2017

Is Stem Cell Transplantation a Practical Treatment for Macular Degeneration?

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A Thesis Submitted to Fulfill the Requirements of the Honors Program at Assumption College

April 2017

Introduction

Macular degeneration is a relatively newly identified eye disease that has been causing the loss of vision in people for ages. The disease is defined as the deterioration of the macula, which is the central part of the retina. The retina consists of a layer of cells that lines the back and peripheral areas of the eye. These cells are called photoreceptors. They receive stimuli from light and send electrical signals to the brain via the optic nerve, allowing humans to see and perceive the world through their eyes. There are two types of photoreceptor cells: rods and cones. Rods are used to detect low light levels whereas cones are used to detect high light levels and color (31). The macula is made up of both rods and cones. The cone cells are located in a specialized part of the macula called the fovea. These photoreceptor cells allow humans to focus their vision, see in color, and see in detail (1). If the cells in the macula die, then vision is lost. Figure 1 provides a diagram of the human eye and its individual parts (14).

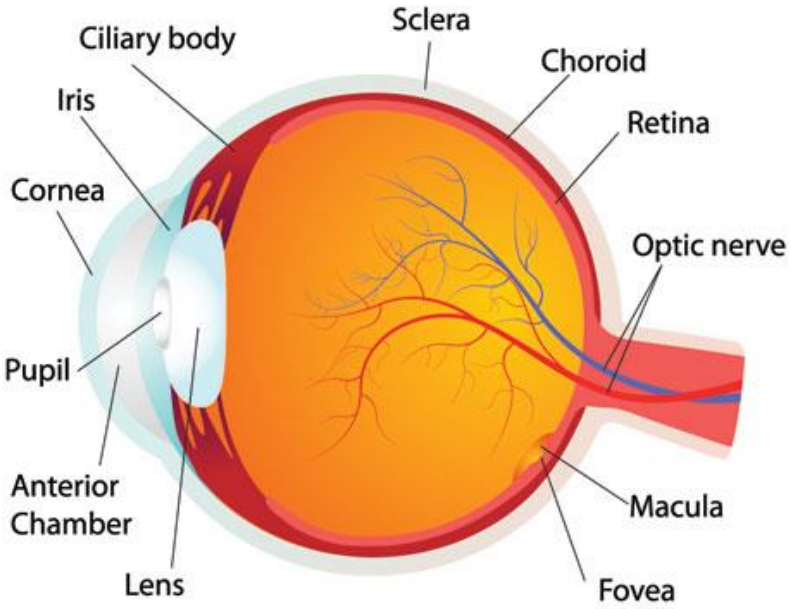

Figure 1 Diagram of the human eye (14)

Macular degeneration comes in two forms: Stargardt disease macular degeneration and age-related macular degeneration (AMD). Stargardt disease is a specific type of macular degeneration because it is genetic and affects children and adolescents (1). It is caused by a recessive mutation that ultimately causes the deterioration of retinal cells. Stargardt disease is vastly less frequently seen than AMD and only appears in one out of 20,000 children or adolescents (1).

AMD is the predominant version of macular degeneration. It currently affects 1.75 million Americans and that number is predicted to increase to 3 million by 2020 with the baby boomer generation reaching ages over 55 years old (4). AMD is caused by the aging process, and adults over the age of 55 are at an increased risk of developing macular degeneration in their lifetimes. There are two types of AMD: dry and wet.

Dry AMD is caused by the thinning of the macula due to drusen pockets that form underneath the retina. Drusen is characterized as the accumulation of extracellular aggregates, such as proteins, lipids, and autofluorescent cellular waste products either in between the Retinal Pigment Epithelial (RPE) monolayer and the membrane attached to it known as Bruch's membrane, or in the subretinal space in between the RPE monolayer and the photo-receptors of the retina (2, 31, 33, 38). The anatomy of the eye consists of the retinal layer of photoreceptor cells, whose outer segments interact with the RPE monolayer across the subretinal space. Figure 2 represents the retinal and subretinal anatomy (21). These pockets then lead to an inhibition of cellular function and ultimately cell atrophy (1).

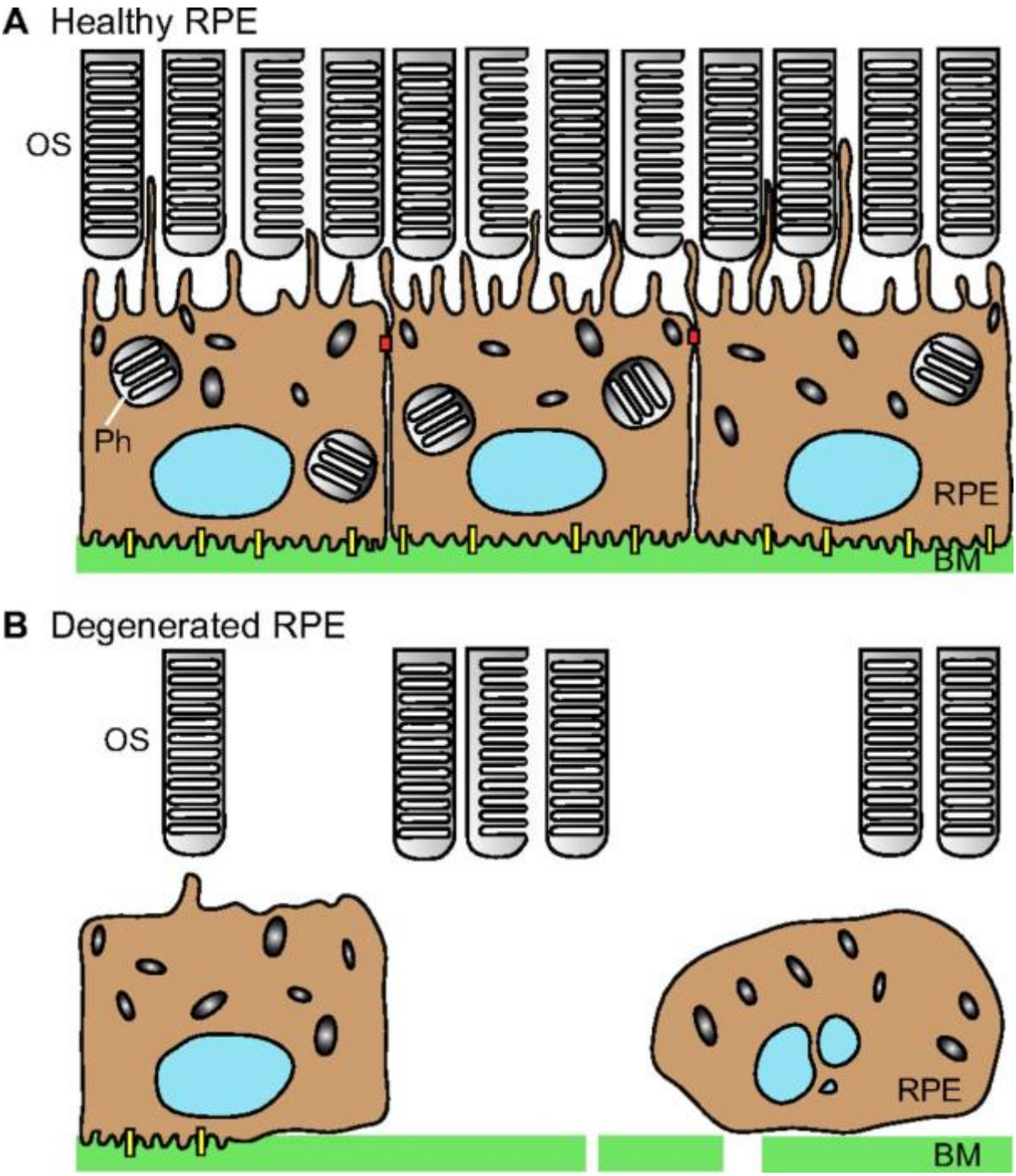

Figure 2 Diagram of retinal and subretinal membranes (21). A) Represents a normal and healthy retina and RPE complex. B) Represents photoreceptor cell death upon RPE cell death in the subretinal space.

Wet AMD is caused by blood vessels that grow behind the retina in the choroid layer. These vessels then begin to leak blood and other substances onto the retinal cells and cause them to scar. The scar tissue that forms on the cells prevents them from functioning and leads

to vision loss. About 85% of AMD cases are dry while the other 15% are wet (1). Figure 3 presents a diagram of the different types of AMD (15).

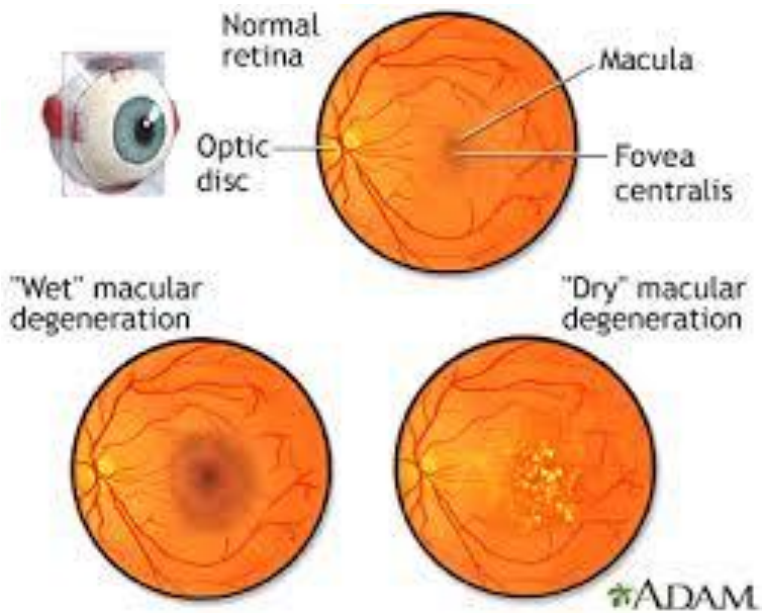

Figure 3 Diagram of the different types of AMD (15)

Both types of AMD are ultimately caused by the death of cells in the RPE monolayer underneath the outer segments of the photoreceptor cells of the retina. The RPE cells play an extremely important role in ensuring the health of the photoreceptor cells. RPE cells can protect photoreceptors from damage caused by light, and repair damage caused to DNA, proteins, and lipids, and most importantly remove elongated outer segments of photoreceptor cells. The latter function is of utmost importance because this process of phagocytosis by the RPE cells keeps the photoreceptors at a constant length and removes toxic wastes produced from the rods and cones (31). If these wastes were to develop, they would likely form drusen pockets and eventually kill the photoreceptor cells of the retina (32, 33). This is why RPE cells are invaluable when dealing with AMD and why they are the subject of stem cell transplantation.

Macular degeneration is a topic of great interest in the world of eye care today because there is no definite cure for any version of it. With the absence of a cure, and many more cases of the disease on the horizon, it makes sense that optometrists and ophthalmologists are searching for treatments and ultimately a cure. Luckily, over the past couple of years, substantial research has been done and some treatments have been discovered. However, a perfect solution has not been found yet, and new techniques are currently being explored.

Existing Treatments

It is important to evaluate the existing treatments for AMD before jumping ahead to stem cell transplantation. Ophthalmologists and optometrists support taking preemptive strikes in reducing one's risk for developing AMD. Stargardt's disease is a heritable trait from a recessive gene and cannot be prevented, but wet and dry AMD may be able to be thwarted through regular exercise, refraining from smoking, maintaining healthy blood pressure and cholesterol levels, and eating many green, leafy vegetables and fish (3). Regular exercise is good for overall general health because it increases oxygenated blood flow to all parts of the body, including the eyes. Photoreceptor cells heavily rely on oxygen in order to make energy and survive. The better blood flow the body has, the quicker oxygen can get to the photoreceptor cells. In addition, it may be possible that the quicker the blood flows through the retinal cells, the more waste and extracellular aggregate can be removed (39). Smoking can cause AMD because it reduces oxygen levels in the blood (1). Having good blood pressure and cholesterol levels is important because if not enough blood gets to the eyes due to cholesterol blockages, then the cells can be damaged. Lastly, a healthy diet with iron-enriched vegetables can help preserve vision in someone who is predisposed to the disease (4). The iron will help oxygen bind to hemoglobin in the blood cells and allow more oxygen to flow to the eyes and promote better cell health. These measures are good ways to lower one's risk of developing AMD; however, they are not foolproof and people still get the

disease, especially if they are genetically predisposed to it. Researchers have found that macular degeneration can be heritable (41).

There are a few key supplements that patients suffering from AMD can take to help reduce the effects of the disease and preserve some vision. The National Eye Institute (NEI)-sponsored Age-Related Eye Disease Study (AREDS) has suggested that taking a combination of vitamins and minerals can help reduce the effects of AMD (4). AREDS suggests that vitamin C, vitamin E, beta-carotene, and zinc oxide can help treat the disease, though there can be some side effects in taking these supplements. Too much beta-carotene may increase the risk of cancer in patients who are smokers, and high doses of zinc may increase one's risk for Alzheimer's disease and prostate growth (4). Too many vitamins or minerals may also affect the body's ability to process other nutrients (4). As it stands, supplements can be beneficial, but may not be right for everyone.

Fortunately, there are still some other techniques to treat AMD. All of the other treatments used to treat AMD only apply to wet AMD. The most popular method is the use of anti-vascular endothelial growth factor (VEGF) injections. Wet AMD is caused by newly sprouting, weak blood vessels that form in the eye and leak blood and other liquids into the retina, causing inflammation and ultimately the death of macular cells (1). VEGF causes the growth of these unwanted blood vessels, and anti-VEGF drugs inhibit them by inducing an anti-VEGF antibody into the eye, which binds to the VEGF and stops it from inducing the growth of the blood vessels (3, 43). Ophthalmologists can now inject the drug into the eye of the patient to stop the growth of these leaky blood vessels. The problems with these injections are cost, inconvenience due to multiple trips to the doctor's office per month, and the possibility of being more susceptible to complications with other eye surgeries. A recent case described a woman who had experienced an autoconjunctival graft compromise after undergoing pterygium surgery. Pterygium is a benign tumor that grows in the eye, and this

woman's surgery aimed to remove the tumor and replace the cell deficient area with a segment of cells taken from another part of the eye. Her surgery was uneventful due to the lack of blood vessels that were able to grow to aid in the integration of the autoconjunctival graft to the wounded area of the eye. This outcome was caused by the anti-VEGF treatment that lowered the amount of blood vessels in the eye (5). Some people may not like these disadvantages of the injections and may look for another treatment.

The second most popular treatment is photodynamic therapy (PDT). This technique requires the patient to have a drug called verteporfin injected into his or her arm. This drug will then flow into the newly growing weak blood vessels in the eye. Once the drug has reached the vessels, a "cold" laser (otherwise known as a low frequency laser) is shone into the eye to activate the drug. A “cold” laser is used so that none of the cells in the eye are destroyed by the laser. The drug then seals off the blood vessels and inhibits their growth, therefore reducing the patient's deterioration of vision (3). Yet again, this treatment is not perfect. According to a case study, PDT has the capability of inducing macular detachment via a process called acute exudative maculopathy (AEM) (6). AEM is an acute fibrinous inflammation that can result in a detached macula (6). Fortunately, this phenomenon is an extremely rare occurrence (1.4 % chance), but scientists are not exactly sure why PDT causes AEM to happen (6). It is a risk and should be noted before undergoing PDT treatments.

There is another available treatment for patients that do not qualify for the previously mentioned therapies. Ophthalmologists can also use a "hot" laser (otherwise known as a high frequency laser) technique to destroy the weak blood vessels that come with wet AMD (3). This treatment is the least frequently used because the laser may also kill other normal and healthy cells around those blood vessels and make vision worse than before the surgery. However, the procedure may stop future vision deterioration and improve one's vision in the long run.

Scientists have also looked into a few different surgical procedures during the last couple of decades in the form of neovascular membrane removal, macular translocation, and RPE cell transplantation. There have been a few clinical experiments where patients with wet AMD have had their neovascular membranes removed. This procedure undoubtedly helps in reducing the amount of leaky blood vessels damaging the macula, but does not aid in the restoration of visual acuity because it does not replace damaged cells with healthy cells. In addition, removing the neovascular membrane may also remove some of the healthy RPE cells in the retina (17). To account for this, some have added the translocation of the macula onto healthy regions of the retina to preserve or improve a patient's vision (17, 28). Unfortunately, this procedure requires the detachment of the retina which can cause some serious health risks such as proliferative vitreoretinopathy, in which the retina detaches a second time due to scar tissue buildup from the initial detachment (28, 29). Scientists had previously tried to transplant allogeneic (cells not from your body but someone else's) RPE cells from a human fetus to avoid detachment of the retina, but these grafts were very often rejected by the body (17). They then moved toward autologous (healthy cells from your body) RPE transplantation, in which a sheet or suspension of RPE cells are grafted subretinally (30). This technique can be successful sometimes and may be able to preserve long-term vision in some patients, but it also comes with a high risk of a detached retina and massive hemorrhages. This is because removing RPE cells from the peripheral parts of the retina and reinserting them into the subretinal space is an extremely invasive procedure (17). In addition, the overall eye health improvement is not as great as the eye benefits of other existing treatments such as anti-VEGF injections (30). Overall, these surgical procedures are complex, time consuming, expensive, and risky. There is a chance that they could prove to be beneficial, but it also important to consider the fact that the cells being transplanted or

translocated through these methods are the same age as the cells being replaced and possess no rejuvenation characteristics (21).

In the recent months, developments have been made to improve the existing treatments for wet age-related macular degeneration (AMD). The most recent advancement has been to combine photo-dynamic therapy (PDT) with anti-vascular endothelial growth factor (VEGF) drugs. A study published in the December issue of *Experimental and Therapeutic Medicine* analyzed the effects of this combined therapy by treating one group of AMD patients only with intravitreal injections of the anti-VEGF drug called Lucentis and treating the other group with both Lucentis and PDT. The study concluded that the combined treatments had a significant improvement of the patients' overall vision and hemodynamic parameters while also reducing visual field defects compared to the patients that only received Lucentis treatment (16.)

This study showed that some improvements have been made regarding the existing treatments. Although the treatments themselves have not been improved much, combining the two seemed to produce a better treatment than what each of them could provide alone. In addition, the paper showed that using a PDT with Lucentis injections lowered the amount of injections that patients needed to improve their vision (16). Anti-VEGF injections must be repeated frequently to produce maximum effect; however, they can produce ocular complications by themselves and can be potentially painful and expensive (16). PDT not only can help improve one's vision in combination with anti-VEGF drugs, but can also improve one's overall health by reducing the number of intravitreal injections they receive.

This improvement of existing treatments is encouraging, but these treatments still do not target the pathogenesis of the disease nor do they cure it (17). However, there may exist a treatment that can stop the disease at its source. Doctors and researchers have been studying

stem cell therapies over the last couple decades, and many experts in the field are hopeful that stem cells will be able to improve patient outcomes or even cure disease (18).

Stem Cell Transplantation

In order for one to formulate an informed assessment on the practicality of stem cell transplantation, one must understand what a stem cell is. A stem cell is characterized by three core properties. They possess the ability to divide and regenerate for long periods of time; they are unspecialized or undifferentiated; and they have the remarkable ability to become a specialized cell type (19). To put it in simpler terms, stem cells have no specific function rather than to continue to reproduce themselves in their nonspecific state until they are triggered into becoming a specific type of cell through epigenetic changes produced by environmental cell signaling or viral transduction (19, 20). Stem cells are extremely promising in the world of medicine because they provide a reservoir of cells that can be manipulated into almost any desired cell type and carry out its specific function.

There are three main categories of stem cells recognized today. They are known as embryonic stem cells, adult stem cells (also known as somatic stem cells) and induced pluripotent stem cells (19). Each category of stem cell gets its name either from where the stem cell is from or how it is derived. Embryonic stem cells come from embryos. The embryonic stem cells that scientists use today have been developed from eggs that have been fertilized in a test tube. This is referred to as *in vitro* fertilization, and none of the embryonic stem cells were fertilized in a woman's body (19). Embryonic stem cells are referred to as pluripotent, meaning that they can only form embryonic tissue that come from the ectoderm, mesoderm, and endoderm, as opposed to extra-embryonic tissue (21). Adult stem cells come from various organs in the body, such as the brain, lungs, liver, adipose tissue, gut, bone marrow, blood vessels, skeletal muscle, teeth, heart, skin, ovarian epithelium, and testis (19, 22). It was once thought that adult stem cells could only differentiate into the same tissue in

which they were found, but it has been discovered that they can cross lineage barriers and function as cells unique to other tissues. These cells do not possess as great a range of differentiation as pluripotent cells and can only be transformed into a limited number of cell types; therefore, they are referred to as multipotent (21, 22). Induced pluripotent stem cells are adult stem cells that have been reprogrammed into pluripotent stem cells by changing the gene expression of the adult stem cell to create proteins and certain factors that are used in maintaining the vital properties of an embryonic stem cell (19). Induced pluripotent stem cells function in the same way as embryonic stem cells, but are conveniently derived from a noncontroversial source.

Stem cells can be differentiated through a number of different methods. Adult stem cells can be turned into induced pluripotent stem cells (iPSC). iPSC and embryonic stem cells can be transformed into any embryonic tissue. Adult stem cells can be specialized into a limited number of specific tissues, and now some cells can even be directly reprogrammed into a different cell type without going through an induced pluripotent step (20).

Stem cells can be extremely beneficial in regenerating diseased or damaged cells for a few reasons. The primary reason is because they can be transplanted into a diseased area and replace the dead or nonfunctioning cells with newly functioning cells of the same type. The other recently discovered effect that differentiated stem cells can have on diseased or damaged cells is called the paracrine effect (23). The paracrine effect is when the differentiated stem cells do not become a part of the tissue, but rather secrete chemical factors that signal the nearby functioning cells to repair the damaged cells. These cells then die or are rejected within 1-2 weeks, but have shown to have produced a long term effect on the regenerating cells (23).

However, stem cells have more major problems that need to be worked out. Unfortunately, a few decades ago when stem cells were newly discovered, scientists found

that it was extremely difficult to properly cultivate stem cells and apply them practically. They discovered that stem cells are extremely complex and hard to deal with, regarding cultivating pure cultures and functional differentiated cells. In addition, there was and still is much backlash against the use of embryonic stem cells. The first major problem with stem cells is a moral one. In order to get the cells from the embryo, the embryo must be destroyed, and many people have strong feelings about that action. For some, it is unethical to kill an embryo even if it can help sick people, bring eyesight to the blind, and save lives (9). Luckily, scientists have developed a method to generate human induced pluripotent stem cells (hIPSC) (9). These stem cells come from adult humans, so no killing is necessary. These cells derive from certain parts of the body, such as fibroblasts in human connective tissue (9). Scientists can use different techniques to change these adult somatic cells into multipurpose stem cells, but one of the most common ways is via viral transduction. This is when scientists take a virus that contains fragments of stem cell DNA that are responsible for translating certain transcription factors and allow the virus to inject the DNA into the cell. The cell then transcribes and translates the injected DNA and produces the desired transcription factors that are needed to reprogram the cell into an induced-pluripotent stem cell (9).

Skeptics may ask where does one go from there? The answer is directing these stem cells into functional RPE cells. In an experiment performed by Choudhary/Booth, both hESC and hIPSC were changed into RPE cells via a method where scientists take a single-layered culture of stem cells and manipulate actin and bone morphogenetic protein signaling pathways with small molecules and recombinant proteins. This induces the change in the stem cells and ultimately leads to retinal pigment cells to be developed in roughly 45 days (10). This method is a good technique to use because it produces a high yield of new retinal cells in a relatively short time and opens up new doors in treating macular degeneration. Recently these stem cells have been used in preclinical and clinical trials.

The second major problem is cultivating pure cultures of differentiated cells before transplanting them into the body (8). A pure culture of stem cells means that all of the stem cells are engineered to act as a certain cell in a certain location in the body. If some cells in the culture were not properly generated as the desired type of cell, then the area of the body that the cells were transplanted in will produce an autoimmune response and a tumor called teratoma may arise in the organism (40). A teratoma tumor occurs when a foreign cell to the germ line area begins to grow and proliferate amongst the other cells that are supposed to be there (40). In this case, the undifferentiated stem cells may be differentiated into cells other than RPE cells by different growth factors or environmental stimulus when transplanted into the eye (40).

As time passed and more research was done, scientists thought they found a way around this obstacle. In Choudhary and Whiting's report, a method had been developed to effectively differentiate and isolate RPE cells from a bundle of undifferentiated embryonic stem cells and obtain a pure sample of the RPE cells that are specialized for transplantation in the desired area (8). The differentiated RPE cells are recognized by the presence of a cell surface marker known as CD59 (8). CD59 is expressed only in RPE cells, which allows scientists to tell the difference between the differentiated cells and the undifferentiated stem cells (8). The samples are then exposed to fluorescent-activated cell sorting (FACS) in order to insure only differentiated cells are collected and ready for transplantation (8). This is of grave importance because if some residual stem cells from the cluster are cultivated and transplanted into an organism, they may cause the growth of a teratoma tumor. This technique is groundbreaking because it now allows stem cell transplantation to have a chance of being a practical regenerative treatment for macular degeneration.

However, this method is not perfect and needs improvement. To date, there is no method of extracting 100% pure differentiated stem cells (24). Scientists have recently been

developing a few new ways to get around this dilemma. One method is to transduce certain induced pluripotent stem cell (iPSC) suicide genes such as iCaspace9 to have the residual stem cells die and reduce the amount of contamination in the differentiated stem cell sample. One study showed that this method induced apoptosis, or cell death, in 95% of the undifferentiated stem cells (25). This did not produce a 100% pure culture, but did significantly reduce the risk for teratoma. Another study used a similar technique with suicide genes, but also inhibited a gene that the iPSC needs to survive called survivin. They found that the cell suicide gene harmed the differentiated cells in addition to the residual iPSC due to its toxicity. By contrast, the survivin inhibitor produced no toxicity and only killed the residual iPSC (24). The data did not produce a 100% pure cell culture, but did provide a new inventive way to reduce the risk of teratoma.

There is also a strategy present in the scientific community that has recently made a comeback. It is called direct lineage reprogramming, and it is the method differentiating cells without entering a pluripotent stage (20). This process uses defined reprogramming factors to change the epigenetics of any cell in order to differentiate it into a desired cell. These factors are lineage-specific transcription factors, small molecules to induce signaling pathways and epigenetic regulators, microRNA, and pluripotent factors (20). This method has even been able to convert human fibroblasts into RPE-like cells (26). However, direct lineage reprogramming has a problem producing fully matured and functional cells because it fails to silence the expression programs of the initial cell population (20).

The third major problem with stem cells is their inconsistency in producing fully functional differentiated cells. Conveniently enough, there is another study out that might be able to fix that problem. These researchers transfected embryonic derived RPE stem cells with modified mRNA *in vitro* to avoid an innate immune response by the cells. The mRNA was then translated by the cells' ribosomes, and the cells produced functional proteins that

resembled those of true RPE cells (27). The mRNA provided a safe entry into the cells and did not elicit any immune response. This study shows that mRNA can be used to engineer RPE cells (27).

The fourth major problem with stem cells is the transplantation itself. The surgical procedure that doctors must do to in order to successfully transplant the cells safely is rigorous (17). In addition, the transplanted RPE cells do not always firmly attach to the RPE monolayer in the subretinal space in a way that will allow the cells to proliferate or function properly. This is not to say that scientists have given up on the matter. Instead they are currently researching ways to improve adhesion of the cells by looking at tight-junction (TJ) signaling proteins in the retina. Researchers have identified two TJ proteins (ZO-1 and ZONAB) that have direct influence over the differentiation of the stem cells and homeostasis of the monolayer (34). The manipulation of the expression of these proteins may lead to better transplantation results. In addition, researchers have also been exploring the idea of creating a carrier device for the RPE stem cells in order to help the cells adhere and function properly on the Bruch membrane. One study developed a honeycomb porous film that mimics the Bruch's membrane (35). The experiment showed increased adhesion and function in pig eyes.

A copious amount of research and trials have been conducted on differentiating stem cells into functional RPE cells; however, there have not been many transplantations on human subjects. There have been trials done on lab rats and mice which yielded positive results. In Bakondi's research, it was shown that the transplantation of isogenic mesenchymal stem cells into the subretinal space of the eye of a rat may be able to protect the retinal cells of rats from degeneration and vision loss (11). In addition, there has also been a study comparing the protective effects of human iPSC-derived retinal pigmented epithelial cells in comparison with human mesenchymal stromal cells and human neural stem cells on the degenerating retina in rd1 mice (12). This experiment showed that human iPSC were the most effective in

preventing retinal degeneration in mice compared to the other stem cells. This study was important because it showed that certain stem cells work better than others, especially when they are specially induced for the retina like the hIPSC were. In these trials the cells differentiated without teratoma and the light detection and overall eye health had improved for the mice, but mice and humans are not the same organism.

At this time, there have been three different stem cell transplantations done on human subjects. Each of the three have differing results, some positive and some very negative. The first trial's results were published in 2015. In the experiment 18 total patients received stem cell transplantation. Nine of them had Stargardt's disease and the other nine had dry AMD. The results varied. The transplantations worked for all of the patients. There were no signs of teratoma or any really serious side effects. The majority of eyes treated saw an increase in pigmentation of the RPE cells, indicating a successful transplant (36). Best-corrected visual acuity had improved in ten eyes, improved or remained the same in seven eyes, and decreased by more than ten letters in one eye on the Snellen Eye Chart, whereas the untreated fellow eyes did not show similar improvements in visual acuity (36). There were also some instances of vitreoretinal surgery and immunosuppression that produced adverse effects in some patients' eyes. The experiment concluded that human embryonic stem cell transplantation could be a viable treatment for macular degeneration (36). However, even with this seemingly positive data that has been produced, there are still skeptics. In Aznar and Tudela's article, the authors write of their suspicions to the advances of stem cell research. Aznar and Tudela reference one experiment where some patients benefitted from the transplant, whereas some experienced no change and some experienced negative effects. This experiment was regarded as a positive and useful finding that proved that stem cell transplantation is a viable way to treat eye diseases. Even so, Aznar and Tudela were not so convinced and deemed the results to be "overly optimistic" (13). They also said that the study was too small to produce

significant data. Granted this was just one experiment that could have been biased or slightly skewed, but this article shows some sort of disagreement in the field of stem cell transplantation.

The second experiment looked at was published in the *New England Journal of Medicine* in 2017. The study consisted of two patients that were diagnosed with "wet" AMD. Only the first patient was operated on because the cells extracted from the second patient ended up having a mutation in the DNA that could have caused a problem during the transplantation of the cells. The results from the transplanted autologous iPSC-derived RPE cells into the subretinal space of Patient #1's treated eye showed that the procedure was successful. There were no serious adverse events recorded after the 25 month follow up (17). The patient's visual acuity did not change, but her VFQ-25 score, a questionnaire form used to gauge one's general vision, social functioning, visual dependency, near vision, and color vision (42), had improved and she said she had "brighter" vision. These results were not miraculous by any means, but they did show a safe transplantation that enlarged the pigmented areas of the monolayer. This high-density area may indicate the recovery of the photoreceptors, but it is too early to say for sure (17).

The third experiment yielded the worst results. In the same *New England Journal of Medicine* issue, another injection of autologous stem cells was used to treat AMD (37). This experiment used adipose tissue-derived stem cells because researchers have found that these cells are easier to obtain and prepare compared to other stem cell sources. However, there is little evidence that cultures of adipose-derived stem cells can be turned into RPE or photoreceptor cells (37). Three elderly patients, each of which had a form of AMD, received bilateral intravitreal injections. Each of them ended up with severe vision loss. The first patient ended up with a detached retina that then turned atrophic and resulted with the patient's inability to detect light. The second patient also sustained a detached retina but

luckily it was later reattached. This patient had a severe vision loss going from 20/50 visual acuity in the right eye and 20/100 in the left to only having waving detection in the right eye and 2/200 in the left. The third patient saw her visual acuity go from 20/40 in the right eye and 20/200 in the left eye to perception of hand motion in the right eye and light perception in the left. She also experienced detached retinas, but they were reattached at a later time (37). This experiment was privately funded not overseen by the FDA.

Conclusion

Macular degeneration is a complicated and fickle beast to tackle. As of now there is no cure, but there are some promising treatments that can make living with macular degeneration tolerable. Perhaps in the future, once more research and experimentation is done, stem cell transplantation will be the cure for it. Yet, there will still be questions that need answering, such as if transplantation is effective, how long will it last? Will patients need multiple surgeries like the multiple injections people get a month for the anti-VEGF drug? How much will it cost? Will everyone be able to afford such a high tech surgery? Would it just be better to develop some other preventative method instead of a cure? These are all questions that will hopefully be answered in the near future.

At this time, I cannot confidently say that stem cell transplantation is a practical treatment for macular degeneration. There simply has not been enough research and clinical trials performed to produce concrete data. Right now, the results are very hit or miss. Some trials work, some trials are safe but do not improve one's vision, and some are disastrous. I must take an utilitarian approach to this thesis question and see if the pros outweigh the cons and vice versa. I have concluded that the pros do not outweigh the cons and that stem cell transplantation is presently too risky to become a practical solution to macular degeneration. It still has problems with tumor production, transplantation methods, and overall efficiency. I cannot condone the use of stem cell transplantation until there is more evidence that it is safe

and effective, unless someone is beyond any pre-existing treatment and has decided to take the risk. However, I am confident that in the near future it will be the obvious long term treatment for AMD. Scientists are close to making it a practical treatment, but they just are not quite there yet. As medical advances and technology continue to grow exponentially, I am sure that we as a society will be ready in the coming decades.

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