ECM Hydrogel Derived from Decellularized Adipose Tissue for Adipose Derived Stem Cell Differentiation to Augment Breast Reconstruction
(Technical Report)

Ignorance and Discrimination: The United States and the HIV/AIDS Epidemic
(STS Paper)

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

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Introduction

Each year, over 100,000 women in the United States require a mastectomy with limited options for breast reconstruction (Simon, n.d.). Current replacements have limitations regarding the inability to support the creation of new blood vessels and cover large defects, as well as defective volume retention rates. On the other hand, hydrogels can support vascularization and differing size defects, while volume retention rates can be controlled and monitored (O'Halloran et al., 2018). With the utilization of adipose tissue, one of the most abundant and consumable biomaterials, a hydrogel may be created with decellularized adipose tissue (DAT). Therefore, the technical project proposal serves to derive a hydrogel from the extracellular matrix of adipose tissue that can thereby support the proliferation of adipose-derived stem cells.

Even though the mortality rate in breast cancer has decreased by 40% in recent years, viruses and diseases such as human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) can still maintain high mortality rates for breast cancer (Simon, n.d.). According to a study in Botswana, women with HIV had a twofold reduction in survival rate for breast cancer even when patients were taking antiretroviral medication and had suppressed viral loads (Sadigh, 2019). Therefore, it is crucial to raise awareness of the correlation between an increase in the mortality rate in HIV/AIDS and breast cancer patients by overcoming the long-lasting stigmas associated with HIV/AIDS that have been created and proliferated by the United States government and its policies. The stigma attached to the HIV/AIDS crisis is deeply rooted in homophobia, xenophobia, and racism due to media outlets and influential people, such as the President of the time, referring to HIV/AIDS as the 'gay plague' (Lopez, 2015). The STS research paper proposal will examine the role of the United

States government creating and proliferating the stigma associated with HIV/AIDS and how these stigmas are deeply rooted in homophobia.

Technical Topic

In 2022, over 200,000 women in the United States will receive the diagnosis of breast cancer; 72% of these women will elect to have a mastectomy, while the other 28% will choose to have breast-conserving surgery (*Breast Cancer Facts and Statistics*, n.d.). Post-mastectomy reconstruction is typically done autologously from the patient's own body with varying muscle flaps known as autologous tissue transfer (ATT), or alloplastic with implants. In combination with either of these methods, autologous fat grafting (AFG) is used to provide contouring which addresses smaller deformities that remain after ATT or implantation methods. The choice of reconstruction method depends on the location of the resected tumor, the choice of the patient, or the need for follow-up treatment, such as radiation (Donnely et al., 2020).

The process of AFG includes taking a small amount of fat from another region of the body and reinjecting it in the site of the resected breast tumor. As only a small amount of fat can be removed from the body, AFG only serves minor defects after tissue transfer or implantation and can be absorbed back into the body due to the poor vasculature at the implantation site. Apart from the poor vasculature, a concern amongst experts exists about the potential for the insertion of fat tissue into what once was a cancerous site. Researchers are currently looking into the concern that it could lead to a reemergence of cancer (Ross et al., 2014). However, the two major complications associated with AFG are the weakness in areas from which fat was removed and the unpredictability of volume retention. The complication associated with fat grafting includes weakness in certain areas following the removal of fat, thus making daily tasks harder for patients who elect fat grafting or tissue transfer (Rabin, 2018). Additionally, a study done on

facial reconstruction AFGs, found that 33% of the initial volume inserted remains after a year (Meier et al., 2009). Thus, the existing complications within fat grafting create a clinical need for a more minimally invasive approach in post-mastectomy reconstructions.

To this end, adipose tissue is the most abundant, consumable, and easily harvested tissue already found in breasts, thus making it easier to use for tissue transfer and grafts. However, as mentioned previously, one of the complications associated with fat grafting is the lack of volume retention. Tissue engineering hopes to overcome this obstacle by creating a support structure that can withstand seeded stem cells and allow these cells to proliferate and incorporate into the surrounding tissue in breasts through adipogenesis (Donnely et al., 2020). By controlling these parameters in a laboratory setting and utilizing an extracellular matrix (ECM) hydrogel, the volume retention rate will significantly improve as a byproduct and the nutrient and waste exchange of cells can be closely examined. The ability to observe these parameters in an injectable hydrogel provides a much more stable and minimally invasive option for patients following post-mastectomies.

Adipose tissue is an optimal choice for the creation of a hydrogel as it provides an abundance of extracellular matrix proteins (ECM) and can secrete numerous growth factors into this matrix, allowing the hydrogel to support stem cell seeding and differentiation. In order to create the hydrogel, human adipose tissue following a liposuction at the University of Virginia University Hospital will undergo decellularization, lyophilization, cryo-milling, and digestion

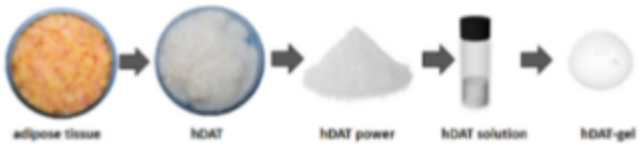

Figure 1: The creation of human decellularized adipose tissue hydrogel utilizing established protocols. *(Bunnell and Gimble, 2018)*

before finally undergoing gelation as the final step of the formation of the hydrogel (Figure 1). The processes will all be done according to established protocols by previous researchers in human decellularized adipose tissue (hDAT) (Bunnell & Gimble, 2018). We aim to measure the mechanical properties associated with both the adipose tissue and the created hDAT hydrogel to ascertain that the hydrogel created contains the same mechanical properties as existing adipose tissue within breasts. Additionally, adipose-derived stem cells (ADSC) obtained from human adipose tissue will be plated and cultured as we finish the formulation and hardening of the hydrogel (Figure 2). These ADSCs will be collected utilizing established protocols, including

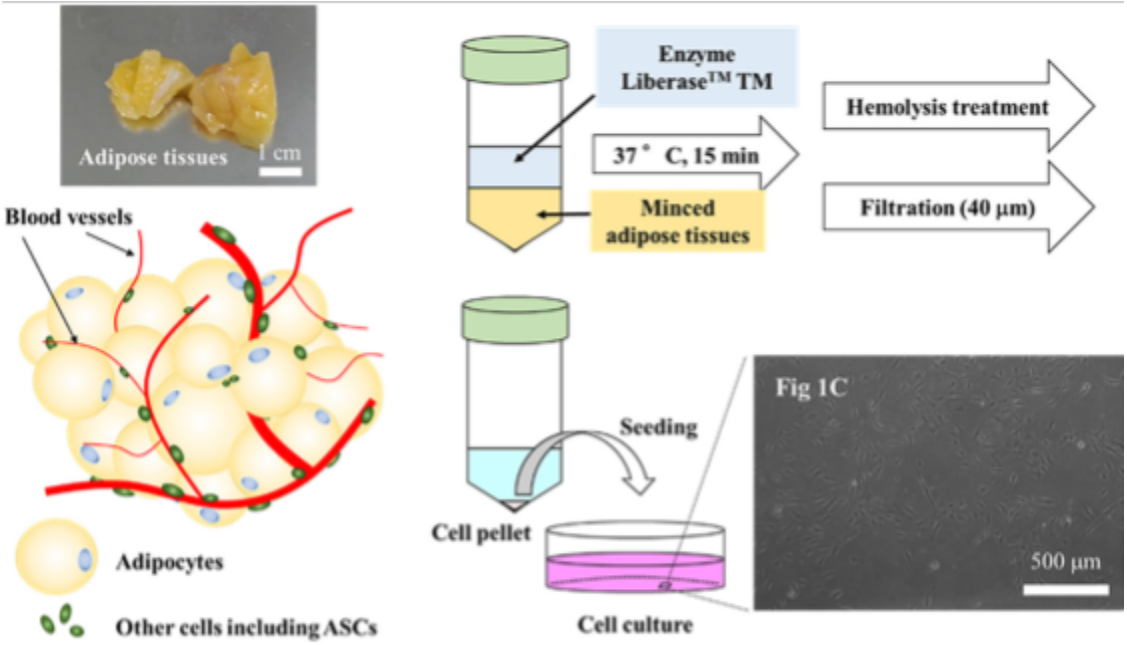

Figure 2: The process that is done for the collection of human adipose-derived stem cells. (*Saito et al., 2020*)

treating human adipose tissue with enzymes and lysis treatments before being filtered and pelletized before being seeded onto a cell culture plate (Saito et al., 2020). Following the creation of the hDAT hydrogel, ADSCs will be embedded into the hydrogel and stained and imaged on a weekly basis to ensure the vascularization and proliferation of the cells. This project would be deemed successful upon the creation of the hDAT hydrogel and the successful embedding of ADSCs with these stem cells proliferating and creating new vasculature in the hydrogel.

STS Topic

Human immunodeficiency virus (HIV) is a virus that attacks the immune system through the hijacking of T-cells and subsequently uses these cells to further replicate their viral material. If allowed to progress, the depletion of the immune system reaches critical levels leading to the development of acquired immunodeficiency syndrome (AIDS). Originally HIV was a virus commonly found in Chimpanzees and mutated to human infections during the 1800s; however, the HIV epidemic would not gain traction or awareness until the early 1980s (*About Hiv/Aids*, 2022). On June 5, 1981, the United States Centers for Disease Control (CDC) released a publication detailing a rare lung infection identified in five previously healthy gay men in Los Angeles. Following this publication, an influx of reports swept through the CDC regarding increased opportunistic infections infiltrating gay communities around the country (*A Timeline of Hiv and Aids*, n.d.). Unbeknownst to all, HIV/AIDS would continue to spread indiscriminately throughout the country with no real name linked to the disease until the latter half of 1982, when the CDC would finally identify AIDS.

As mentioned, HIV/AIDS spread indiscriminately across the globe and has continued to plague communities thirty years later, with over 40 million people dying following their battle with the virus (World Health Organization, n.d.). During the 1980s and 1990s, at the height of the epidemic, HIV/AIDS would be commonly referred to as the "gay plague" or "gay-related immunodeficiency disease (GRID)" due to the initial link to the gay community in the CDC's 1981 study. Although the initial linkage was made without malice and served as a simple observation on behalf of researchers, the stigma of HIV being a "gay disease" would continue to persist and haunt the members of the gay community for decades to come. The influence in which this stigma had on politics and funding allocations towards research would continue to

impact legislation and public opinion through the years, especially with the surgence of Monkeypox in 2022 (Chee Tao Chang et al., 2022).

Due to the lasting effects of the stigma HIV carries, it is essential to analyze the policies and legislature enacted by the U.S. government through the lenses of the political technology framework. The framework elaborated on by Langdon Winner, a political theorist who focuses on social and political issues as they relate to modern technology, delves into two definitions of political technologies. One tells about the process of technological development determining the politics of an artifact that can be used to further a power dynamic, and the other is about inherently political technologies that are "compatible with a particular kind of political relationships" (Winner, 1980). In the case of the HIV/AIDS crisis, the epidemic did not start as an inherently political technology. Instead, it gained political traction through the creation of policies and legislation to establish a power dynamic between the government and the LGBT community. The created power dynamic was one of control, fear, and shame as policies affected military enrollment, immigration, and funding allocations towards research. The critiques associated with political technologies include that technological advancement or specific displays of power can serve as an "excuse" to ignore political morality (Winner, 1980). Thus, it is essential to take this critique into consideration to establish the need to create equitable and equal political decisions regarding technology. A chronological timeline will examine the policies adopted in response to the HIV/AIDS crisis and how these policies caused the crisis to become a political device in various sectors of the government.

Methodology

Research Question: How has the HIV/AIDS crisis been utilized to create a power gap between the LGBT community and the U.S. government?

The STS research paper will examine the United States legislature passed in the 1980s and 1990s as a political technology to stigmatize HIV and AIDS further. Creating a chronological timeline of homophobic policies associated with the epidemic and the response caused throughout the country will aid in the legislature's analysis. Documentary research and policy analysis methods will be incorporated into the research process to complete this timeline. Documentary research papers will be used by reading newspaper articles from the 1980s and 1990s to identify the growing polarization and mischaracterization of the HIV/AIDS epidemic and the LGBT+ community. Articles that will be analyzed include: '*Magazine's HIV claim rekindles "gay plague" row*', '*The Reagan administration's unbelievable response to the HIV/AIDS epidemic*', and '*Homophobia out of the closet in the media portrayal of HIV/AIDS*' (Clarke, 2006; Howard & Yamey, 2003; Lopez, 2015).

On the other hand, policy analysis methods include reading policy and legislation that the United States government implemented in various sectors of the government. The examination of some of the policies in greater depth will include military testing for new recruits, medical examination of immigrants, and the refusal of President Reagan to allocate any substantial funds to the CDC (Bill Keller, 1985; Centers for Disease Control and Prevention, 2009; Padamsee, 2017). If a potential link between a governmental policy and homophobia in these government sectors exists, there will be a further investigation and discussion into the policy and its contents.

Conclusion

In the technical project, the final deliverable will be the creation of an injectable ECM hydrogel utilizing human decellularized adipose tissue. The human adipose-derived stem cells seeded into the hydrogel will be stained and imaged to ensure the cells' vascularization and survival over time. Additionally, mechanical testing will show the similarity between the

hydrogel and adipose tissue, giving a more realistic option for breast reconstruction. We hope to show non-toxicity and quicker healing rates in irradiated nude mice to move forward with potential clinical trials in the future.

For the STS research paper, a chronological timeline following news and research articles will examine the policies and legislation passed by the United States government regarding the HIV/AIDS epidemic and the public option of those infected with the virus. The political technological framework will demonstrate that the HIV/AIDS crisis was not an inherently political technology but became an attempt to establish a power dynamic between the LGBT community and the U.S. government through fear-mongering and homophobia.

Resources

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