A Novel Encapsulation Device for Mouse Neural Stem Cells

(Technical Paper)

Considering the Ethical Implications of Stem Cell Research

(STS Paper)

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Introduction

With advances in technology and increased funding allotted for research of regenerative medicine treatments (Hossain & Milne, 2018), the future of regenerative medicine and its practical implementation for clinical usage is quickly becoming a reality. Specifically, there has been a major increase in stem cell research over recent years (de Miguel-Beriain, 2015) as stem cells appear to be a key player in regenerative medicine research (Cossu et al., 2018). As a result of this increase in the utilization of stem cells for regenerative medicine, researchers have had to delve into the implications of both the technical aspects of effectively harvesting and delivering stem cells clinically as well as the ethical considerations of stem cell collection and usage. Consequently, two major concerns have arisen that threaten the future of stem cell research: the limiting factors of time and monetary cost to coat the stem cells in a protective hydrogel, and the possible rejection of stem cell research by members of society and organizations based on moral grounds.

First, encapsulating stem cells with a protective hydrogel coating is currently a manual process that is tedious, time consuming and is prone to human error (Highley, 2019; Whitewolf, 2019). The cell coating procedure also requires the use of expensive polymer solutions; additionally, it generates high energy costs due to an energy intensive centrifugation process (Whitewolf, 2019). These costly limiting factors deplete funds and time spent by lab members that could be allotted to other aspects of stem cell research. Second, if stem cell research continues to advance without any regard to ethical considerations, this unchecked progression could lead to dehumanizing practices, as well as violating the rights and privacy of donors and those who receive stem cells for treatment purposes (MacPherson & Kimmelman, 2019; Volarevic, 2018).

In an attempt to improve the efficiency of the current cell coating process and therefore eliminate the barriers that arise due to extensive time requirements and high monetary costs, the technical aspect of this project will focus on designing, prototyping and testing a device that will automate the process of encapsulating stem cells with a hydrogel coating. The STS research will focus on considering and understanding the key ethical aspects of stem cell research so that stem cell utilization in applications such as regenerative medicine can still progress while adhering to carefully determined ethical standards.

Technical Topic: Designing a Hydrogel Cell Coating Device for Stem Cells

When utilizing stem cells in regenerative medicine, it is critical that the stem cells be encapsulated in some form of protective outer coating in order for the cells to survive an injection into a test subject (Romero et al., 2015). Many researchers currently use bulk hydrogel encapsulations to protect cells as they are injected into the body and travel toward their target (Dias, Elicson, & Murphy, 2017). These hydrogels provide excellent protection for the cells; however, the hydrogels do not permit a high density of cells to be injected into the body. Therefore, some labs have recently begun encapsulating cells with only a few layers of polymer rather than a using a multi-layer hydrogel with cells contained within a larger cell matrix. This two to three layer polymer coating allows for a higher density concentration of the cells to be injected into the patient, while at the same time allowing for the protection of the cells.

However, even a new development of a two to three polymer layer coating on the cells needs improvement. Specifically, this process is currently done manually, which leads to a number of different inefficiencies. Execution of the cell coating process by hand-pipetting the solutions containing the polymers is a tedious, time-consuming process. Additionally, the centrifugation process and the exchanging of solution can be extremely energy-intensive and place unnecessary strain on the cells (Whitewolf, 2019). Finally, the manual coating process is prone to technician error form improperly pipetting or pipetting to forcefully causing damage to the cell samples (Whitewolf, 2019). If the manual cell coating process is continued, labs will be forced to wield large amounts of money and resources to perform the energy-intensive procedures within the process. Therefore, our capstone group is attempting to automate the cell coating process by designing, constructing, and testing a device that will account for inefficiency in the current manual process.

The device will consist of a main chamber with four tubes connected to the main chamber as shown in Figure 1. At the bottom of the chamber, there will be a porous membrane filter, and the cells will be placed on top of the filter. One of the two tubes connected to the bottom of the chamber will allow a phosphate-buffered saline (PBS) solution to flow upwards, causing the cells to rise up off of the membrane filter and be suspended in the solution as it fills up the main chamber. After this, one of the tubes connected to the top of the chamber will allow

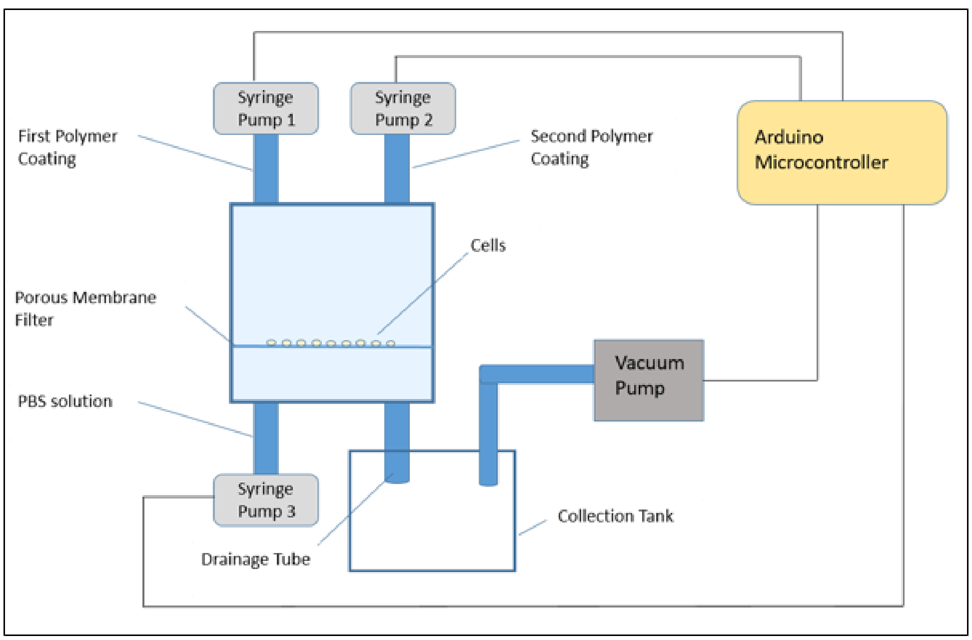

Figure 1: The basic design of our capstone team's hydrogel coating device with labeled components (Created by Author).

the first polymer coating solution to pour into the main chamber. The polymer contained within the first coating solution will bind to the cells. After sufficient time is given for the binding of the polymers, the excess polymer and solution will be sucked through the porous membrane filter into a drainage tube connected to the bottom of the main chamber. The membrane filter pores will be large enough to let the unbound polymers through, but small enough that the cells will not go through. The drainage tube, which is connected to a vacuum pump will suck the excess fluids into a separate collection chamber. Once all of the fluids have been drained out of the main chamber, the cells will now be resting on the porous membrane filter.

The process of suspending the cells will be repeated, except this time, the second tube connected to the top of the membrane will allow the flow of the second polymer solution into the main chamber to bind with the cells. Once again, the excess fluid will be drained out into the collection chamber and now the cells will be finished with the coating process. The three tubes containing solutions will be attached to syringe pumps controlled by an Arduino microcontroller that will allow the user to set flow rates for each respective solution. The vacuum that will suck excess fluids through the drainage tube into the collection chamber will also be controlled by the microcontroller. Our capstone team will program the microcontroller so the user can simply set the flow rates and then press start, allowing full automation of the cell coating process.

STS Topic: Considering the Ethical Implications of Stem Cell Research

As mentioned earlier, stem cell research has the potential to provide many cell-based therapies and make conceptual regenerative medicine concepts reality. However, utilizing stem cell-based interventions requires the harvesting of stem cells from a variety of sources, as well a direct injection of these cells into a test subject. And while stem cell-based therapies could prove to be incredibly useful in regenerative medicine, there is much debate regarding the morality and ethics of the harvesting and utilization of stem cells (Sandel, 2004). Pervasive and numerous questions of whether stem cell research and its applications should be permitted — and funded — has raised significant uncertainty about the future of stem cell research and regenerative medicine. In order to move forward with research, it is crucial that literature on stem cell ethics is closely reviewed so all concerns are addressed in order to develop comprehensive standards on which practices are and are not acceptable to keep researchers in check.

The first ethical issue to consider is the harvesting of stem cells. There are two main sources stem cells can be harvested from: embryos and non-embryonic sources, including umbilical cord blood, bone marrow, and other somatic cells (Sugarman, 2008). Both types of sources raise separate ethical issues upon evaluation. When considering collection of stem cells from non-embryonic sources, the primary concern regards privacy of both the donor and the recipients of the stem cells (Sugarman, 2008). When considering embryonic stem cell collection, some argue that the destruction of an embryo for cell harvesting is the destruction of human life, while others claim that an embryo is merely a precursor to life and should not be granted its own rights (Sandel, 2004). Thus, the heart of the issue is how one defines an embryo; however, controversy remains on such definitions as well (de Miguel-Beriain, 2015, p. 2). Researcher Iñigo Miguel-Beriain hopes this debate can be resolved by developing a scientific technique that will allow for the production of “stem cell lines (which nowadays almost nobody considers to be embryos themselves) that are suitable to be used for research and therapeutic purposes without destroying human embryos” (2015, p. 3).

While producing stem cell lines may seem to be a viable solution, it raises its own set of ethical considerations. The main issue involved with stem cell lines regards what a donor is consenting to when they agree to donate a sample of their stem cells. A donor’s sample may be used for one set of experiments; however, this sample could be used to create several cell lines, which could in turn be used to create even more cell lines. Therefore, a singular sample may be used in the future to create an infinite number of cell lines and derivatives, which could be nearly impossible to keep track of. This in turn renders the donor ignorant to the reality of how their cells and their derivatives are being used. Currently, the consent process for stem cell donors only includes information about the general physical and social risks of donating. If we are to take into account the ethical considerations of the donor's right to know how their stem cells and derivatives are being utilized, then, as Sugarman states, "issues related to future uses, intellectual property, ownership, and control over cell lines and their derivatives should be incorporated into the consent process" (2019, pg. 2).

While these are just a few of the ethical issues that must be considered when conducting stem cell research, these and any other pertinent ethical issues must be considered when progressing forward with stem cell research. The ethical implications of a specific topic are often much more extensive than they may seem upon initial consideration, and the consequences of such implications on society must be taken into account, especially in regards to stem cell research. Additionally, when considering the future of stem cell research, one should consider one of the important concepts discussed in Howard Rheingold's "Look Who's Talking," which is that just because a technological advancement is becoming feasible does not imply that we should move forward with such an advancement without taking time to consider its consequences and implications for society (1999). In my project and in similar projects that concentrate on stem cell research, it is imperative to consider and discuss the ethical concerns brought forth by society in order to form a set of cohesive moral standards. Once these standards are in place, they can serve as guidelines to direct the course of future research.

Conclusion

When attempting to advance stem cell research, it is paramount to consider both the technical and sociotechnical aspects of the research. If this project is implemented successfully, than the future of regenerative medicine and stem cell research could be improved both technologically and socially. If our hydrogel cell coating device is successfully designed and built, it will increase the effectiveness of stem cell encapsulation by automating the process and therefore minimizing the costs of the solutions, as well as reducing the time necessary to complete the process. Additionally, a thorough explanation of the literature of stem cell ethics will benefit the overall field of stem cell research by providing us with a strong foundation and an improved understanding of the field in order to further guide it in future research.

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