

EVs and You: Delivered Hot and Ready, or Your RNA is Free!

By Ryan Stagnaro

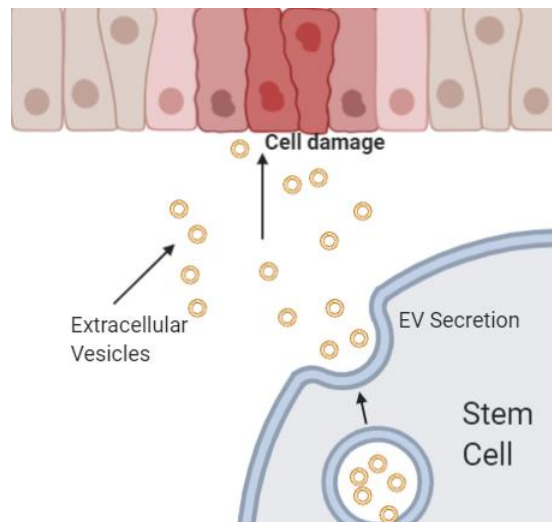
Shelter-in-place living during a global COVID19 pandemic is frustrating, for more reasons than one. And the worst part? The time of year that it started. Allergy season. Even now my roommates are keeping their distance due to my runny nose and teary eyes. This could all be easily fixed if I just had some more allergy medication; however, that's not so simple when you're trying to limit the number of trips you make to the store to every other week. Maybe if I put in a special order for the medication online and have it delivered? Perhaps then I can get rid of these allergies and my roommates will stop shunning me for fear that I have COVID19? Done, I've ordered the anti-inflammatory medication, now I just need to wait for the delivery person...

Pandemic or not, most of us have been in a situation similar to this, worrying about pollen and other outside allergens. Unfortunately, some people have to worry about more than just having a mistaken immune response to particles floating in the air, as they have mistaken immune responses to their own body. This is an autoimmune condition, which afflict an estimated 23.5 million people in the United States alone. Many autoimmune conditions, such as multiple sclerosis (MS), can lead to devastating permanent damage. When someone has a disease like MS their own immune system begins to see itself as a threat. MS is like an allergy, but instead of your body reacting to the pollen in the air or the shrimp in your food, it is reacting to parts of your own cells. In the case of multiple sclerosis, your body mounts an immune response to parts of your nervous system, which leads to extensive damage and potential paralysis. In order to treat this type of illness, we need to both calm down the immune system, and repair the damage that was caused.

If only the cells impacted by MS could put in a special order for some anti-inflammatory particles from mesenchymal stromal cells!

Mesenchymal stromal cells (MSCs) are the coolest stores on the block in the stem cell biology community. These cells act as a sort of support system that provides helpful factors dedicated to healing, repairing, and keeping your cells active—similar to how a store can provide whatever you need to live and thrive. Studies indicate that MSCs release healing and anti-inflammatory factors to calm down the immune system and prevent more damage to affected tissue, which could help individuals with MS.

Unfortunately, MSCs are large, and although they have a ton of useful particles available, their size makes them slow and inefficient at delivering these helpful molecules. Especially given that like this quarantined student, most cells can't leave their home and need to wait patiently for their delivery.



Luckily, MSCs provide healing and anti-inflammatory factors similar to the way you can receive antihistamines from Amazon, through a package in the mail.

Extracellular Vesicles (EV) are microscopic packages of helpful particles that are produced by MSCs to be given to cells as a supporting mechanism. These EVs allow MSCs to heal surrounding cells and prevent damage as seen in the image to the right. Scientists have found that they are able to harvest these EVs straight from a sample of MSCs. These EVs are very similar to a cardboard box delivered to your doorstep, but instead of a doorstep, they are delivered directly to the cells in need.

Past research has shown that injection of MSCs into an animal reduces damage and inflammation resulting from autoimmune diseases. New studies being performed suggest that injecting a patient with EVs derived from MSC have an even more robust positive influence on the afflicted tissue when compared to injection of whole MSCs.

Treatment of autoimmune diseases are tricky, but using small EV packages instead of using larger slower MSCs will allow for much greater efficiency in delivering what the cells need. Scientists have demonstrated that EVs are able to deliver their helpful particles anywhere in the body to help combat debilitating issues such as autoimmune inflammation and cell death.

When it comes to autoimmune and inflammatory diseases, every minute counts, and EVs will make sure your delivery arrives quickly. “Delivered hot and ready, or your RNA is free!”

References

Clark, K. *et al.* Placental Mesenchymal Stem Cell-Derived Extracellular Vesicles Promote Myelin Regeneration in an Animal Model of Multiple Sclerosis. *Cells* **8**, (2019).

Kao, C.-Y. & Papoutsakis, E. T. Extracellular vesicles: exosomes, microparticles, their parts, and their targets to enable their biomanufacturing and clinical applications. *Curr. Opin. Biotechnol.* **60**, 89–98 (2019).

Shi, Z., Huang, H. & Feng, S. Stem cell-based therapies to treat spinal cord injury: a review. *Jnanabha* **5**, 125–131 (2017).

Wang, A. *et al.* Placental mesenchymal stromal cells rescue ambulation in ovine myelomeningocele. *Stem Cells Transl. Med.* **4**, 659–669 (2015).

Yamout, B. *et al.* Bone marrow mesenchymal stem cell transplantation in patients with multiple sclerosis: a pilot study. *J. Neuroimmunol.* **227**, 185–189 (2010).