Tissue-Engineered Organs and Its Relevance to Society

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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

At one point of time, the thought of engineering organs to be used in replacement of those naturally formed sounded preposterous. Now with the development of tissue engineering, a field that utilizes life sciences and engineering to research and produce biological material for the purpose of implementation within an organism to substitute or improve tissue or organ function, it has become apparent that the production of artificial organs is not far out of the realm of reality (Langer & Vacanti, 1993). This technology has been driven from an unmet demand for healthy organs that is observed through the current system of organ transplantation and its extensive list of awaiting patients. In 2021, there was a total of 107,217 patients on the waiting list, but only 41,355 transplant surgeries were performed that year (Health Resources & Services Administration, 2022). This disparity results in 17 patients dying each day from failure to receive an organ, and the patients who do receive an organ still have an average wait time of three to five years (Health Resources & Services Administration, 2022; National Kidney Foundation, 2016). This research paper analyzes the way in which research and development of artificial organs is affected by ethical debate and potential actions that can be performed to maximize public support for the technology through the obliging of widely held moral standards.

Theory of Co-Production

To illustrate the interdependency between the development of artificial organs and the ethical standards set by society, analysis of various sources will be viewed under the lens of co-production. The theory of co-production is defined by Sheila Jasanoff (2004) as the way in which society and technology are interlinked to influence each other. To think about how varying aspects of society drives the development of technological knowledge as the technology embeds itself in communities to change the conditions of people, Jasanoff organizes the framework into

four instruments: identities, institutions, discourses, and representations. She defines identities as either human/non-human or individual/collective sources in which individuals gains stabilization through reasoning during chaos. Summarizing Bruno Latour's definition, institution is defined "as society's inscription devices…vehicles through which the validity of new knowledge can be accredited" and "the safety of new technological systems acknowledged" along with serving "as sites for the testing and reaffirmation of political culture" (Jasanoff, 2004, p. 40). Discourse is the use of language, usually with intention to manipulate, to sway audiences and solve problems. Representation is informed by human agency and behavior as means for politics and culture to influence scientific practices (Jasanoff, 2004). These instruments allow for bridges to form between "the cognitive, the material, the social, and the normative," all through four recurrent themes: the materialization of new technoscience, the resolution of its controversies, the processes that allow for its broadened implementation, and "the adjustment of science's cultural practices in response to contexts in which science is done" (Jasanoff, 2004 p. 6, 38). Essentially, when a new technology is developed, it requires coherency between the society's perception of normality and what is new so that the public is willing to integrate the advancement with pure and useful intention.

Demand for Alternative Methods to Traditional Organ Transplant

The current standard of care for patients suffering from organ failure include pharmacological therapies to minimize symptoms or orthotopic organ transplantation, in which an organ is surgically removed from a donor (typically deceased) and inserted in replacement of the ill patient's dysfunctional organ. Despite advances in these existing healthcare treatments, organ failure has still become a leading cause of mortality all over the world due to limitations in obtaining donors (Wang, 2019). Not only is there a donor shortage, but organ transplant comes at

the risk of immune rejection. To eliminate these limitations, researchers have started explorations in the manufacturing of lab-grown organs.

Studies regarding artificial organ technologies focus on determining the proper utilization of three main components: cells, scaffolds, and biomolecules. Of these three, selection of cell types has displayed the most delay to the overall progression of artificial organ technology. This is because the most promising cells line, human embryonic stem cells (hESCs), have faced ethical objections from many (Moreno-Borchart, 2004). This cell line is recognized as important to the development of these organs since it can be differentiated to promote proliferation of different tissue types and can be sustainable for long-term production, characteristics that allow them to be applicable for expansive treatments and patient populations (Howard, Buttery, Shakesheff, & Roberts, 2008). Human embryonic stem cells are sourced through donations of remaining embryos from in vitro fertilization procedures. Donors give explicit consent for their fertilized eggs to be destroyed during the process of extracting clusters of cells to create the cell lines for research (California Institute for Regenerative Medicine, 2009). Much of the argument surrounding the use of embryonic stem cells is in regard to the sanctity of life and the determination of at which moment life begins. Other ethical debates that influence public support for artificial organs are questions that lack scientific answers, such as those that regard the "commercialization of human biological material…firms who want to make a profit – and…issues of donation and control of human biological material" (Welin, 2008, p. 686).

Analysis of Ethical Debates and National Policies

Past Legislation Regarding hESCs

During previous presidencies, the laws regarding hESCs were frequently argued, even in some occurrences exposing contradicting viewpoints between legislative and judicial branches.

The discourse of when life begins had been long debated before any findings of hESCs were made and many of these same arguments were used to drive the curating of initial legislation regarding hESC research. During the Reagan and George H.W. Bush administrations, restrictions of federal funding on fetal research emerged as a result of an uproar of debates regarding the legalization of abortion, the central argument being that "the absence of public consensus regarding the moral status of the fetus and the embryo precluded both the development of regulation constraining such research and the use of public funds to support it" (Gottweis, 2010, p. 555). Due to this sentiment, the first article in the books that defined some form of regulation for federal support of any research utilizing human embryos was the Dickey-Wicker amendment, first adopted in 1996. This amendment was attached to legislation concerning the National Institutes of Health (NIH) and prohibits federal funds from being used for any work that involves creating human embryos solely for research purposes or inflicts destruction to an embryo, directly going against the 1993 recommendations of the NIH's Human Embryo Health Research Panel in which they deemed it appropriate for donated embryos from IVF to be used for research and wanted approval for federal funding of certain embryonic research (Gottweis, 2010; National Institutes of Health, 2021).

The Dickey-Wicker amendment still left a lot of room for varying interpretations and on January 15th, 1999, Harriet S. Rabb of the Office of the General Counsel of the U.S. Department of Health and Human Services (DHHS) determined that funds were not prohibited from being used on research that utilizes human stem cells as these cells themselves were not human organisms due to their inability to develop into a life form (Rabb, 1999). While this did not overturn any prohibition of funding for research that is dependent on the harvesting of hESCs from embryos, as that still falls under the clause for causing death, Rabb's ruling opened doors

for increased public funding and support into projects that utilized cell lines that had already been created from private-funded harvests and culturing from discarded IVF embryos. In August of 2000, with the support of President Bill Clinton, the NIH announced their support for providing federal grants for the study of hESCs; although, it came on the brink of the presidential election of George W. Bush's, a vocal opposer of stem cell research (Smaglik, 2000). President Bush held socially conservative Christian values and it was known he believed "each of these human embryos is a unique human life, with inherent dignity and matchless value," thus influencing him to reinstate bills that prohibited tax-funded research that destroyed human embryos and limited all research on hESCs to only those that utilized already existing cell lines (The White House Office of the Press Secretary, 2006). Democratic President Barack Obama, a supporter of hESCs and stem cell research, aimed to remove any limitations set upon their study as he believed in their potential to create new medical treatment discoveries. During his time in office, President Obama issued an executive order that was meant "to remove these limitations on scientific inquiry, to expand NIH support for the exploration of human stem cell research, and…enhance the contribution of America's scientists to important new discoveries and new therapies for the benefit of humankind," allowing for the NIH to conduct any human stem cell research to the extent of the law and revoking Bush's previous policy (The White House Office of the Press Secretary, 2009a). However, this win for biomedical research was short lived. Just one year later, a lawsuit against the NIH was filed and Federal Chief Judge Royce C. Lamberth released a temporary injunction that blocked President Obama's executive order and halted NIH funding to hESC projects. He stated, "If one step or 'piece of research' of an [hESC] research project results in the destruction of an embryo, the entire project is precluded from receiving federal funding" (Harris, 2010). This ruling went against all stances of Presidents Obama, Bush,

and Clinton. One year later, in the U.S. Court of Appeals, it was determined that Judge Lamberth did not have the power to release the injunction or halt NIH funding, but the final decision still needed to rest in his court (Conger, 2011). Back in his court, Lamberth reversed his initial ruling and dismissed the case all together (Rovner, 2011). This vacillation occurs behind the scenes with each administration, especially during their transitional periods.

Current Landscape

Currently, human embryonic stem cell (hESCs) research is legal in the United States, but it is limited by federal and institutional regulations. Even today, the greatest hinderance to funding of research involving hESCs is still the Dickey-Wicker amendment. It places dependency on private funding to create new stem cell lines, unlike previous scientific discoveries that were financially supported by federal taxes, motivating more and more scientists to focus their research to the field. The constant change of support between different presidential administrations and varying interpretations of the amendment by court judges inflicts stress on researchers and their institutions, since they are constantly trying to prove the importance of their experiments to obtain reliable funding. Another of these regulations includes a 14-day limit that prevents research on an in vitro human embryo past 14 days post-fertilization and is recommended by several international scientific society guidelines, including the US National Academies of Sciences, but is not enforced by federal law (Matthews & Moralí, 2020). While not enforced, it is public opinion (though some may say of a minority) that upholds researchers to this standard, as they hope to minimize any outrage or controversy regarding the origin of their study. The government's lack of a coherent position allows for the spread of mistrust amongst community members and is partly responsible for any misinformation being shared.

Legislation Regarding Commercialization and Donation of Human Biological Material

There are no transparent rights that strictly define ownership to specific parties in the case of donated human tissue (Hakimian & Korn, 2004). However, there have been previous Supreme Court cases that have set some precedent when determining ownership for this material when it has become profitable. One of these cases was in 1990, when the Supreme Court of California ruled in Moore v. Regents of the University of California that "individuals do not have rights to a share in profits earned from research performed on their bodily materials" and enabled researchers to retain legal ownership over material they take from individuals, as long as it is donated under informed consent for the purpose of medical advancement (Nott, 2020). Following this ruling and that of similar lawsuits after, it has been generally assumed that any once bodily material or substances have been obtained from a patient through donation, they can be used for the development of any biological material, including cell lines and genomic sequences; these products are distinctly separated from their origin material, thus stripping the donor from any ownership (Schleiter, 2009). Because there is no national policy with wide-range applicability for researchers or patients to refer to, many individuals fear that artificial organs may be commercialized in a way that devalues human life or creates disparity between those in need. In an industry that is currently estimated at a market value of nearly $25.9 billion and is projected to have a compound annual growth rate of nearly 10 percent between 2020 to 2027, there surely has to be societal agreement regarding the value of life and tissue so that there can be transparency in profit distribution once these organs hit the market (Grand View Research, 2020).

Recommendations for Future Studies, Policy, and Regulations

Jasanoff expressed the importance of recognizing key identities, institutions, discourses, and representations when studying the interdependency between a technology and the society it will conform with. In the ethical debate of using human embryonic stem cells for the further progression of artificial organs, a potentially revolutionary solution to the epidemic organ shortage, it is the moral identities of individuals and religious/cultural institutions that are either upholding a stance against the use of these cells or defending the use of them in hopes of saving others. While government as an institution has failed to create policy with a distinctive stance in neither the case of hESCs or ownership of material, scientific and educational institutions have maintained their support for this field of research and have released articles and thought-pieces to provide evidence for their need of stem cells and push for better funding towards their work. Discourse has been driven between the public, scientists, and government officials in hopes of determining balanced legislation that will promote new advancements in healthcare while maintaining a moral standard that is agreed on by as many as possible. This representation of morality is still cause for widespread disagreement between the varying parties.

When relating the theory of co-production and its themes to the topic of hESCs and artificial organs, it can be determined scientists are on the edge of materialization of new technoscience, delving into the resolution of its controversies, and developing the processes that allow for its broadened implementation. However, they are largely struggling to achieve a solution to benefit the execution of the technology. Because the lack of public embrace for this new science and increased debate over ethicality, researchers are being forced to adjust the ways in which they present their findings and the methods they use to obtain funding or the processes they use to drive their experiments so that more people will be willing to engage with this

technoscience. As predicted, the developmental process of artificial organs is affected by society as much as it affects society.

U.S. Senator Mitt Romney (2008) once advised "Starving research and development is like eating the seed corn". While initially referring to the automobile industry, his point is applicable to any technological advancement and its successful growth. Science cannot move forward without proper support from the public. In the case of using hESCs for research and expanding the studies for artificial organs, it is critical for all stakeholders to understand the perceptions of one another and to realize their own influence in establishing a compromise that will allow for the biomedical field to optimize the technology while also preparing the general public to accept the origins of the product and support its implementation. So far, representation through legislation has been unclear due to stubborn identities and institutions that have driven most discourse to be combative and argumentative, instead of solution-based, the way it is meant to be. While there is no way to accommodate to every belief or need of every person, some steps can be taken to achieve balance.

The first action that can be taken is to understand why some groups disagree with the use of hESCs and to determine if there would be any way to eliminate portions of the harvesting process that create conflict for these communities. According to Ron Stoddart, the executive director of Nightlight Christian Adoptions, one religious agency of many that have filed lawsuits against the NIH and executive offices for allowing federal funding of hESC-based research, "[They] do not want to see stem cell research that would destroy embryos…if there was a way of extracting the stem cells without destroying them, I would not be opposed to it" (Harris, 2010). This viewpoint is conceived from the religious belief that life begins at conception and thus it would be against its sanctity to harm a fertilized egg that may have a chance to grow into a fetus

if implanted. While this notion may be dismissed by the majority of Americans, a large portion, nearly one-third of respondents in a study conducted by the University of Nevada at Reno, do not approve of using IVF-extracted stem cells to treat serious diseases (Bates, 2011). When distributing federal funds and campaigning to gain public trust in healthcare, it would be beneficial to consider this third of the population. Solutions could include: introducing legislation that only allows for non-implantable IVF embryos to be used, increasing funding to research alternative methods of hESC extraction, or looking into how stem cells from other sources, such as cord-derived, can be reprogrammed for use. These methods most likely will extend the timeline for artificial organ development, but they may be good to consider if it opens more potential for better funding and increased acceptance.

If these alternative methods are not considered optimal by scientists and there is more evidence to suggest that the current extraction process needs to be maintained for research and development to proceed efficiently, it may be best for government agencies to solidify regulations amongst institutions. While it is expected for new pieces of legislation to receive backlash, the repetitive flip-flop between judicial courts and political parties helps no one. Instead, laying down strict rules for all researchers and institutions to abide to will allow for faster results to be produced, since there will not be the constant legal battles that were observed in the past, in which funds were halted and studies were forced into limbo. Meanwhile, institutions and healthcare officials can focus their efforts on spreading factual information to the public and teaching them the benefits of stem cell research, in some cases eliminating any misconceptions they may have. Being able to provide solid evidence of the benefits that stem cell research provides and the opportunities it gives suffering patients may change the heart of individuals.

Lastly, to address the concerns biomedical researchers, healthcare advocates, and the public may have regarding the commercialization of artificial organs, the best option would be to compile clearly defined guidelines for their utilization and distribution. One drawback of technological implementation is that science is often ahead of policy. Usually, technology is developed under good pretenses but a lack of regulation allows for it to be used for malintent. Using past experiences, such as cases over self-ownership, autonomy, donorship, and informed consent can help when drafting these regulations. Currently, the American Medical Association offers Code of Medical Ethics Opinion 7.3.9 which states that physicians have to obtain informed consent from the tissue donor and disclose any potential commercial applications to them to use their biological materials in research (American Medical Association, 2022). While this recommendation is already followed by the majority of physicians and researchers, because it is not defined as a law, there has been room for the manipulation of donors. To maintain transparency, protect donors, and hold scientists accountable, this recommendation should be concreted into law. Additionally, to limit ownership disputes and ensure equitable distribution of any organs manufactured, an amendment discussing bioartificial organs should be written into the Uniform Anatomical Gift Act (UAGA) and similar regulation to that set by the current National Organ Transplant Act (NOTA). The UAGA is a federal framework that facilitates the utilization of anatomical gifts or human organ and tissue donations (Sadler, Sadler, & Stason, 1968). NOTA and subsequent policies followed by the national Organ Procurement and Transplantation Network ensure patients experience equal access and opportunity to receive organ donations through effective allocation that is not discriminative on the basis of race, sex, gender, age, or other irrelevant categories (United Network for Organ Sharing, 2014). Enacting

regulation such as these will help maintain value in every human lifeform, from each cell to person.

Conclusion

Former President Barack Obama said, "Medical miracles do not happen simply by accident. They result from painstaking and costly research…When government fails to make these investments, opportunities are missed" (The White House Office of the Press Secretary, 2009b). In a political system such as the one in the United States, where policy is meant to be a broad representation of its people, it is fundamental to scientific discovery to have public support for every technology being researched. Simultaneously, as Jasanoff realized through her theory of co-production, for this technology to ease in implementation, scientists have to be as willing to conform to society's beliefs as much as individuals are willing to conform their identities to benefit the masses. Engineered organs can be the solution to a worldwide organ shortage. It can be the saving grace to multitudes of suffering patients who have no other alternatives to turn to. For this to occur, national policy needs to be set in place to protect the interests of institutions, donors, and patients through clear guidelines and expectations. Also, scientists have to be willing to look towards alternative methods of research to comply with the moral standards of communities they may disagree with. If these alternatives are not beneficial to the masses, individuals have to be willing to set aside their personally held beliefs to acknowledge the overall good occurring. With transparency, preparation, and compromise from all parties, there will be an increased potential for the development of artificial organs, their equitable distribution, and more communities willing to engage in utilization of this form of treatment.

Resources

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