Co-production of Politics and Human-Derived Biological Material Donation and Use

A Research Paper in STS 4600

Presented to the Faculty of the School of Engineering and Applied Sciences
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Engineering

Author

Lauren Harkins
April 05, 2020

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

Signature _____ Date _____

Approved _____ Date _____
Dr. Rider Foley, Department of Engineering and Society

Introduction

B-Cell acute lymphoblastic leukemia (B-ALL) is the most common type of acute lymphoblastic leukemia, accounting for around seventy-five percent of all cases (Terwilliger & Abdul-Hay, 2017). There are approximately five thousand new cases of B-ALL and over one thousand deaths due to B-ALL in the United States each year. The long-term remission rate for adult patients with B-ALL is only between thirty and forty percent (Terwilliger & Abdul-Hay, 2017). This low rate of remission is due to the lack of inexpensive and effective targeted treatments.

Unlike some types of cancer, B-ALL offers the advantage of having known biomarkers to help target the anti-cancer drugs to the cancerous area. For the other cancers, scientists are working to find a biomarker to improve treatment options. One way to find a biomarker is by sequencing tumor specimens to identify overexpressed or mutated genes that are specific to the cancer type. Scientists rely on donated tumor samples from patients to identify biomarkers. These samples are often stored in facilities referred to as biobanks. Biobanks are often associated with actual physical samples, but they can also hold genetic data from people (De Souza & Greenspan, 2013). The various specimens and genetic data stored in biobanks are used in research for a wide range of applications, not just discovering new biomarkers for cancer.

Various policies and best practices have been created by academic, private, and governmental agencies to ensure that human-derived biological material specimens are of the highest quality so accurate data can be obtained, and patients' rights are upheld (De Souza & Greenspan, 2013). However, it is important to fully analyze how all of branches of the United States government are impacting all aspects of biological material donation, specifically regarding patient rights, such as consent to donate, ownership rights, and the use of the donated

samples, not just impact on quality. A timeline is used to help visualize the interwoven nature of these two topics. The research also highlights the impact of this co-production on science and politics, and how communication between scientists and policymakers must be open and wanted for both parties to benefit.

Human-Derived Biological Materials and Biobanks

The story of Henrietta Lacks is one of the most famous cases of human-derived biological material used for research. In 1951, cancerous tissue samples were taken from Henrietta without her consent, a common practice at the time (Beskow, 2016). Those cells were used to make the HeLa cell line. The HeLa cell line is the first immortal cell line grown in a laboratory. Immortal cell lines are capable of surviving and dividing outside of the body for extended periods of time when normal cells would typically die. Immortal cell lines are heavily relied upon in medical research. Over eleven thousand patents were derived from research using the HeLa cell line (Ursano, 2012). HeLa cells were used to develop techniques for genome mapping, which resulted in Henrietta Lacks' entire genome being published online (Beskow, 2016). Her cells were also involved in developing the polio vaccine and chemotherapy (Ursano, 2012). Today, scientists still collect specimens from patients, but informed consent is required.

One of the most controversial human-derived biological materials is human embryonic stem cells (hESCs). Scientists derive hESCs from the inner cell mass of human embryos before the implantation in the uterus (Semb, 2005). The most common source of human embryos before implantation is from *in vitro* fertilization, where an egg and sperm are combined outside of the body. hESCs are pluripotent, meaning they can differentiate into any cell type in the human body. hESCs have many possible research applications due to their pluripotency. One application is modeling genetic diseases by creating hESC lines that have specific mutations

linked to specific diseases. Another application of hESCs is the generation of specific cell types from hESCs through differentiation to replace lost cells in a person's body (Semb, 2005).

While hESCs are one example of human-derived biological material, anything taken from a patient, like tissue from Henrietta Lacks, is considered to be human-derived biological material. The most commonly collected sample type is human tissue, followed by plasma and whole blood (Edwards et al., 2014). Other commonly collected sample types include salvia, urine, and even hair and toenails. Amniotic fluid, breast milk, mucus, and bone are more rare specimen types, but still collected (Edwards et al., 2014). After collection, all of these specimens needed to be properly stored for later use in research. Scientists have turned to facilities called biobanks for storage.

A biobank is defined as "a biorepository that accepts, processes, stores and distributes biospecimens and associated data for use in research and clinical care" (De Souza & Greenspan, 2013). Biobanks can contain a variety of specimens, from cells to genetic sequences. There are several classifications of biobanks, such as disease-centric, population-based, and virtual. Disease-centric biobanks collect a variety of specimens (blood, cerebrospinal fluid, urine) from patients with a specific disease, such as acquired immunodeficiency syndrome (AIDS) at the University of California San Francisco's AIDS Specimen Bank. Population-based biobanks collect samples from random members of a large group, often a country's population, like the Danish National Biobank. Virtual biobanks, such as Specimen Central, contain data and images from various specimen that is stored and can be accessed online (De Souza & Greenspan, 2013). Despite the variety in biobank types, all of them contain specimens that are used in research.

Biobanks are very important for medical advancement because of the data and specimens they provide to researchers. Using animal cells and tissue models can only mimic the behavior

of humans and human cells to a certain point, so having human-derived materials is necessary to gather accurate data. Biological samples, like fibroblasts and blood cells from a patient, can be used to derive induced pluripotent stem cells, a growing area of research that has important applications in tissue engineering and regenerative medicine. Biopsies from cancerous tissues can be used in the identification of biomarkers for a variety of cancers which can provide essential information for early stage detection of cancer and creating immunotherapies.

Socio-Technical Elements of Human-Derived Biological Material

Many groups of people are affected by the donation and use of human-derived biological materials such as patients, scientists, scientific institutions, and the federal government. The patients are the most obvious group affected as they are the ones who are donating their own biological material. Scientists rely on these donations to be able to perform experiments and gather data to better inform medical advances. Another group that is affected is the future patients that can benefit from the detection methods and the new treatments that have been created from research involving human-derived biological materials. Scientific institutions have become involved in ownership disputes with scientists over the donated materials. The federal government plays a critical role in creating regulations for the use, various levels of consent, and privacy laws regarding donated material.

By 1999, there were already three hundred million specimens stored in biobanks in the United States, increasing at a rate of twenty million per year (Eiseman & Haga, 1999). Therefore, it is crucial that biobanks themselves, as well as the samples contained in them, are properly regulated through laws and policies. Lack of regulation can harm the research being done using the biological samples, as subpar samples could have negative impacts on the research. It can also harm patients who donate samples if their identity and personal information

is revealed. For example, research may show that a certain ethnic group is more likely to suffer from a certain disease which can lead to stigmatization or discrimination of the group. Furthermore, ethical and legal questions can be raised when the proper policy system is not in place.

The framework that is used in my analysis of biobanks and human-derived biological materials is co-production. This theory was proposed by Sheila Jasanoff in her 2004 book, "The States of Knowledge: The Co-Production of Science and the Social Order". Jasanoff argues that science and society are jointly created and influence the creation of one another (Jasanoff, 2004). In my analysis, the science is specifically in relation to the donation, storage, and use of human-derived biological materials. As for society, I concentrated on political structures and ethical underpinnings of the institutions, formal rules, that govern this socio-technical system. Furthermore, I focused on the *interactionist* strand of co-production. The *interactionist* strand of co-production highlights the processes of altering power and order. This strand also focuses on how conflicts between science and politics are resolved as well as the cooperation between them. The *interactionist* strand seeks to explain the overlap of science and society when there is change to the existing socio-technical relationship (Jasanoff, 2004).

Research Question and Methods

The question addressed in this research paper is: How have United States government's policies and the donation of biological materials influenced one another over time? This question allows us to view science and politics as the dynamic, interwoven socio-technical systems that they are. It is important to analyze political impacts on regulation at all stages of the process: donation or collection, storage, and use in research. This question is important to ensure that the donation and use of biological materials and the policies surrounding them are

created to benefit the public. It is also important to analyze what factors are important to ensure the positive collaboration of science and politics.

This analysis uses secondary evidence, specifically sources from all three branches of the United States government. From the executive branch, I looked at executive orders, patents, and agency policies. For the legislative branch, I looked at laws issued, policy documents, and congressional testimonies. For the judicial branch, I focused on four case laws: *Moore v. Regents of the University of California, Association for Molecular Pathology v. Myriad Genetics, Greenberg v. Miami Children's Hospital Research Institute, Inc*., and *Sherley v. Sebelius.* This evidence was gathered by doing a literature search for each of the different sources from the late twentieth century to present day.

For my data analysis, I took a historical approach. This analysis style allows me to see the growth of politics and science over time. In my analysis, I created a timeline spanning the past forty years, from 1980-2020. This timeline contains significant events derived from the evidence for all three branches of the United States government. Additionally, it contains significant scientific developments in the donation, storage, and use of human-derived biological materials in the United States. This timeline allows me to full analyze the co-production of science and politics. This research analyzes how scientific events created political responses, and how political events created scientific responses by looking at the organization of the timeline. I can use the timeline to analyze the what caused the different conflicts and cooperation between science and politics through the *interactionist* strand of the co-production framework.

Results

The policies of the United States' government and the donation and use of human-derived biological materials are interwoven and have significant impacts on one another. In the following analysis, I looked at two cases involving patient rights in relation to donation and storage and human embryonic stem cells (hESCs). These cases highlight how the interwoven nature of science and politics can benefit or harm current and future patients.

Donation and Storage of Human-Derived Biological Materials

Both the donation and storage of human-derived biological materials has changed over time. This analysis focuses on patient rights in regards to donation of biological samples. Patient rights can include informed consent and ownership rights of the donated samples.

In 1984, a cell line was created from samples taken from a patient named John Moore. This then led to the court case *Moore v. Regents of the University of California*. In this case, Moore sued the researchers over the fact that they took samples from him to make a patented cell line without his knowledge (Schleiter, 2009). The court ruled that the researchers must disclose their interests (research or economic), but that the cell line was an invention and therefore patentable without the patient having any ownership rights.

In 1987, Sanger sequencing (a method to find the sequence of DNA) was automated so that sequences could be found more quickly (Shendure et al., 2017). This led to the sequencing of many genes that were linked to disease. In 1994, a gene BRCA1 was linked to breast cancer, and its sequence was identified (Mersch et al., 2015). This led to a lawsuit, *Association for Molecular Pathology v. Myriad Genetics*, in 2013 (Cartwright-Smith, 2014). In this case, the court ruled that companies cannot patent naturally occurring DNA sequences but can patent synthetic complementary DNA. In 2019, senators Thom Tillis and Chris Coons proposed a bill that would alter what can be patented (Sherkow, 2019). Many people feared that this would

overturn the Supreme Court's ruling in *Association for Molecular Pathology v. Myriad Genetics* that natural DNA sequences cannot be patented. In another judicial case that took place in 2003, *Greenberg v. Miami Children's Hospital Research Institute, Inc.*, patients sued over the use of their tissues to gain a patent for a disease testing kit, as the tissues were originally donated for research purposes only (Schleiter, 2009). Fearing the halt of research, the courts ruled that the institute should have warned the patients, but the patients still have no ownership.

Ownership rights are not the only concern in patient rights. Another concern is the donor's right to privacy. Passed in 1997, the Code of Federal Regulations (CFR) Title 45 § 46.101 is in place to attempt to ensure the anonymity of patients donating biological materials (Andrews, 2005). Without this law, biobanks can put the patients who donated samples at risk because of the personal information that can be revealed.

These scientific and political events surrounding the donation and storage of human-derived biological material are shown in Figure 1, below:

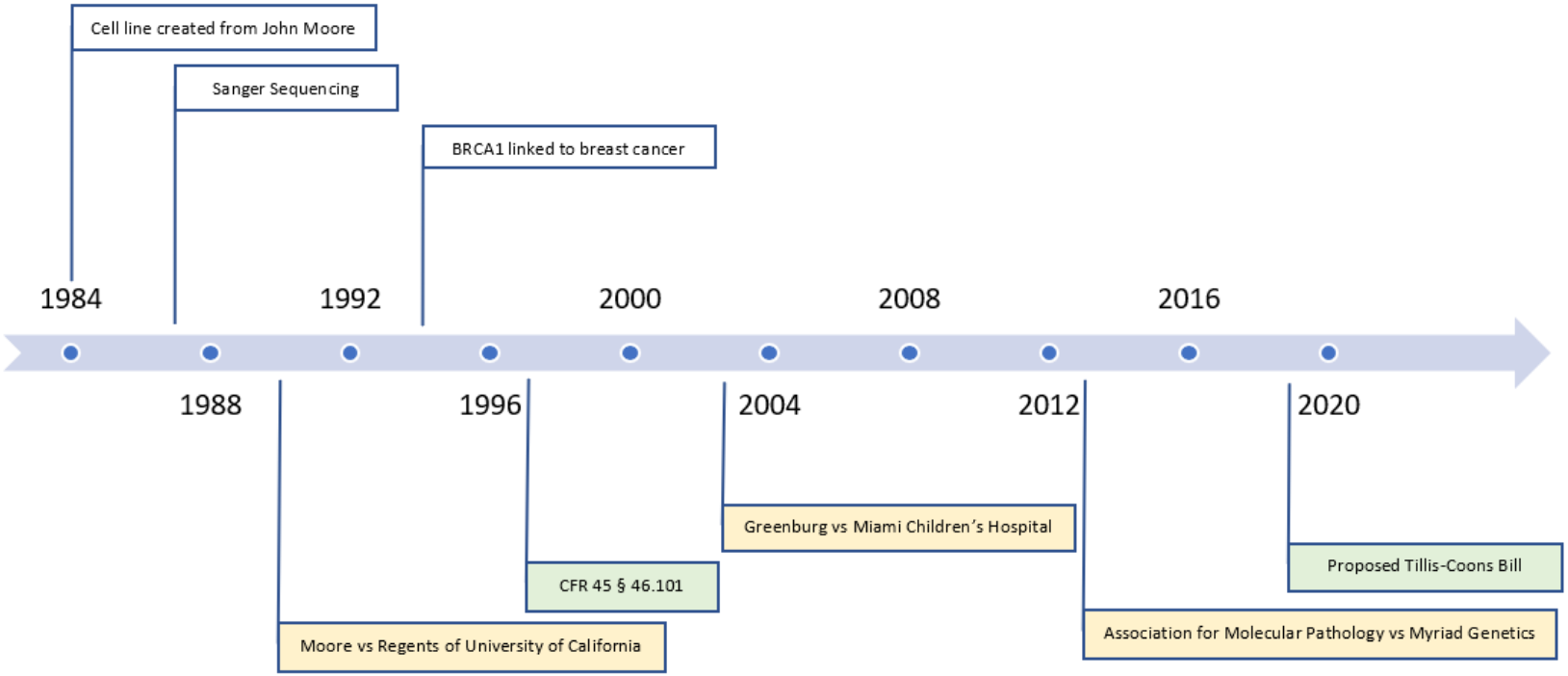

Figure 1. Timeline of Donation and Storage of Human-Derived Biological Materials from 1980 until present day. Scientific events are above the timeline, while political events are below the timeline. For the political events, events highlighted in yellow are from the judicial branch, while the events in green are from the legislative branch.

In this case, the political structure influenced science. Because of judges' rulings, scientists are able to commercialize their research without providing benefits to the donor. However, the courts did side in a way that benefitted in the public by not allowing companies to patent gene sequences. Patents on gene sequences linked to disease prevent scientists from identifying mutations in the gene and can hinder pharmacological research to find drugs to cure the disease (Andrews, 2002). With CFR Title 45 § 46.101, policy is affecting science, especially in relation to donation. Scientists now have to go through more steps and paperwork before using the donated samples. This has the potential to slow down research, but it is more beneficial to the donors as their privacy is protected.

Human Embryonic Stem Cells

The first hESC was created in 1998, followed promptly by the first patent on the creation of hESC (Eguizabal et al., 2019). The hESC lines were created from embryos that had been discarded after in vitro fertilization. However, the Dickey-Wicker Amendment was previously passed in 1996 (Rodriguez et al., 2011). This amendment bans funding for research involving embryos that are harmed or destroyed, and has been continually renewed since it was first passed with very limited changes. People began to argue that creating the hESCs from the discarded embryos violated the Dickey-Wicker Amendment.

In 2001, then-President George W. Bush signed an executive order specifically banning federal funding of hESCs (Murugan, 2009). However, researchers were allowed to continue doing research with hESC lines that had been created before the executive order was in place. In 2004, scientists discovered the potential of hESCs to revert to germ cell lineages. They believed that this ability to differentiate into any cell type in the body would be critical in regenerative medicine research. However, to get the most accurate data and to have the potential to be used in

people, researchers needed hESCs of the highest quality. Unfortunately, many of the hESC lines derived prior to President Bush's executive order were not high quality due to contamination or outdated procedures to derive the cell lines.

In 2009, then-President Barack Obama issued an executive order overturning President Bush's executive order banning federal funding for hESC research. In response to President Obama overturning the executive order, researchers Dr. James Sherley and Dr. Theresa Deisher filed a lawsuit against Kathleen Sebelius, the Health and Human Services Department Secretary, and Francis Collins, Director of the National Institute of Health (NIH) (Greene et al., 2011). They believed that the NIH guidelines on hESC research violated the Dickey-Wicker Amendment. However, a judge ruled that the NIH guidelines did not violate the Dicey-Wicker Amendment in 2011 in the case *Sherley v Sebelius* (Greene et al., 2011). It was argued that the Dickey-Wicker Amendment does not apply to hESC lines that have been derived since they are cell lines and no longer embryos. In 2014, the first clinical trials involving hESCs began, involving one of the cell lines derived in 1998.

These scientific and political events surrounding the creation and use of hESCs in research can be seen in Figure 2.

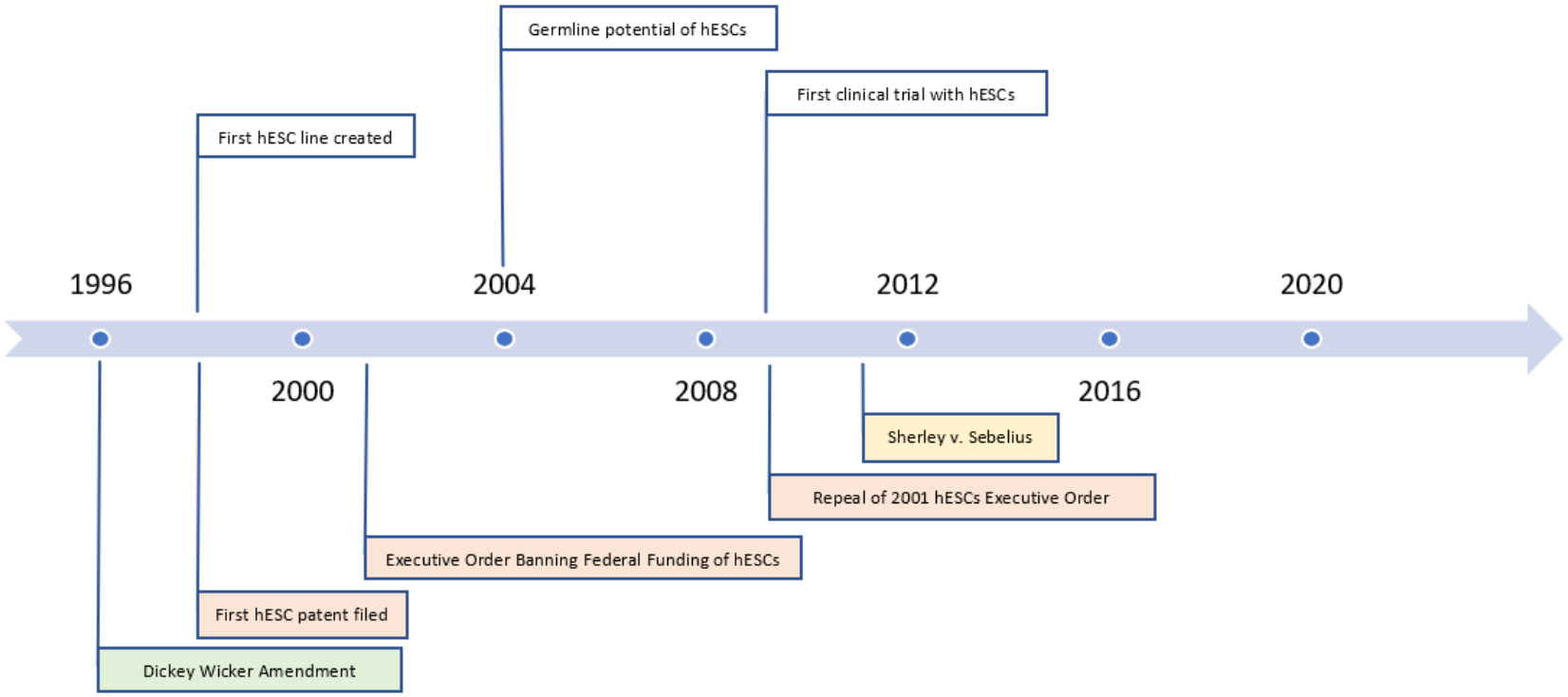

Figure 2. Timeline of human embryonic stem cells (hESCs) from 1990 until present day. Scientific events are above the timeline, while political events are below the timeline. For the political events, events highlighted in orange are from the executive branch, the events in green are from the legislative branch, and events in yellow are from the judicial branch.

In this case, science influenced politics. This discovery of cells derived from human embryos inspired an ethical debate on the definition of when life starts and what constitutes harm to an embryo, which led to the executive order by former President Bush. The executive order then in turn influenced science, as United States researchers could no longer create new hESCs in their laboratories located in the United States. Additionally, then-President Bush had announced that more than sixty hESC lines would still be available for research (Hynes, 2008). However, the actual number was closer to twenty, with many of those cell lines not suitable for research. This limited number of hESC lines further hindered the scientific progress in fields like regenerative medicine that rely on hESCs.

Discussion

The above cases offer evidence of the co-production of science, the donation and use of human-derived biological material, and society, the political structure in place in the United States. Both cases highlight policies from all three branches of the United States government, illustrating that all three branches influence human-derived biological material and, in turn, are influenced by it.

Due to the interwoven nature of science and politics, it is important to highlight the critical communication between scientists and politicians when it comes to informing science policy. Politicians may be trying to draft beneficial laws, but they also may lack the understanding to actually make a positive impact. One example of this good intention with poor execution was a mandated forty-six question questionnaire for bone donation to reduce the possible spread of HIV (Hoeyer, 2014). The doctors admitted to rarely actually asking all of the questions on the form. The doctors prioritized answering their patients' questions and addressing their concerns over spending the time to ask all of the mandated questions. Additionally, there

have been no documented cases of HIV transmission via bone donation. While the politicians that created this questionnaire had good intentions (reducing the spread of HIV), they failed to effectively communicate with the doctors to ensure a positive impact. Similarly, this miscommunication between politicians and scientists can be seen with former President Bush's executive order. It is likely that President Bush was not purposely lying about the availability of hESC lines for research. It is probable that he was not aware of the various issues such as contamination and using outdated procedures to derive the hESC lines that limited the number of usable cell lines. If there was more effective communication between scientists and politicians, perhaps President Bush's inaccuracies about his executive order could have been avoided. With the proper communication, all parties involved, including patients, are properly informed and can benefit. In both of these cases, there is a space between what is known and what is being done.

In 2005, the World Health Organization (WHO) met to discuss bridging this space, which they refer to as the "know-do gap" (World Health Organization, 2005). They identified that this gap exists between research and policy as well as knowledge and action. They identified improving knowledge translation as critical to bridging the gap. WHO defines knowledge translation as "the synthesis, exchange and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people's health" (World Health Organization, 2005). WHO identified that there are certain factors that can push, pull, or help exchange that either facilitate or hinder knowledge translation causing cooperation or conflicts, respectively.

In the donor rights case, several factors were causing conflicts. The advent of sequencing rapidly changed research in a way that the political structure did not know how to prepare for. Additionally, there were financial benefits to allow companies to patent genes that appealed to

the capitalistic values of the United States. Fortunately, cooperation prevailed as information was exchanged between the two sides to explain the detrimental side to research of patenting genes. In the hESC case, the main factor driving the conflict was the failure to exchange information and the lack of demanding evidence. After learning the cells came from embryos, many people did not care about the rest of the science behind hESCs. It rapidly devolved into a debate of when life starts, not the scientific value of creating these cell lines. President Obama facilitated cooperation by creating an agenda to bring more scientific evidence to government decision-making. Exchanging information with scientists provided President Obama with the evidence showed that overturning President Bush's executive order would help research to benefit the people of the United States. These two cases highlight the importance of open communication to facilitate cooperation. However, the hESC cases highlights that both sides have to want the evidence and communication or else we have reverted back to conflict.

While my findings provide a good introduction to the co-production of politics and the donation and use of human-derived biological materials, it is not without its limitations. The biggest limitation is that the scope of this issue is extremely broad. I investigated all three branches of the United States' government. The category of donation and use of human-derived biological materials is also very expansive and can easily lead into other subjects like informed consent. Instead of the entirety of human-derived biological material use and donation, I decided to focus on three areas: human embryonic stem cells, biobanks, and patient rights. I also tried to limit my research to politics on a federal scale which is still very broad. Co-production could be analyzed on a more regional level by looking at state and local government policies.

If I could do this paper again, I would pick a much narrower scope for the paper. While my timeframe was narrow enough, my scientific and political focus was much too broad. Given

the chance to redo, I would pick a narrower scientific concept, such as only human embryonic stem cells. On the political side, I would focus on a singular branch of the government at one level, such as the executive branch exclusively at the federal level. This narrower focus would allow me to go more in-depth in my research and analysis of the subject.

With this knowledge from my analysis, I can advance my engineering practices. I will work to promote the engagement of scientists with science policy creation to ensure that the good intentions are actually achieved. I will work to communicate more effectively with policymakers and other non-science audiences to help bridge the know-do gap. Next year, my research will involve donated human organs. It will be critical for me and my team to effectively communicate with the donors about what we are doing. We will also need to effectively communicate with policymakers to make sure we are abiding by all policies and to help improve policies going forward.

Conclusion

Science and politics are a complex, interwoven socio-technical system that have influenced one another over time. The two cases analyzed in this research paper show that the influence of science and politics on one another can either benefit or harm current and future patients. Therefore, proper communication between scientists and policymakers is critical to benefit patients by preventing any unnecessary panic, allowing progress in research to be made, and creating more useful laws. Working together, scientists and politicians can promote knowledge translation and narrow the know-do gap. However, there has to be a demand to share information and evidence from both sides. Failure to properly communicate and want information from one another will result in more conflicts between science and politics instead of cooperation.

References:

Andrews, L. B. (2002). Genes and patent policy: Rethinking intellectual property rights. *Nature Reviews Genetics*, *3*(10), 803–808. https://doi.org/10.1038/nrg909

Andrews, L. B. (2005). Harnessing the Benefits of Biobanking. *Journal of Law, Medicine, & Ethics*, *33*(1), 22–30.

Beskow, L. M. (2016). Lessons from HeLa Cells: The Ethics and Policy of Biospecimens. *Annual Review of Genomics and Human Genetics*, *17*(1), 395–417. https://doi.org/10.1146/annurev-genom-083115-022536

Cartwright-Smith, L. (2014). Patenting Genes: What Does Association for Molecular Pathology v. Myriad Genetics Mean for Genetic Testing and Research? *Public Health Reports*, *129*(3), 289–292.

De Souza, Y. G., & Greenspan, J. S. (2013). Biobanking Past, Present and Future: Responsibilities and Benefits. *AIDS*, *27*(3), 303–312. https://doi.org/10.1097/QAD.0b013e32835c1244

Edwards, T., Cadigan, R. J., Evans, J. P., & Henderson, G. (2014). Biobanks containing clinical specimens: Defining characteristics, policies, and practices. *Clinical Biochemistry*, *47*(0), 245–251. https://doi.org/10.1016/j.clinbiochem.2013.11.023

Eguizabal, C., Aran, B., Chuva de Sousa Lopes, S. M., Geens, M., Heindryckx, B., Panula, S., Popovic, M., Vassena, R., & Veiga, A. (2019). Two decades of embryonic stem cells: A historical overview. *Human Reproduction Open*, *2019*(1), 1–17. https://doi.org/10.1093/hropen/hoy024

Eiseman, E., & Haga, S. B. (1999). *Handbook of Human Tissue Samples*. RAND.

Greene, J., Kerr, O. S., & Klarman, M. J. (2011). Sherley v. Sebelius. *Harvard Law Review*, *125*(2), 626–633.

Hoeyer, K. (2014). Blood, death, and data: Engaging medical science and technology studies. *STS Encounters*, *6*(2), 1–26.

Hynes, R. O. (2008). US policies on human embryonic stem cells. *Nature Reviews Molecular Cell Biology*, *9*(12), 993–997. https://doi.org/10.1038/nrm2528

Jasanoff, S. (2004). *States of Knowledge: The Co-Production of Science and the Social Order* (1st ed.). Routledge. http://ebookcentral.proquest.com/lib/uva/detail.action?docID=200656

Mersch, J., Jackson, M., Park, M., Nebgen, D., Peterson, S. K., Singletary, C., Arun, B. K., & Litton, J. K. (2015). Cancers Associated with BRCA1 and BRCA2 Mutations other than Breast and Ovarian. *Cancer*, *121*(2), 269–275. https://doi.org/10.1002/cncr.29041

Murugan, V. (2009). Embryonic Stem Cell Research: A Decade of Debate from Bush to Obama. *The Yale Journal of Biology and Medicine*, *82*(3), 101–103.

Rodriguez, S., Campo-Engelstein, L., Tingen, C., & Woodruff, T. (2011). An Obscure Rider Obstructing Science: The Conflation of Parthenotes with Embryos in the Dickey–Wicker Amendment. *The American Journal of Bioethics*, *11*(3), 20–28. https://doi.org/10.1080/15265161.2010.546472

Schleiter, K. E. (2009). Donors Retain No Rights to Donated Tissue. *AMA Journal of Ethics*, *11*(8), 621–625. https://doi.org/10.1001/virtualmentor.2009.11.8.hlaw1-0908.

Semb, H. (2005). Human embryonic stem cells: Origin, properties and applications. *APMIS*, *113*(11–12), 743–750. https://doi.org/10.1111/j.1600-0463.2005.apm_312.x

Shendure, J., Balasubramanian, S., Church, G. M., Gilbert, W., Rogers, J., Schloss, J. A., & Waterston, R. H. (2017). DNA sequencing at 40: Past, present and future. *Nature*, *550*(7676), 345–353. https://doi.org/10.1038/nature24286

Sherkow, J. S. (2019). Patent Eligibility Reform and the Public Health. *The Milbank Quaterly*, *97*(1), 654–658.

Terwilliger, T., & Abdul-Hay, M. (2017). Acute lymphoblastic leukemia: A comprehensive review and 2017 update. *Blood Cancer Journal*, *7*(6), 577. https://doi.org/10.1038/bcj.2017.53

Ursano, R. J. (2012). "Science calls her HeLa." *Psychiatry*, *75*(2), 101–102. https://doi.org/10.1521/psyc.2012.75.2.101

World Health Organization. (2005). *Bridging the "Know–Do" Gap*. WHO.