Looking for a cure to Spina Bifida using different mesenchymal stem cell sources

By Scott Walker

If you've ever known a person with Spina Bifida, the words may conjure up images of them unable to walk without the use of metal leg braces or crutches. If this person had a severe form of the disease, you also know about the excess cerebrospinal fluid that can build up until it has to be drained from their head by a shunt.

Spina Bifida is a birth defect caused by impaired development of the spinal cord. When the spinal cord develops normally, a flat layer of cells forms a closed tube (just imagine rolling up a piece of paper into a tube – same thing). In people with spina bifida, the tube does not close all of the way. This so called "neural tube closure defect" causes damage to neurons within the spinal cord. Death of spinal cord neurons can lead to paralysis and a deadly condition known as hydroencephalus in which fluid accumulates on the brain and has to be drained through an implanted shunt. Severe cases can also cause a portion of the spinal cord to jut out of the newborn baby's back.

A cutting edge new surgical treatment seeks to cure this congenital disease before it can inflict any of these horrors. This treatment would use stem cells derived from a baby's own placenta. (Placenta develops from the same early embryonic cells that the actual embryo does, so they carry the same genetic make-up).

Figure 1: The left spina bifida sheep received a control with no stem cells. The sheep on the right was treated with P-MSCs and is able to walk. This experiment was previously performed in the Wang lab[2].

A routine in utero diagnostic procedure can be used to safely harvest a small piece of placental tissue from the pregnant mom. The placenta is a rich source of specific types of adult stem cell called the Placental Mesenchymal Stem Cell (P-MSC). It turns out that P-MSCs can repair neurons in the spinal cord without directly replacing them.[2]

The hope is that a baby's spinal cord could be repaired using the amazing regenerative properties of these cells while the baby is still in the womb.

P-MSCs act as little cell factories by constantly pumping out a veritable plethora of proteins signal to nearby cells to thrive and grow[1]. These proteins can even suppress the immune system, which can reduce potentially harmful inflammation and promote the growth and survival of surrounding cells.[3] . A truly unique and powerful ability; P-MSCs do not actually become part of the tissue. They act for a few weeks to a month before disappearing forever, but it is all the time they may need to provide life-changing benefits for countless unborn babies.

It turns out the placenta is not the only safe way to obtain an MSC from a developing baby. The amniotic fluid that constantly bathes the unborn baby is also rich with MSCs. These MSCs are called amniotic fluid MSCs or AF-MSCs.

Amniotic fluid samples large enough to isolate cells from can be obtained using another common in utero diagnostic test called amniocentesis. Much like members of a family, while P-MSCs and

AF-MSCs may share a name and look similar, it is possible for them to behave very differently. It could be that AF-MSCs are even more effective at healing damaged spinal cord neurons and would serve as a more potent treatment for spina bifida.

Comparing these two different cell types was the focus of my work in the laboratory of Dr. Farmer and Dr. Wang at University of California, Davis –Department of Surgery.

Direct comparison of two cell types can be challenging because if the cells come from different donors, they would naturally have genetic differences (all people have different genetic profiles).. Thankfully, in our study we were able to obtain both MSC types from a single donor, eliminating all the genetic variation that occurs between different people's cells.

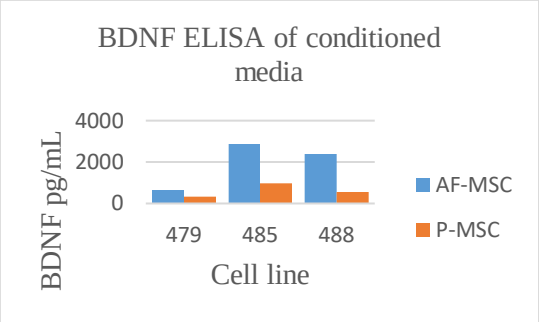

Figure 2: Levels of BDNF secreted by both AF-MSC and P-MSC adjusted for cell number, AF-MSCs have much higher secretion.

Cells isolated from different tissues may be very different from each other in several important protein messages, chief among them being factors called:

- Brain Derived Neurotrophic Factor (BDNF)
- Hepatocyte Growth Factor (HGF)
- Vascular Endothelial Growth Factor (VEGF)

VEGF and HGF may help regenerate vascular tissue (think blood vessels) and promote formation of new blood vessels. Our research showed that AF-MSCs secrete almost no VEGF or HGF.

BDNF is critical for development and function of neural tissue and, therefore, may be instrumental for neuron protection in the aforementioned surgical intervention for spina bifida. Our work showed that AF-MSCs make almost three times as BDNF than P-MSCs!

Future experiments are needed to definitively measure which MSC is better equipped to functionally protect ns from dying, but this research has certainly helped clarify how MSCs function to regenerate tissue. This could translate into important real world applications for difference source MSCs in the treatment of spina bifida.

We are hopeful our findings will ultimately help provide successful and safe regeneration of neurons in fetuses that would otherwise be born with spina bifida.

References

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