A Cure For Osteoarthritis: Next Generation Mesenchymal Stem Cells
By Andrew Ciccheto

Sadly, the odds are not in your favor. Data indicates that once you turn 65 you have more than a 60% chance of developing osteoarthritis (OA)[1]. If you are already over 65, I imagine you are likely nodding your head in unfortunate agreement.

OA is a debilitating disease that causes joint pain brought on by chronic inflammation and cartilage degeneration that worsens with time. People suffering from OA deal with pain on a regular basis. Can you imagine simple tasks like walking the dog or grocery shopping being dreaded, painful undertakings? Or a more extreme example: can you imagine not being able to run to safety in the event of an emergency? You should not be shrugging your shoulders in apathy at these examples; remember that you and your loved one have a greater than 1 in 2 chance of being faced with these scenarios later in life. Something must be done about this devastating, painful disease.

So what's the cure? It seems that for such a pervasive disease, surely there would be some medical remedy. Unfortunately, the only treatment options currently available are pain medications or, in more severe cases, surgical replacement of the arthritic joint.

However, exciting new research indicates mesenchymal stem cells (MSCs) may be the answer to treating OA. These incredible cells have been termed the *paramedics of the body* for their ability to modulate the immune system and regenerate damaged tissue, which are two prominent targets of OA. MSCs produce a variety of molecules to activate the body's own healing machinery. In some cases, MSCs permanently engraft in the patient and differentiate (i.e., develop) into bone or cartilage thereby replacing lost tissue. Significantly, clinical trials of MSCs have shown their unwavering safety; there have been no deleterious consequences of MSC transplantation into human patients[2]. However, effectiveness of MSCs has been inconsistent across human studies, likely due to the inherent variability of living cells.

To solve the variability problem, modified (and unharmful) viruses have been used to deliver genes of therapeutic interest into MSCs. Viruses have naturally evolved to put genetic information into host cells (usually causing disease), but now we have learned how to use them to put beneficial DNA into the host genome (instead of disease-causing DNA). This, in essence, allows the recipient cells (MSCs) to produce medication in a reliable fashion.

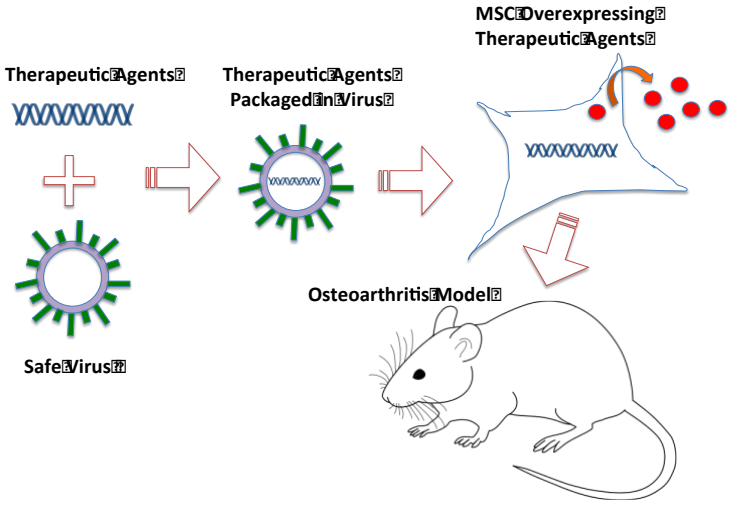

Figure 1. Using virus to deliver therapeutic genes to MSCs, in turn making them more potent for OA treatment.

We used this virus-delivery mechanism to supply MSCs with genes coding for important anti-inflammatory proteins and a cartilage growth factor to increase MSC therapeutic potency. These superior *Next Generation MSCs*, as scientists are calling them, represent a cutting-edge combined cell and gene therapy platform that is showing promise as an OA treatment option.

But not so fast! Genetic manipulation of MSCs requires additional studies to ensure their acclaimed safety profile is retained post-modification. When viruses deliver genes to cells, they insert the genes at random locations in the host cell DNA. If this random gene insertion was to occur in the middle of another important gene within the MSC DNA, it could have dire consequences. It turns out the odds of this happening are very low, but we must be comprehensive in our testing to ensure MSCs meant for improving health do not do the opposite. Therefore, a battery of experiments have been conducted to demonstrate that the MSCs are still behaving normally (aside from the intended changes).

Our experiments evaluating MSC growth, shape and size show that the cells appear and function as expected. We have also measured the level of therapeutic gene expression, much like gauging the dose of medicine needed to treat a disease. This assessment will allow for a calculated drug delivery system when using our *Next Generation MSCs* to treat OA.

We have also used functional experiments that have validated the exaggerated immune suppression capabilities of *Next Generation MSCs* - an important aspect of OA treatment. White blood cells (the same ones that cause OA) were limited in their ability to grow and promote inflammation. The genes inserted into MSCs by the virus were responsible for accomplishing this task; unmodified MSCs were much less effective.

Next, we investigated the ability of *Next Generation MSCs* to make cartilage. It seems that the genetic modification does in fact help MSCs turn into cartilage! Production of new cartilage could help rebuild the cartilage that has been lost in OA patients.

Could it be that *Next Generation MSCs* are the answer to one of the world's most prominent musculoskeletal diseases? We will find out once this technology moves to first-in-human clinical trials. Stay tuned.

References:

1. Lawrence, R. C., Felson, D. T., Helmick, C. G., Arnold, L. M., Choi, H., Deyo, R. A., . . . National Arthritis Data, W. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum, 58(1), 26-35. doi: 10.1002/art.23176

2. Barry, F., & Murphy, M. (2013). Mesenchymal stem cells in joint disease and repair. Nat Rev Rheumatol, 9(10), 584-594. doi: 10.1038/nrrheum.2013.109