

Undergraduate Thesis Prospectus

Developing a Decellularized Adipose Tissue
Hydrogel to Promote Soft Tissue Regeneration
(technical research project in Biomedical Engineering)

COVID Vaccine Opposition: Free Choice,
Safety Concerns, and Misinformation
(sociotechnical research project)

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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General research problem

How can disease burden in the U.S. be reduced?

The U.S. ranks 7th in gross domestic product (GDP) per capita (WPR, 2022). Nevertheless, ranked by life expectancy, the U.S. places in the mid 40s among all countries worldwide (Worldometer, 2022). The U.S. Centers for Disease Control and Prevention (CDC) reports a declining life expectancy in the U.S. In 2021, CDC estimated life expectancy at 76.1 years, the lowest since 1996 (CDC, 2022a). National health expenditure accounts for about 20 percent of U.S. GDP, amounting to \$4.1 trillion dollars in 2020 (CMS, 2022). The leading causes of death in the U.S. include heart disease, cancers, and COVID-19, which together claimed an estimated 1.65 million lives in 2020 (CDC, 2022b).

Developing a decellularized adipose tissue hydrogel to promote soft tissue regeneration

How can breast tissue be regenerated post-mastectomy?

The advisor for this BME project is Patrick Cottler, PhD in the plastic surgery department at UVA. I am working with peers Vy Nguyen and Andrea Kian on this capstone project. In the treatment of breast cancer, a patient may undergo a mastectomy, the surgical removal of one or both breasts. 40% of people diagnosed with breast cancer require mastectomy to ensure local and systemic disease control, amounting to more than 100,000 U.S. women each year (BWH, 2022). There are several existing strategies for breast reconstruction following mastectomy. Autologous fat grafting (AFG) is a procedure by which fat is harvested from the abdomen or thighs via liposuction and injected into the breast to reconstruct shape (CC, 2018). Autologous tissue transfer (ATT) is currently the most favorably viewed large volume reconstructive procedure; tissue such as fat, skin, and muscle is harvested from the body and used to reconstruct the breast

(AMC, 2022). Prosthetic implants, silicone gel-filled or saline-filled sacs placed under the chest muscle, are commonly used post-mastectomy to restore breast shape (NCI, 2011). However, all these methods have severe shortcomings. AFG is suitable only for small volume defects and is at risk of being absorbed back into the body if the fat fails to integrate completely into the new tissue environment. ATT is a costly solution that requires a high level of surgical expertise, a longer recovery period, and only is possible if there is enough excess tissue to transfer to the breast area (Breastcancer.org, 2022). Implants are susceptible to infection, migration to undesired areas, immune response to the foreign object, and there is a need for regular replacement (O'Halloran et al., 2018).

The goal of our project is to develop a hydrogel, which will be a 3-D cross-linked network composed of the extracellular matrix of adipose (fat) tissue, capable of supporting adipose-derived stem cells that are able to differentiate into mature fat tissue in order to regenerate the appearance and mechanical properties of the breast following mastectomy. Our hydrogel will need to be injectable, promote cell growth and blood vessel formation, be able to withstand the mechanical environment of the native tissue, and be non-toxic and non-immunogenic. We will follow and refine wet lab protocols to create the hydrogel and isolate adipose-derived stem cells, verify cell viability through culturing within the hydrogel, perform mechanical indentation testing to measure the stiffness and strength of the hydrogel and native tissue, and potentially pioneer an *in vivo* implant study on irradiated mice. At the end of the project, we hope to have a hydrogel that induces fat growth with potential use for large volume breast reconstruction following mastectomy.

COVID Vaccine Opposition: Free Choice, Safety Concerns, and Misinformation

In the U.S. since 2020, how have social groups that distrust public health guidance for the prevention of the transmission of coronavirus advanced their agendas?

The World Health Organization declared COVID-19 a global pandemic on March 11th, 2020. Four days later, the U.S. began to implement state-wide shutdowns to prevent the spread of the infectious, airborne virus. Despite social distancing and masking efforts, the CDC estimates 350,000 deaths due to COVID in 2020 (CDC, 2021c). The Food and Drug Administration (FDA) issued an emergency use authorization (EUA) for Pfizer's COVID-19 vaccine on December 11th, 2020, followed shortly by a Moderna EUA 7 days later (CDC, 2022d). An EUA facilitates the availability of vaccines during public health emergencies; all vaccine EUAs require final or interim analysis of a phase 3 clinical efficacy trial of well over 3,000 vaccine recipients, demonstrating that the known and potential benefits of the vaccine outweigh the known and potential risks (FDA, 2020). Receiving 2 or 3 doses of a COVID-19 vaccine is associated with a 90% reduction in risk for emergency ventilation and death, and models estimate that non-ICU hospitalization, ICU hospitalization, and deaths decrease by 64%, 66%, and 69% respectively (Moghadas et al., 2021; Tenforde, 2022). While many Americans welcomed vaccines, others distrusted them. Among those who distrusted the vaccines, some organized to propagate distrust.

Maciuszek et al. (2021) found that opponents of vaccination discount the knowledge of vaccination proponents, and vice versa. The explanation may be ingroup favoritism, outgroup negativity, or naive realism. Cowan et al. (2021) found evidence suggesting that political party affiliation has become a source of identity that shapes personal decision making. This partisan identity is a bigger factor than differences in demographics, institutional trust, or concern about COVID-19. Getting a COVID vaccine may now be viewed as something a Democrat may do,

whereas a Republican would not. Bolsen and Palm (2022) theorize that the COVID-19 vaccine itself is politicized due to its development and approval process coinciding with the presidential campaign and election of 2020.

Many Americans oppose the COVID vaccines as government intrusion. According to one, for example, they are a “big government thing where they’re trying to control the public” (Burnett, 2022). According to another, “you shouldn’t be able to force that stuff on people, it's step one, and then it'll be step two.” When asked what step two was, he replied with “who knows” (CNN, 2021). Some Americans distrust the vaccines because they suspect dangerous side effects, a fear often rooted in misinformation. One person believes the vaccines are a “de-population tool” with “malevolent stuff in it” (Burnett, 2022). Another believes that the vaccines are “snapping the DNA in half” (CNN, 2021).

According to the Center for Countering Digital Hate, 12 well-known figures, called the “Disinformation Dozen” by their critics, “produce 65% of the shares of anti-vaccine misinformation on social media platforms” (Bond, 2021). Prominent “Disinformation Dozen” member Dr. Joseph Mercola stated on his podcast “Take Control of Your Health” that his “favorite intervention for COVID-19 and other upper respiratory infections” is “nebulized hydrogen peroxide” (DOTB, 2020). This podcast has been shared over 4,600 times on Facebook (CCDH, 2020). Many health professionals have spoken out against this remedy, the Asthma and Allergy Foundation of America stating that hydrogen peroxide “can be toxic if ingested or inhaled” and “can cause respiratory irritation” (AAFA, 2021). Dozen member Dr. Sherri Tenpenny tweets regarding masks that “the longer you wear one, the more unhealthy you become” (CCDH, 2020). At an Ohio statehouse hearing organized by Republicans to debate a bill around civil liberties and vaccines, Tenpenny claims that the vaccines are “magnetized,”

claiming of those vaccinated that “you can put a key on their forehead, it sticks” (NBC News, 2021). Tenpenny’s Twitter account has since been permanently suspended for violating its COVID-19 misinformation policy.

“Disinformation Dozen” member Robert F. Kennedy Jr. founded Children’s Health Defense (CHD), a nonprofit that issues anti-vaccine propaganda. CHD claims it values “exposing truth,” “righting wrongs,” and “protecting our future,” according to its website’s main page (CHD, 2022). Digging deeper into the website reveals CHD’s more specific goals of “exposing the truth about vaccine injury” and “exposing fraud and corruption within the CDC and the pharmaceutical industry.” CHD publishes multiple articles per day designed to spread misinformation about COVID, recently including titles such as “6 Reasons You Might Be at Higher Risk of Injury From a COVID Vaccine” and “More Man-Made Pandemics and Pushing Kids to the Front Lines.” CHD, previously totalling over half a million followers on Facebook and Instagram, is now banned on both platforms.

The National Vaccine Information Center (NVIC) claims to be dedicated to “preventing vaccine injuries and deaths” and advocates for “voluntary vaccine choice” (NVIC, 2022). NVIC posted on Facebook “this is not how vaccine testing normally happens” and “big pharma will profit from the coronavirus” in March of 2020, along with over 300 other posts concerning COVID and vaccines from February to April. Kalichman et al. (2021) identified NVIC and three other individuals and groups, one of whom is Dr. Sherri Tenpenny, as leading propagators of misinformation and conspiracy theories disguised as legitimate sources of medical information. A Facebook analysis revealed that this early deception outpaced public health information from the CDC and FDA and hampered the rollout of COVID vaccination (Kalichman et al., 2021).

Lawmakers who oppose mandatory vaccines, citing reasons of personal autonomy or safety, can change COVID vaccination policies. Thirteen states, most of them predominantly Republican, ban vaccine mandates for employees (LeadingAge, 2022). Texas Governor Greg Abbott has said the vaccines are “safe, effective, and our best defense against the virus,” but argues that vaccination must be “voluntary and never forced,” suggesting that vaccine mandates are an infringement of civil liberties (Allen, 2021). Florida Governor Ron DeSantis states that “nobody should lose their job due to heavy-handed COVID mandates” and that the COVID vaccines “have not gone through enough testing and clinical trials,” justifying opposition to vaccine mandates as government intrusion and on grounds of safety and efficacy (Sarkissian, 2022; Staff, 2021).

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