DETERMINING THE EFFECT OF CARBON SOURCES ON *GARDNERELLA* BIOFILM FORMATION AND DESIGNING A BIOFILM DISRUPTOR

INVESTIGATING HOW DIFFERENT CULTURAL BELIEFS OF ASIAN-AMERICAN GROUPS SHAPE THEIR PARTICIPATION IN CERVICAL CANCER SCREENING

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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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General Research Problem

What is the public understanding of women's reproductive and sexual health care in the United States?

The most common vaginal infection in reproductive-age women is bacterial vaginosis (BV), with a prevalence rate of 27% in North America (Peebles et al., 2019). BV develops when there is a change in the bacterial composition of the vagina that causes a decrease in "good" bacteria and an increase in "bad" bacteria (Machado & Cerca, 2015). Current treatment plans are antibiotics such as Metronidazole, Clyndamycin, and Tinidazole (*Bacterial Vaginosis - Diagnosis and Treatment - Mayo Clinic*, n.d.). However, there is an issue of frequent recurrent cases within three to twelve months due to antibiotic resistance (Peebles et al., 2019). Based on previous research it is assumed that the development of a biofilm from the pathogenetic bacteria causes this resistance. However, there is a current lack of information on the metabolic mechanisms involved to develop an effective treatment for recurrent BV. This is a concern, as it is important to treat BV when it is discovered to prevent adverse outcomes. My capstone group aims to investigate the components of the biofilm, understand how they affect biofilm synthesis, and then develop a biofilm disruptor using the gained information.

When researching BV, the recent discovery of its positive association with cervical human papillomavirus (HPV) infection stood out to me (Gillet et al., 2011). HPV is a serious concern as thirteen types are oncogenic, cancer causing, and can lead to the development of cervical cancer (CC) (*Basic Information about HPV and Cancer | CDC*, 2022). While early stage CC can be treated with methods such as chemotherapy or surgery to remove the cancer, cervix, and/or the uterus, late stage is often not curable (*Cervical Cancer - Diagnosis and Treatment - Mayo Clinic*, n.d.). In order to detect CC in early stages, females should get routine cervical

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cancer screening. Even though this is a known way to prevent CC, the percentage of women in the United States overdue for screening has risen from 14% in 2005 to 23% in 2019. When analyzing the overdue data by race and ethnicity, Asian women had the highest percentage, 31% (*Rate of Overdue Cervical Cancer Screening Is Increasing - NCI*, 2022). These rates also vary among Asian American subgroups, with Korean American women having greater odds of never receiving screening than other subgroups (Yoo et al., 2011). My aim is to investigate the low rate of screening among Asian American women. Specifically, I will focus on the subgroup of Korean American women.

Both BV and cervical cancer screening relate to women's reproductive and sexual health. Although this topic has gained support in research funding and campaigns to spread awareness of its importance, there is still a stigma that limits its progression. The two projects will help with the progression of women's health care. The technical topic aims to further developments in treatments for disease that affect females, while the STS topic aims to understand social and cultural barriers associated with females seeking and receiving reproductive and sexual health care.

Determining the effect of carbon sources on *Gardnerella* biofilm formation and designing a biofilm disruptor

How do various carbon sources affect Gardnerella biofilm formation?

As mentioned earlier, recurrent cases of BV are common due to antibiotic resistance, meaning that in many situations treatments are ineffective. BV poses a threat to both women's health and the health of their future children, as it is associated with an increased risk of preterm birth, pelvic inflammatory disease, and the acquisition and spreading of sexually transmitted diseases (STDs), including human immunodeficiency virus (HIV) (Machado & Cerca, 2015). In

order to prevent these effects, BV patients have to routinely take antibiotics, leading to $4.8 billion spent in its treatment annually across the globe (Peebles et al., 2019). Gaining a better understanding of the metabolic mechanisms responsible for recurrent cases is imperative to developing an effective treatment plan.

BV infection is characterized by the overgrowth of pathogenic anaerobes, an organism that grows without air, in the vagina. The dominant group of anaerobes associated with BV is *Gardnerella* (*G.*) which can form a biofilm by synthesizing extracellular polymeric substances (EPS). EPS are polysaccharides, proteins, extracellular DNA, and lipids, in this case, originated from bacterium. When they aggregate, they form a biofilm that encapsulates and protects the pathogenic anaerobes (Di Martino, 2018). Previous research has shown that this biofilm is associated with decreased antibiotic susceptibility.

Our group's first aim is to identify the polysaccharide composition of the *Gardnerella* biofilm. We chose to look at the polysaccharide composition because it provides the EPS with the most strength. This will be done *in vitro*, outside a living organism, using synthetic vaginal media (SVM). Using this media, the *G. vaginalis* (ATCC 14018) and *G. piotti* (JCP8151B) strains will be grown to a mature biofilm state. The compositions will be characterized via immunofluorescent lectin and matrix staining. This will allow for the polysaccharides to be visualized and quantified using fluorescent microscopy, determining the specific ones present and their levels in the EPS.

The experiment is then repeated with select carbon sources, also known as monosaccharides. Since these carbon sources form the EPS composition of the *G.* biofilm, the use of different carbon sources may lead to alterations in the biofilm. Therefore, studying them will allow us to identify how these alterations manifest across *G.* strains. We will quantify the

biofilm formation using gold standard crystal violet staining method, which provides another way to visualize the effect of carbon sources in physiologically relevant conditions.

Lastly, using the data collected from the above experiments, we aim to predict and test inducers of *Gardnerella* biofilm dispersals. For our project the inducers we will use are enzymes. By gaining an understanding of the biofilm's composition, we can select enzymes that target the identified carbon sources in the EPS and hopefully damage it, allowing for increased antibiotic activity. This will be done using SVM altered with the enzyme inducers and co-incubated with mature biofilms. These changes will also be characterized through scanning electron microscopy. If compounds capable of inducing biofilm dispersion are identified, these can be used to develop efficient treatments for recurrent BV cases. This research will help further the understanding of the *Gardnerella* biofilm present in BV and contribute to the development of a novel treatment.

Investigating how different cultural beliefs of Asian-American groups shape their participation in cervical cancer screening

Why are there low rates of cervical cancer screening for Asian American women, specifically the subgroup of Korean American women?

Cervical cancer is the fourth most common cancer for women globally, contributing to 6.9% of new cases diagnosed in 2020 ("Worldwide Cancer Data | World Cancer Research Fund International," n.d.). Within the US there are around 13,000 new cases and 4,000 deaths annually (Burger et al., 2021). Even with these known statistics, the rate of American women overdue for CC screening is increasing, with higher rates among Asian American women (*Rate of Overdue Cervical Cancer Screening Is Increasing - NCI*, 2022). Through the STS paper, I want to investigate the impact of beliefs and practices within Asian American communities, specifically Korean Americans, that are contributing to these high rates. I will focus on how these cultural

components are used to help design intervention programs and the outcome of them. In order to do this, there needs to be an understanding of what CC screening is and how it can be perceived as off-putting.

Cervical cancer screening is valuable as it allows for precancerous cervical cell changes to be identified and treated, preventing further development. The two main screening methods are the HPV test and the pap smear. The HPV test checks cells for infection with the oncogenic strains of HPV. The pap smear collects a sample of cells and checks them for pathologic changes caused by HPV that can lead to CC if left untreated. Both of these tests are done during a pelvic exam. During the exam a speculum is inserted into the vagina and used to open it, allowing for a brush to collect samples from the cervix. The samples are then examined in a lab, looking for infection and/or abnormality. Screening recommendations are varied between age groups. For women 21-29 years old, the United States Preventive Services Task Force (USPSTF) recommends a pap smear every three years, as long as continued normal results. For women 30-65 years old, the USPSTF recommends a pap test every three years, a HPV test every five years, or a HPV/pap co-test every five years (*Cervical Cancer Screening - NCI*, 2022). Overall, the examination is fast and not harmful.

The ease of the procedure itself implies that there are other social factors preventing Asian American women from getting screened. Current understanding of the disparity assigns barriers into three main groups. The first of these is lack of understanding of cervical cancer. This issue occurs due to prevalence of misinformation, mostly about how someone develops and prevents CC (Fang et al., 2011). However, there have been conflicting results regarding this barrier, with some studies concluding that understanding was non-significant (Yoo et al., 2011). The conflicting data indicate a need for more research to be conducted. The second group of

barriers is lack of access to healthcare. These challenges include lack of insurance, cost, and language difficulties that deter women from seeking screening (Fang et al., 2011). Even if Asian American women have access to healthcare many of them do not utilize gynecological care as they need permission and support from male relatives (Gor et al., 2011). This ties into the third grouping of cultural beliefs which highlight gender-specific roles in Asian culture. There is a strong value placed on modesty among females that deters them from receiving pap smears. There are other beliefs about health being related to luck and that care should only be utilized when there is a clear problem (Fang et al., 2011). These aspects need more research as cultural beliefs vary among different subgroups of Asian Americans, meaning they can have varying levels of impact towards the likelihood of screening compliance (Yoo et al., 2011).

Research shows that there is no general method for producing effective intervention programs for Asian American women. The effectiveness depends on many factors such as location, type, and population. Shortcomings from these interventions are due to limited information on good quality interventions, intervention studies only focusing on Asian Americans, and lack of cost effectiveness and long-term sustainability (Lu et al., 2012). I plan on looking at the intervention programs designed for Korean American women to gain a better understanding of the problem of low CC screening compliance rates.

In order to understand the conceptualization and approach to the problem these programs take, I will first research the cultural beliefs and practices of Korean Asians. I will specifically read studies about gender dynamics and opinions and access to health care. Then I will examine the intervention programs that have been aimed to raise compliance rates for CC screening to see if they utilized the knowledge of these beliefs and practices to understand why they have been successful or not. This will be done by researching intervention programs that have been

implemented throughout the US, seeing if the approach utilized aligns with Korean American culture.

Conclusion

I hope to progress the development of effective intervention programs that promote cervical cancer screening among the Asian American population. My STS research will identify how cultural components should be utilized to conceptualize programs to address the issue of females not receiving cervical cancer screenings, specifically focusing on Korean American women. This ties into the larger issue of stigma surrounding women's reproductive and sexual healthcare.

The typical person feels uncomfortable discussing reproductive organs, issues, treatments, and sexual health. This has led to a lack of understanding of care for reproductive health issues in the common public and the scientific community. In recent years there has been more research conducted to further this field. My technical topic is part of this movement. We hope to better understand the *Gardnerella* biofilm composition and use this to select enzymes that will disrupt it. Such an advancement would improve women's sexual health and lessen the stigma around reproductive health.

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