Russo et al. (2020) were successful in demonstrating the adaptive capacity of the MSCs to ischemic environments by subjecting the MSCs to a cell viability test under stroke conditions.

**Mitochondrial transfer supports tumor growth and proliferation**

Results from mitochondrial transfer have been promising, but there are emerging studies that have effects that are not as desirable such as the promotion of growth and migration of cancer cells[4].

A study in 2016 by Vulcano et al. investigated whether WJ-MSCs affect the proliferation of validated lung cancer stem cells (CSCs)[5]. The study found out that similar to its bone marrow counterpart, WJ-MSCs have different effects on different tumors. The results show that WJ-MSCs have a contrasting effect on adenocarcinoma- and squamous cell carcinoma-lung cancer stem cells (LCSC). This is the first study to show that WJ-MSCs increase the proliferation of LCSC that are derived from adenocarcinoma. On the other hand, WJ-MSCs inhibited the cell growth of LCSC derived from squamous cell carcinoma when observed in vitro, but do not have the same effect in vivo.

The role of Wharton's Jelly derived mesenchymal stem cells in cancer research is currently under debate. On one hand, the studies supporting its use for regaining the lost mitochondrial functions of cells promise great benefits. However, the studies claiming that the WJ-MSCs effect on the increased growth and proliferation of lung cancer cells cannot be taken lightly. More studies on this matter, such as an in-depth investigation that is designed to understand the molecular mechanisms that work behind the effects of WJ-MSCs on various LCSC subtypes, will help settle if this promising new cancer therapy is indeed beneficial or not.

**References**

1) Li C, Cheung MKH, Han S, et al. Mesenchymal stem cells and their mitochondrial transfer: a double-edged sword. *Biosci Rep*. 2019;39(5):BSR20182417. Published 2019 May 3. doi:10.1042/BSR20182417

2) Lin HY, Liou CW, Chen SD, et al. Mitochondrial transfer from Wharton's jelly-derived mesenchymal stem cells to mitochondria-defective cells recaptures impaired mitochondrial function. *Mitochondrion*. 2015;22:31-44. doi:10.1016/j.mito.2015.02.006

3) Russo E, Lee JY, Nguyen H, et al. Energy Metabolism Analysis of Three Different Mesenchymal Stem Cell Populations of Umbilical Cord Under Normal and Pathologic Conditions. *Stem Cell Rev Rep*. 2020;16(3):585-595. doi:10.1007/s12015-020-09967-8

4) Bergfeld SA, DeClerck YA. Bone marrow-derived mesenchymal stem cells and the tumor microenvironment. *Cancer Metastasis Rev*. 2010;29(2):249-261. doi:10.1007/s10555-010-9222-7

5) Vulcano F, Milazzo L, Ciccarelli C, et al. Wharton's jelly mesenchymal stromal cells have contrasting effects on proliferation and phenotype of cancer stem cells from different subtypes of lung cancer. *Exp Cell Res*. 2016;345(2):190-198. doi:10.1016/j.yexcr.2016.06.003