THE FUTURE OF TUMOR REVERSION THERAPY: HOW SOCIETY DECIDES THE INTERPRETATION OF A TECHNOLOGY

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By

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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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DEVELOPENT OF AN AUTOMATED BALL LAUNCHER AND EVALUATION OF TRAJECTORY OF TUMOR REVERSION THERAPY

A treatment that can undo cancer without collateral damage may sound like science fiction, but it may soon be a reality. Although cancer survival rates have significantly increased in the past three decades, the treatments that defeated the cancer typically result in some form of permanent damage or significantly increase the likelihood of another life-threatening disease. (Miller et al., 2019). The risk of most cancer treatments is that they may damage healthy cells in their attempt to kill cancer cells, but if tumors could be reverted into normal cells, then the risk would be eliminated. There are theoretically many ways that tumor reversion can be accomplished, but which will produce the first clinically approved tumor reversion therapy in a human being?

The STS thesis paper analyzes and compares three ongoing areas of research that have the potential to facilitate the reversion of tumors into healthy tissue: the replication of the embryonic microenvironment, creative utilization of gene editing, and the direct manipulation of bioelectric networks. Various aspects of society play a role in determining which technologies are used to develop tumor reversion therapy. Attention, and subsequent funding, from the scientific community have a large factor in determining which of those three will produce a reliable tumor reversion treatment. Additionally, new cancer treatments need to go through additional regulation and standards before medical practitioners consider adopting them. Each research area also has the potential to produce controversy and raise ethical concerns about the developing technology. The STS thesis is organized to explore the relationship between these social factors and the development of tumor reversion therapy through the framework of Social Construction of Technology, which was designed by Bijker et al. (1987) and revised by Klein and Kleinman (2001). The impact society has on each of the research areas is analyzed through

the framework of the Social Construction of Technology to answer the following question: How do the interests of the scientific and medical communities, as well as the regulatory and ethical concerns of society, influence which emerging technologies will produce the first clinically approved tumor reversion therapy?

During the Covid-19 pandemic, pet dogs spent most of quarantine bennefitting from increased attention in the company of their owners (Jezierski et al., 2021). However now that quarantine is lifted, pet dogs will be subject to emotional pain induced by the sudden drop in attention and time with their owners (Stephan et al., 2021). The goal of the technical thesis, or the capstone project, is to alleviate separation induced emotional pain experienced by dogs through the production of an automated ball launcher to play fetch with the dog while its owner is away. Electrical engineering student Alexander Byrd and computer engineering students Andrew Childers, Austin Turner, Hayden Sarpong, and Ji Sun Hong aimed to gain experience applying electrical and computer engineering by designing an automated ball launcher that could rotate and wirelessly communicate. The capstone project is motivated by a strong affection towards pets and an interests in gaining hands on experience designing a machine that incorporates mechanical parts, such as motors and servos, with electrical and computer engineering applications.

The STS and technical thesis are loosely coupled as their subjects significantly differ, but they share similar principles. Both the STS thesis and the technical thesis are motivated by a curiosity to explore applications of electrical engineering beyond circuitry and by a desire to produce new methods of alleviating unnecessary physiological pain. Both illustrate the importance of drawing information from different scientific communities to. Additionally, both analyze the myriad of different constituents that could comprise a technology. The technical

design process considers how the physical components of the automated ball launcher were selected. The STS thesis illustrates the importance of accounting for social factors regarding each option in addition to the physical properties of a technology's constituents.

SOCIETAL FACTORS INFLUENCING THE DEVELOPMENT OF THE FIRST CLINICALLY APPROVED TUMOR REVERSION THERAPY

THE SOCIAL CONSTRUCTION OF TUMOR REVERSION THERAPY

The analysis of the different methods for designing tumor reversion therapy will be done through the framework of the Social Construction of Technology, or SCOT. Professors of Science, Technology, and Human values Klein and Kleinman (2002, p 28) describe SCOT as a means for analyzing how the social environment impacts the design process of a technology. The interactions between the social environment and the technology are categorized into four components in SCOT: interpretive flexibility, relevant social groups, wider context, and stabilization (Johnson, 2005, p 1793). SCOT was chosen as the framework because its components serve as well-defined fields of comparison for technologies with similar purposes but different social environments.

The interpretive flexibility component of SCOT examines how research in gene editing with CRISPR, emulating embryonic environments, and altering bioelectric networks with electroceuticals are potential candidates for development of the first tumor reversion therapy. The relative social groups component will discuss the significance of specific organizations involved in development or regulation of the emerging technologies. The wider context component will focus on each technology's reception by broader communities and how other applications of the technology alter the public's perception of it. The stabilization component will discuss how the developing technologies are changing and predict their involvement in developing the first tumor reversion therapy.

Figure 1 shows how the first three components can all relate or affect the artifact without needing to influence one another. The interpretation and wider context, also sometimes called the

technological frame, are usually influenced by the social groups, but SCOT emphasizes the importance of their influence on the technological artifact instead of each other. Stabilization is the change in the content of each group due to feedback from the wider context and social groups.

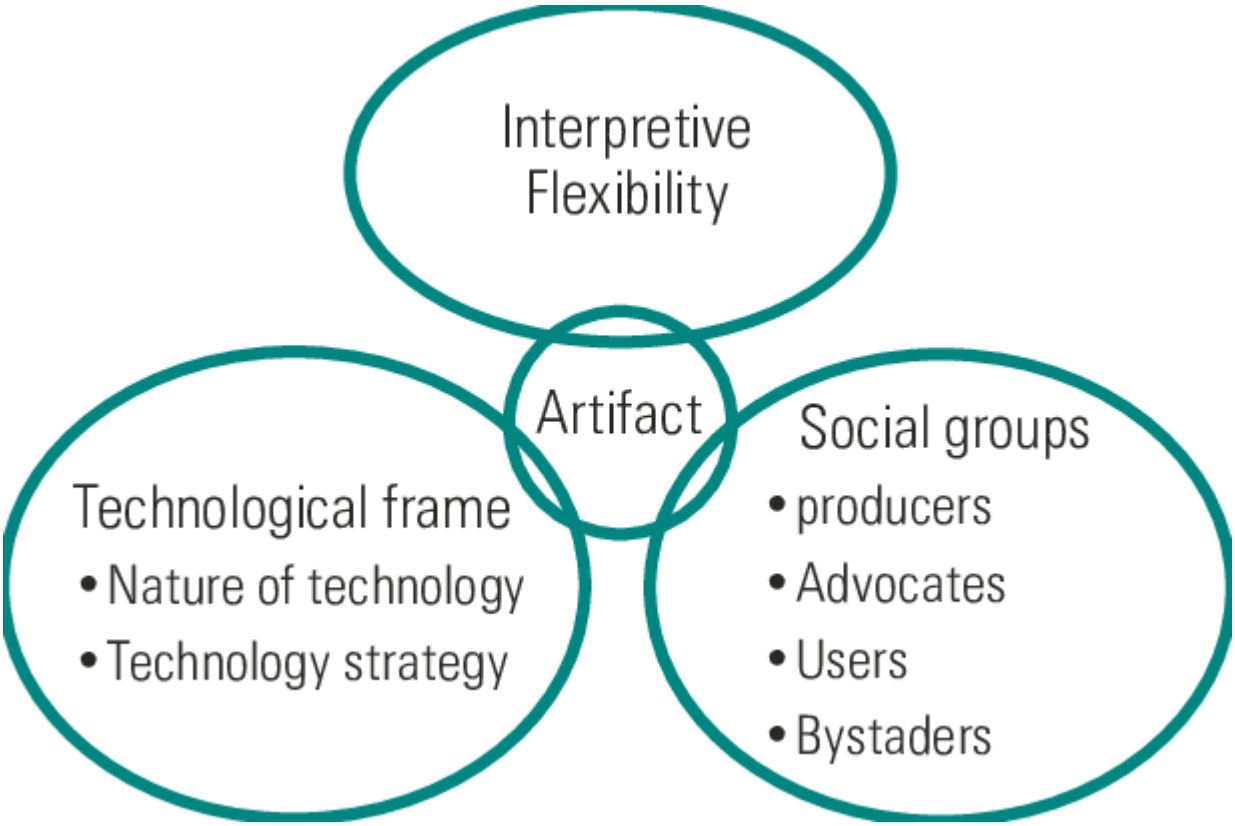

Figure 1. Components of SCOT. This Venn diagram illustrates that social groups, technological context, and the flexible interpretation clause of SCOT allow each to influence the artifact directly even if they do not directly influence one another (Yousefikhah, 2017).

INTRODUCING THE INTERPRETATIONS OF RESEARCH WITH POTENTIAL TO DEVELOP TUMOR REVERSION THERAPY

The interpretative flexibility component of SCOT allows for multiple interpretations of the same technological artifact. Klein and Kleinman (2002, p 29) define technological artifact as the overarching purpose or generally accepted idea of what defines a technology and its interpretations as the different inventions or methodologies that implement the technology. For example, pickup trucks, race cars, and buses are all interpretations of automobiles, the technological artifact in this instance. When the technological artifact exists to solve a problem, flexible interpretation can be extended to different interpretations of the problem's cause in addition to different implementations of its solution. Tumor reversion is the technological artifact in this instance, and it would entail integrating the tumor into the part of the body it has displaced. This integration would look like cancer cells turning into healthy cells to replace the ones it had killed, and then excess cancer cells that would undergo apoptosis, programmed cell suicide. Tumor reversion is still in its nascent stages of development, so it is unclear which research areas will result in the first tumor reversion therapy. Flexible interpretation provides the necessary foundation for comparing gene editing, embryonic microenvironment envelopment, and electroceutical manipulation of bioelectric networks as potential interpretations of the technological artifact tumor reversion therapy.

Undoing cancer requires a greater understanding of what causes cancer than the prominent theories that society currently accepts. Flexible interpretation accounts for different theories describing the cause of cancer. The conventional explanation for cancer is the Somatic Mutation Theory (SMT) which describes cancer as the product of genetic mutations on the cellular level (Boveri, 1929). Tumor reversion following SMT would be achievable by

identifying the cancerous gene then altering it in each cancer cell. Cancer cells are only capable of manifesting behaviors that a stem cell could exhibit, so in this sense cancer can be considered a phenotype (Prehn, 1994). The prospect of identifying and correcting every genetic mutation in every cancer cell may seem like a daunting task with under SMT, but it only becomes impractical in large or decentralized tumors. Soto (2011) proposed the Tissue Organization Field Theory (TOFT) to describe cancer as a systematic discrepancy in a tissue or cellular network. TOFT implies that a tumor could be reverted if the organization within the tissue was returned to its proper state. The TOFT theory seems better suited for tumor reversion, but it can be impractical if the correct state of the cellular network or how to return to it is unknown. Both theories hold truth, but their usefulness depends on the type cancer being analyzed.

Gene editing, or gene therapy, technologies are the most appropriate for treating cancers that are characteristic of SMT. Dr. Jennifer Doudna and Dr. Emmanuelle Charpentier (2014) discovered that the Cas9 enzyme produced by Clustered Regularly Interspaced Short Palindromic Repeats, CRSIPR, was capable of identifying and altering DNA with incredible precision. Similar Cas enzymes can alter genetic material, so the technology is often referred to as CRISPR or CRISPR/Cas technology. In addition to changing DNA, some Cas enzymes are able to target genes that have already been transcribed into RNA, which express the genetic material stored in DNA (Patsali et al., 2019). CRISPR/Cas technologies have been tested and proven to be able to identify and repair genetic mutations that can lead to breast and ovarian cancers (Papsavva et al., 2019). Furthermore, the Cas13 enzyme can revert RNA that has transcribed the cancerous mutations to prevent its proliferation in cancer cells (Papsavva et al., 2019). Scientific Journalist Kim (2022) reported that a revolutionary clinical trial demonstrated that CRISPR/Cas technologies can be safely and effectively administered into the human blood

stream (Kim, 2022). Overall, proof that gene therapy can safely be implemented into the blood stream provides a versatile means of targeting tumors with CRISPR/Cas technologies. Once the appropriate genetic mutations are identified, CRISPR/Cas technologies can suppress or revert their expression and then amend the mutation to prevent its proliferation as a tumor.

TOFT asserts that malignant tumors spread throughout the body and induce cancer in neighboring cellular networks, but they are not the only cells that can reprogram their neighbors. Professor Bizzarri (2010) at the University of Rome observed that malignant cancer cells injected into a developing chick embryo would be differentiated into healthy somatic cells once the chick fully developed. Another experiment at the University of Rome observed that human breast cancer samples injected into unfertilized chicken eggs ceased to exhibit the random and erratic reproduction of cancer cells, formed duct-like structures characteristic of mammary glands, and started producing the components of milk (D'Anselmi, 2013). These findings proved that cancer cells could be reverted into healthy somatic cells when encompassed by an embryo, or embryo-like, microenvironment. The exact mechanisms causing this reversion are unknown but enveloping the tumor in an embryo-like environment is the most reliable method and factually supported means of reverting tumors.

Unfortunately, it is not easy to replicate in adult human beings. To accomplish this form of tumor reversion, a tumor must be surrounded embryonic, or embryo-like, stem cells. However, manually injecting and encompassing a tumor with stem cells would be more impractical and potentially more dangerous than traditional cancer treatments. to manually inject so the cells already encompassing the tumor will need to produce the embryonic microenvironment. Yu et. al (2007) at the University of Wisconsin discovered that the introduction of certain chemicals, known as transcription factors, caused somatic cells to become

undifferentiated into human induced pluripotent stem cells, or hiPSCs. The hiPSCs behave very similarly to embryonic stem cells and share their potential to be differentiated into different cell types, but they are less versatile and can only be induced certain types of somatic cells (Girlovanu et al, 2015). The hiPSCs are less likely to be rejected by the immune system since they share the patients DNA when they are derived from their own somatic cells (Lie et al, 2020, p 8-9). Zhou et al. (2018) demonstrated that CRISPR could be used on patient-derived hiPSCs to remove a genetic mutation causing muscular atrophy in spinal cord. The hiPSCs were then reintroduced to the spinal cord and caused cells that still had the genetic mutation to differentiate into healthy motor neuron cells that did not exhibit the atrophic phenotype (Zhou et al, 2018). This trial proved that stem cells could be safely introduced in the body, alter the problematic phenotypes, and then integrate itself into the body. A tumor reversion therapy could be implemented by a combining CRISPR/Cas and stem cell technologies.

Regenerative abilities to heal any wound, remodel any deformed feature, and replace any lost appendage are becoming more reality than fiction, and the same electroceuticals that are advancing regenerative medicine may also promise tumor reversion therapy for cancers characteristic of TOFT. Electroceuticals are a class of drug that directly alters the electrical signals between cells. Networks of bioelectric signals handle organizing, instructing, and regenerating complex multi-cellular structures called morphologies, so altering the bioelectric signals between the cells allows scientists to alter their morphology (Levin, 2021). Electroceuticals are . A novel way to view cancer is not just as a malfunctioning cell, but as a cell that rejects the network it was a part of and attempts to produce a new one. Luckily, altering the bioelectric network of a tumor can cause it to reintegrate into its original morphology as healthy cells (Chernet, 2013). Tumors essentially act like a separate organism from the one they

were once a part of. Since cancer cells no longer share a morphology with their earlier bioelectrical network, they can often be identified by irregularities in their membrane potential (Kuwahara et al, 2021, p. 7). Experiments have also shown that introducing certain bioelectrical signals to cancerous cells can inhibit their proliferation (Lansu, 2013, p. 6-7). Additionally, the introduction of bioelectrical signals to cancerous cells can cause the cancerous cells to reintegrate, or normalize, into the organism they previously diverged from (Chernet, 2013). A more disturbing discovery Chernet (2013) made was that some electrical signals could induce cancer in previously healthy cells, or force cells neighboring a tumor into joining it rather than vice versa.

Altering bioelectric networks to revert tumors is safest when the new bioelectric state is a well-studied one; such as the process of embryonic tumor reversion. As of 2020 (Sharma), nearly 100 of the key interactions between embryonic microenvironments and cancer cells have been identified, but there may be over a hundred more interactions to discover before we can accurately replicate the tumor reversion observed in embryonic microenvironments. The most promising model for these interactions identifies the relevant electroceuticals needed to cause Tumor-Associated Macrophages in the microenvironment to start killing cancer cells instead of healthy cells in ovarian tumors (Tripathi, 2021). This method can revert the tumor if enough cancer cells are killed to disrupt the tumor's network enough to allow a surrounding embryo-like microenvironments to revert the remaining cancer cells into normal cells rather than killing every cancer cell outright. Large tumors will still run the risk of causing collateral damage before the tumor reversion occurs under this model, but it is still a promising form of tumor reversion therapy.

Although electroceuticals seem to be the most promising technology for tumor reversion therapy, they are notably limited by their ability to reach the cells. CRISPR/Cas technologies could introduce the ability for cells to administer their own electroceuticals at controlled rates and quantities (Nanos and Levin, 2021). The most promising tumor reversion therapy would incorporate gene editing with CRISPR/Cas technologies, principles of envelopment with embryo-like environments, and altering bioelectric networks with electroceuticals. However, just because it is the most ideal design, does not mean that there is a willingness or demand for such a large collaboration.

Interpretive flexibility also allows for the interpretation of multiple technologies as a potential representation of tumor reversion therapy. Figure 2 illustrates that embryonic enveloping, gene editing, and morphology manipulation can all be considered a potential medium for tumor reversion therapy with their respective blue, yellow, and red circles. Additionally, varying degrees of collaboration between these fields of research would introduce additional interpretations that are described in the overlap between the circles in Figure 2. The descriptions of the technology in each overlapping section are just a single interpretation of how those technologies may interact to form tumor reversion therapy, as there could be more interpretations involving the same combinations.

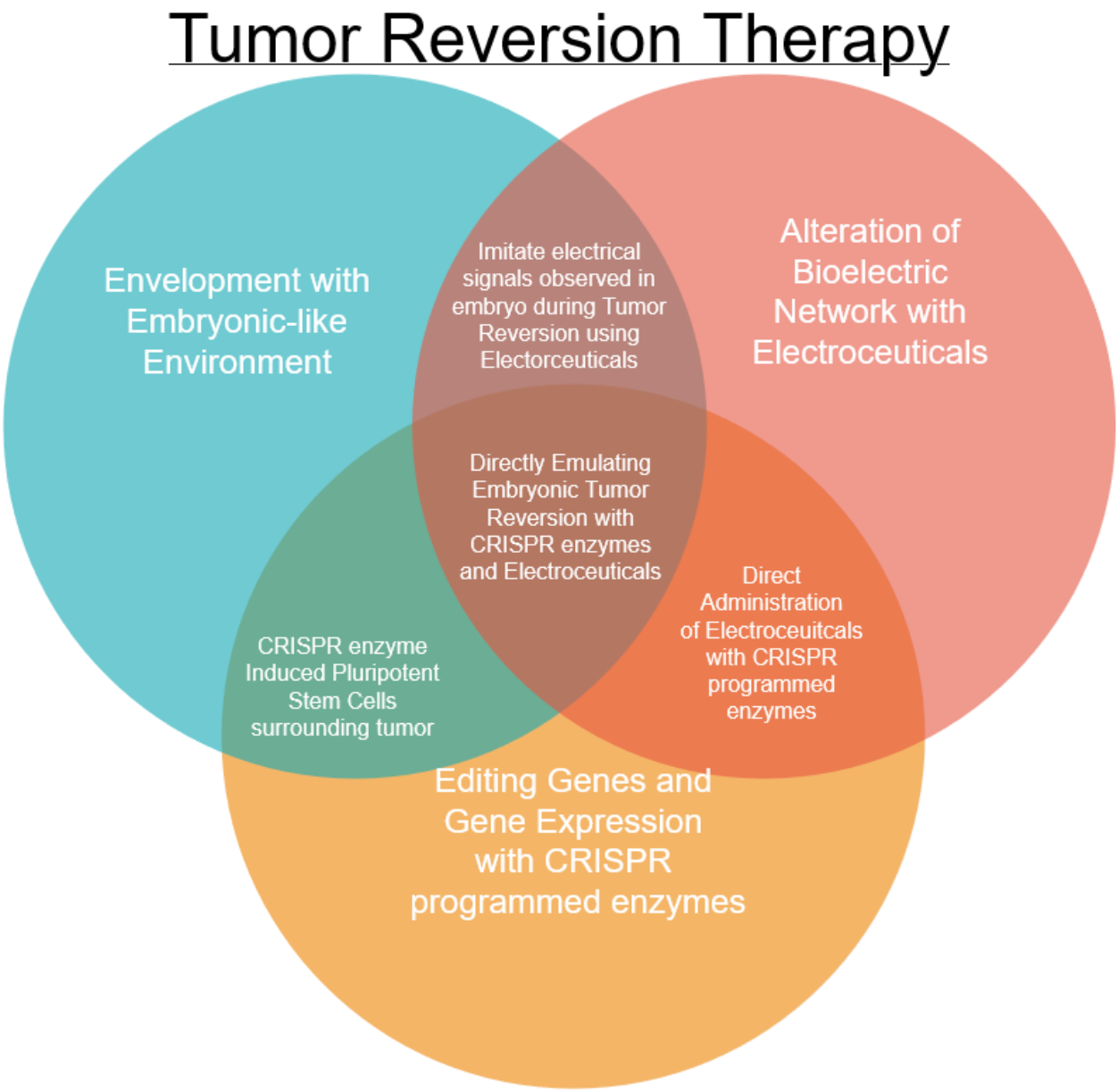

Figure 2. Interpretive Flexibility of Tumor Reversion Therapy. This Venn Diagram depicts how different technologies, whether unique from or in collaboration with one another, can still be considered the same technological artifact under interpretive flexibility. (Byrd, 2022)

THE RELEVANT SOCIAL GROUPS INVOLEVED IN RESEARCH IN DEVELOPMENT OF TUMOR REVERSION THERAPY

The relevant social groups are the driving forces behind the development of the technology. A social group is considered relevant when it contributes to the development of the

technology in some significant way, and the contribution does not need to be technological in nature (Klein, 2001, p. 29-30). The boundary between social groups is determined by their interpretation of the technology; people that share the same interpretation of a technological artifact and attitude towards that interpretation are part of the same social group (Bijker and Pinch, 1987, 30). Klein (2001, p. 30-31) critiques that the relevant social groups component of SCOT does not provide a metric for comparing the influence each group has, so it may lead to the fallible assumption that all groups contribute equally to the design process. Accounting for this concern, the most relevant social groups of the development of tumor reversion therapy are regulatory agencies involved in biomedical research preceded followed by the research and medical organizations developing the therapy.

The Food and Drug Administration, or FDA, are responsible for evaluating clinical trials for new medical treatments. Gaining the FDA's approval is a necessity for over-the-counter drugs, but FDA clearance is more significant when it comes to life-or-death medical procedures. Preclinical studies using non-human subjects must indicate that an experimental procedure could have medical applications before it gets the FDA clearance for clinical trials to start (American Society of Gene & Cell Therapy, 2021). Tumor reversion therapy is still in the preclinical stages but evaluating the medical treatments using experimental technologies provides insight into the process tumor reversion therapies using the same experimental technologies must undergo. For example, the FDA has placed additional regulations on stem cell based medical treatments, with the only stem cells derived from bone marrow currently being approved, so tumor reversion therapies aiming to envelop tumors with embryo-like environments may have more roadblocks in development than other methods (Food and Drug Administration, 2020). Conversely, the FDA has developed an expedited approval program to speed up clinical trials for regenerative

medicines, which would benefit research into electroceutical-based morphology manipulation thanks to its applications in regenerative medicine as well as the potential for tumor reversion (Food and Drug Administration, 2021; Levin, 2021). Many of the drugs considered electroceuticals are already in clinical trials or FDA approved, so new treatments using those electroceuticals have a strong foundation of existing clinical information at their disposal (Churchhill et al., 2019).

Towards the beginning of the Covid-19 pandemic, the FDA authorized the temporary deployment of a plethora of experimental diagnostic procedures to expedite the development of a reliable Covid test (Achenbach, 2020). Among the experimental procedures were several CRISPR/Cas based treatments regarding circulatory illnesses. These clinical trials were revolutionary because they were the first to demonstrate that CRISPR-Cas9 can be safely administered into the human blood stream (Kim, 2022). Even before the emergency protocols, there were already seven ongoing clinical trials using CRISPR/Cas technology, one of which aimed to knockout harmful RNA transcription in cancer cells to effectively inhibit them (Patsali et al., 2019). The FDA has set a promising precedent of allowing clinical trials of many CRISPR/Cas based treatments.

The versatility and modifiability of CRISPR-Cas9 can revolutionize medicine, so several parties are interested in being involved with it. The discovery of its gene editing capabilities earned University of California-Berkley (UCB) professors, Dr. Doudna and Dr. Charpentier, the Nobel Prize in Chemistry (Gotskind, 2021). However, legal disputes started when the (Regalado) 2015 edition of the Massachusetts Institute of Technology (MIT) Technology Review credited the development of CRISPR-Cas9 to the head of a research team at Harvard, George Church. This led to the Broad Institute, a Harvard and MIT collaboration, becoming engaged in a legal

battle with Dr. Doudna's team at UCB for the patent rights for the use of CRIPSR-Cas9 in gene editing (Taylor, 2021). Between significant applications of the other Cas proteins being discovered and the FDA's emergency measures, CRISPR/Cas research has become a lucrative and competitive field. Although competition typically raises quality, potential conflict over patent rights may discourage researchers from sharing info on any CRISPR/Cas based tumor reversion therapy in development.

Dr. Michael Levin is one of the biggest contributors towards research and development of new applications for electroceuticals. Dr. Levin began his works at the Allen Center for Discovery at Tufts University, but has since also founded his own laboratory, Levin Labs, and his own company Morphoceuticals Inc. Recently, a collaboration between the Broad Institute and Allen Discovery Center discovered a combination of electroceuticals that prevent the spread of glioblastoma (Mathews, 2022). Glioblastoma is a deadly and difficult to treat brain cancer that cannot be safely removed or killed without also significantly harming or killing the patient (Mathews, 2022). This breakthrough is promising since stopping its spread is a small milestone towards reverting the glioblastoma altogether. In other words, cancer suppression and prevention are necessary phenomenon to understand before cancer can be reverted. A consequence of this collaboration may reduce the likelihood of Levin's teams being able to collaborate with the teams developing CRISPR/Cas technologies at UCB.

Research teams in other countries are taking a more systematic approach for developing treatments with newer technology. The high demand to treat rare and presently untreatable genetic diseases has led a non-profit organization in France to start the development of a modular platform for CRISPR/Cas based gene therapies and could lead to faster and cheaper clinical trials for rare genetic diseases once completed (Kim,2022). Rather than needing to develop a separate

treatments that need approval like in the US, this team's goal is to make a versatile tool capable of treating many diseases involving genetic material, which would benefit tumor reversion therapy. Several Universities in India are collaborating to develop a sophisticated program that can model multiple bioelectrical, metabolic, genomic, or other types of interactions between cells and their microenvironment (Sharma, 2020). This program would try to simulate every key interaction of embryonic tumor reversion to predict which processes are necessary for tumor reversion to occur so that it can be reverse engineered (Tripathi, 2021). The program likely will not be completed in the foreseeable future, but once it identifies which of the interactions are responsible for the tumor reversion, it might be possible to replicate that interaction in adults using electroceuticals, CRISPR, or even existing medications. Even without all the information, it may provide new methods of treating some cancers or other maladies within this decade.

THE WIDER CONTEXT OF TECHNOLOGIES WITH POTENTIAL TO FOR TUMOR REVERSION THERAPY

The wider context component of SCOT addresses the implications of the technology for society beyond just its relevant social groups. Wider context is the most ambiguous component of SCOT, since it encompasses everything that the technological artifact, its interpretations, and its relevant social groups does not address (Klein and Kleinman, 2001, p 30). An example of the wider context of automated manufacturing could be the consideration of the environmental damage and elimination of jobs such a technologies may cause or an analysis of political and cultural factors propagating or inhibiting the technology. Klein and Kleinman (2001, p 40-42) critique that the distinction between groups in the wider context and relevant social groups is unclear or rarely defined. The groups involved in the wider context of the thesis will be limited to broad cultures and communities rather than concentrated organizations. The thesis limits the

wider context component to the examination of applications and consequences of an interpretation beyond the context of its technological artifact.

The technologies that could result in tumor reversion therapy have a plethora of other purposes, and their ethical implications are more complex than the case of a hammer. The tests needed to develop technology in embryonic envelopment requires potentially lethal experimentation on human embryos. Gene editing technologies blur the line between eugenics and preventative treatment for genetic malformities. Research into morphology manipulation is being used to create synthetic lifeforms, which forces society to question its responsibility to nature and definition of life. These ethical conundrums will be explored in further detail in this thesis.

Of all the discussed emerging technologies, CRISPR-Cas9 has the most media coverage. Controversy concerning CRISPR-Cas9 started when Regalado (2015) published the article "Engineering the Perfect Baby" in the 2015 edition of the MIT Technology Review. The article indicated that a majority of the scientific community involved with CRISPR-Cas9 intend on altering the human genome to make future generations smarter and healthier without significant concern for ethicality of eugenics (Regalado, 2015). Specter (2015), from the New Yorker, justifies this sentiment in "The Gene Hackers" by asserting that although fears of eugenics make sense, the fearful will eventually see the benefits and recognize they outweigh the risks. However, such reassurances were easily drowned out by shocking headlines such as Hall's statement that "scientists are set to cross a long-standing bioethical red line" in a 2016 publication in the Scientific American. Hall (2016) compares scientist's promises that gene editing will improve humanity to Adolf Hitler's promise to "create the perfect race" to illustrate how easy it is well intentioned scientists to be led astray down the dark road of eugenics. Beyond

eugenics, Maxmen (2015) discusses the potential for CRISPR to be used to develop bioweapons and mutant species in the Wired Magazine. People that didn't read about CRISPR-Cas9 would learn of its significance in laymen terms from a song of the same title that poses the question "is every congenital malady bettered sufficient to warrant unfettered?" (ACappellaScience, 2016). Although the scientific community seems to believe gene editing is worth the risk, the public is still distrusting of it and may be hesitant to accept medical treatments that may forebode applications in eugenics.

Controversy surrounding CRISPR still exists, but the pandemic has signifacantly increased the funding and appreciation for medical research. It is unclear whether opposition towards gene editing operations known as gene therapy will return with the same force, but for now researchers and investors are taking advantage of their freedom. Several insurance companies are now providing medical coverage for ongoing clinical trials in gene therapy, which makes procedures involving CRISPR/Cas technologies more available (American Society of Gene & Cell Therapy, 2022). There is a high demand for CRISPR/Cas gene therapies for rare genetic diseases that are presently lacking in effective treatments. While this may seem favorable for the development of tumor reversion therapy using CRISPR/Cas, funding may be diverted towards treating congenital diseases rather than new forms of cancer treatments. Scientific journalist Kim (2022) points out that it would be impractical to invest significant time and money into developing alternative cancer treatments with CRISPR/Cas technologies when they could hold a monopoly in treating genetic diseases that don't already have viable treatments. There is unlikely to be any significant breakthroughs in tumor reversion using CRISPR/Cas until researchers have exhausted its applications in hereditary diseases. Although a majority of research involving CRISPR/Cas technologies focuses on its niche in traeting genetic diseases,

developing those gene therapies could still indirectly provide unforeseen benefits in tumor reversion.

Discussions regarding human embryos are often polarizing. Religious concerns regarding embryonic stem cell research significantly limits where it can be performed. For example, the catholic church is strongly opposed to any research involving human embryos. This limits researchers in Rome to experimentation with non-human embryos, but it will take a great deal more research before any discoveries can be applied to humans without any human subjects (D'Anselmi et al, 2013). However, the demographics opposing embryonic research still encourage stem cell research that does not use human embryos for their applications in regenerative medicine (United States Council of Catholic Bishops, 2022). Therefore, advancements in human induced pluripotent stem cells, or hiPSCs may be required before embryonic tumor reversion can be emulate. The hiPSCs are not as problematic as embryonic stem cells, but they are less versatile and cannot induce as many types of somatic cells (Girlovanu et al., 2015). Furthermore, there is no guarantee that surrounding a tumor in hiPSCs will have the same effect as encompassing tumor in an embryo. Embryos are more than just a collection of stem cells; they are a complex biological network with malleable morphology. An experiment that induced stem cells in a mouse brain found that the new cells automatically integrated into the existing neural network; proof that stem cells can be safely integrated into existing networks, even the most complicated ones (Niu et al, 2013). This means that hiPSCs may be able to act emulate the complexity of embryos, but without experimenting with embryos it will be difficult to develop. Although hiPSCs and embryos are not the only source of stem cells, Tong et al. (2015) found human adult stem cells in articular cartilage and induced them into bone cells to treat osteoarthritis. Furthermore, very small embryonic-like stem cells, VSELS,

have been found in several adult bone tissues, but they are rare difficult to find and do not remain stem cells for long (Ratajczak et al, 2019). The adult stem cells in the body may hold potential for tumor reversion therapy, but they are even less understood than embryos. It is unlikely that there will be any advancements towards tumor reversion therapy that emulates how embryonic tumor reversion in regions where the culture or religion disapprove of embryonic stem cell research.

Altering bioelectric systems with electroceuticals is valuable for regenerative medicine, but it has more disturbing applications as well. Electroceutical based morphology manipulation can engineer synthetic lifeforms, which may raise ethical concerns about the technology. Without needing to alter the DNA, synthetic lifeforms can be created by essentially overriding the biological systems that tells cells which organ they are a part of and how to repair the organ if it is damaged (Ebrahimkhani et al., 2021). Synthetic life forms that have already been created can perform simple tasks, such as moving, but more sophisticated synthetic lifeforms are being produced to develop biocomputers and new forms of automation. At the Allen Discovery Center, Kriegman et al. (2020) are developing a system to automate the design and production of synthetic life forms; in other words, they are making a program that figures out what combination of electroceuticals are needed to manipulate a morphology for performing a given task and then it creates it. A trope in science fiction media is that robots will gain sentience and overthrow their human overlords, but organic lifeforms do have a will to live, so designing sophisticated biocomputers may become problematic.

Designing new species to be biological machines ought to raise ethical concerns, but synthetic organisms have not had enough media coverage for the public to ask these questions. The Government Ethics Committee (2022) acknowledge that creating synthetic lifeforms may

force humanity to question what it means to be alive, but their greater concern is the potential for biological weapons that could be developed. Despite concerns for biological weapons, or maybe aim for them, the federal government is providing grants and research funds for further research into synthetic organisms. According to a Markets and Markets(2021) report, the synthetic life market is already worth 10 billion dollars and is expected to reach 30 billion dollars by 2026. More than half of the organizations involved in the synthetic market are based in the US. Despite trends seen with CRISPR/Cas technologies, it seems that ethical concerns are unlikely to inhibit research into synthetic organisms. Development of synthetic organisms would significantly increase scientific understanding of biological networks, so there are clear benefits to tumor reversion therapy in electroceutical based morphology manipulation.

TRAJECTORY OF STABILIZATION TOWARD TUMOR REVERSION THERAPY

The dynamic nature of technology and society is addressed by the stabilization and closure component of SCOT. Stabilization is the cycle of feedback generated from the relevant social groups and the wider context of a technological artifact that causes an interpretation of it to gradually satisfy more social groups (Klein and Kleinman, 2001, p 30). Closure occurs when the cycle ends, and all relevant social groups reach a consensus for the interpretation of the technological artifact. Bijker (1987, p 44) states that closure can be reached by resolving the controversies surrounding a technological artifact or by redefining the problem the technology is addressing. However, the stabilization aspect of this component is the greater focus of the thesis since the thesis aims to analyze how society affects the process of designing the first tumor reversion therapy rather than predicting how a controversy-free tumor reversion therapy could be reached to achieve closure. Stabilization will account for how aspects of society influence the trajectory of different technologies towards the development of the first tumor reversion therapy.

Each developing technology was found to have a different trajectory regarding the cancer treatment. Enveloping tumors in embryonic-like microenvironments appears to be the most unlikely method to produce the first tumor reversion therapy; it has the least funding and recent media coverage of the three technologies, and its most prominent research teams are limited by cultural or religious concerns regarding experimentation with human embryos in the countries they are based. The gene editing tool CRISPR has the most public attention, but ethical concerns regarding its potential for eugenics or bioweapons, ongoing legal battles over patent rights, and the high demand in other medical applications distracts from its development towards developing cancer treatments. Morphogenetic manipulation using electroceuticals has the most support from the medical communities due to its many applications in regenerative medicine, many of the drugs considered electroceuticals are already approved for use in humans, and the controversial applications of the technology in developing synthetic lifeforms have surprisingly increased its funding from governments and private businesses hoping to develop bio-computers. However, the regular administration of the correct electroceuticals, in the correct places, and in the correct doses to revert tumors would require either long term hospitalization or a significant degree of patient participation, both of which are difficult to find. Realistically, research into embryonic microenvironments is needed to know which electroceuticals to use and where, and nanobots or CRSPR-produced biological agents are needed to administer the electroceuticals in regular intervals over long periods of time to produce the morphogenetic code necessary to revert a tumor

PROSPECT OF TUMOR REVERSION THERAPY

Tumor reversion therapy may still be a long ways in the future, but it appears that electroceutical research into morphology manipulation has the most potential to develop tumor reversion therapy before embryonic enveloping or gene editing with CRISPR/Cas. Electroceuticals directly impact the mechanisms responsible for cancer propagation, so it has the potential to be an effective tumor reversion therapy. Electroceutical morphology manipulation research has less regulatory barriers as most of the drugs used for electroceuticals are already approved for human and clinical use. Morphology manipulation using electroceuticals has the most support from the medical communities due to its many applications in regenerative medicine, many of the drugs considered electroceuticals are already approved for use in humans, and the controversial applications of the technology in developing synthetic lifeforms have surprisingly increased its funding from governments and private businesses hoping to develop bio-computers. A treatment that uses electroceuticals to manipulate the morphology of the tumor by altering its bioelectric network will likely be the first clinically approved tumor reversion therapy.

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