DESIGN OF A UNIFORM AND TUNABLE LIGHT SOURCE FOR PHOTOLYSIS-BASED EXPANSION OF 3D CULTURED MESENCHYMAL STEM CELLS

NO LONGER SUFFERING IN SILENCE: HOW MEDICAL RACISM AFFECTS CANCER PATIENTS, AND HOW IT CAN BE COMBATED

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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 Project

How can the overall medical treatment of cancer patients in the U.S. be improved upon?

It is estimated that there will be 1.9 million new cancer cases diagnosed and 608,570 cancer deaths in the U.S. during 2021 (American Cancer Society, 2021). Until a cure is found, the treatment of cancer patients is the highest standard of care that can be provided. Treatment is a broad term that is often considered in solely a medicinal and physiological capacity. While medicines and therapeutics are undoubtedly vital to their care, the social treatment of patients– specifically minority patients – by their medical professionals is often overlooked but equally imperative.

Avoiding Enzymatic Breakdown: A Larger Platform for Photolytic Expansion

How can damage to 3D mesenchymal stem cells be avoided when efficiently passaging them for treatment and experimental use?

My technical research project is being completed through the Department of Biomedical Engineering under advisor Dr. Griffin. Graduate student Nicholas Cornell will be co-advising. This group capstone project will be completed alongside Hannah Bolen and Golnar Mostashari.

Background Information

3D mesenchymal stem cells (MSCs) have a variety of applications in both modeling and developing therapeutic treatments of diseased states. MSCs can be used in the advanced therapy of cardiovascular diseases, immune disorders, and cancer (Mandal et al., 2019). The culturing of MSCs is therefore absolutely vital in the continued development of novel treatment for various forms of cancer. A 3D hydrogel scaffold is used to maintain the viability and function of the cells

(Kim et al., 2019). Once the MSCs are ready to be passaged and/or harvested for use, the 3D hydrogel scaffold must be degraded to obtain only the MSCs.

A current common method of passaging MSCs uses proteolytic enzymes in order to degrade the 3D hydrogel scaffolds. This poses a problem because the proteolytic enzymes used to target the scaffold are also detrimental to the cell-generated local extracellular matrix (ECM) and cell surface proteins. This damage can result in the MSCs losing stem cells markers on the outside of the cell, a decrease in cell potency, and an increase in post-seeding lag times for cell expansion. In order to address this problem, Dr. Griffin has developed a photosensitive microporous annealed particle (MAP) hydrogel (Griffin et al., 2015) which is degraded when exposed to a specific wavelength and intensity of light. This light exposure will pose no threat to the current or future well-being of the MSCs, making it ideal for use in passaging.

While this technology is useful in procuring healthy MSCs, millions of cells are required for use in any application or experimentation. Presently, the MAP gel is used with MSCs in individual wells of a 96-well plate. When harvested, a small light that covers an individual well is used. This is time consuming and can result in varying consistency of the MSCs due to the fact that conditions may change in the first well by the time the last well is harvested. In order to successfully culture a significant amount of MSCs in a more efficient and consistent manner, a larger light source platform is necessary to simultaneously degrade the MAP gel in all 96 wells.

Project Specifications

The goal for this project is to create a light source platform for the 96 well plate that will be able to provide light at a wavelength of 365 nm and an intensity of 0-20 mW/cm2 +/- <20%. The constraints for this device will concern the conditions it must be able to withstand if it is to be used repeatedly. The platform must be able to withstand the temperature (37° Celsius),

humidity (95%), and CO2 concentration (5%) that exists inside an incubator and a tissue culture hood. The main point of concern among these three constraints is the humidity; the device must be sealed tightly in order to avoid the high humidity damaging the inner electronics of the LEDs. The power source for the platform will be outside of the tissue culture hood. Additionally, the 3D printing materials available will limit the material of the platform (i.e., metal vs plastic).

The platform will be conceptually designed using Autodesk Fusion 360. After a design is finalized, the non-electronic components will be 3D printed and the LEDs will be soldered into place. Since this will be used in close proximity to cells, the temperature of the platform is important. Literature suggests that MSCs can be exposed to temperatures up to 48°C with no significant negative effect (Reissis et al., 2013). A heat sink may be added to direct heat flow away from the device if the temperature rises above 45°C. Once the device has been created, a radiometer will evaluate its ability to provide light at the desired intensity. After characterization, the device will be validated by testing its degradation of MAP gel. If it is able to do so consistently, it may be tested in MSC harvesting/viability experiments as well.

At the end of the project, we will have a platform that is able to degrade MAP hydrogel scaffolding at a larger scale than is currently possible. This will allow for higher efficiency of high-throughput experiments and for more MSCs to be produced at one time. The increase in the scale of the degradation would be convenient for both research purposes and the production of MSCs for therapeutic treatments.

No Longer Suffering in Silence: How Medical Racism Affects Cancer Patients

In the past 30 years, how have advocacies worked to alleviate cancer health inequalities that minority groups in the U.S. have faced?

In the U.S., access to superior medical care is not equal; some inequities correlate with race, sex, and other demographics. Medical racism has been defined as "the systematic and widespread racism against people of color within the medical system. It includes both the racism in our society that makes Black people less healthy, the disparity in health coverage by race, and the biases held by healthcare workers against people of color in their care" (Bronson, 2021). Esnaola and Ford (2012) found that the cancer mortality rates among black people in the U.S. are on average 8.54% higher than among whites. Based on skin color alone, one could be nearly 10% more likely to die from a scientifically nondiscriminatory disease. If focus is only placed on the technological advancement of medicines and not the ways in which society can affect treatment, the overall care of cancer patients will never be comprehensively addressed.

Research on the steps required for antiracist treatment of Black, Indigenous, People of Color (BIPOC) adolescent and young adults (AYA) has been conducted. The term BIPOC is complicated, due to its perception as an amalgam that ignores the differences between the people it describes (Grady, 2020). BIPOC is used in this analysis because it is the category described by the research, but the controversy must be addressed. The Patient-Centered Outcomes Research Institute (PCORI) recommends that programs avoid tokenizing the BIPOC AYAs and instead follow a "transparency-honesty-trust" model (Cheung et al., 2021). This allows for genuine patient engagement, but the lack of BIPOC in leadership roles in the field of research poses a challenge. There has been research into the cancer surveillance systems implemented in the U.S. which strive to collect more comprehensive data on cancer occurrences across races, and the Intercultural Cancer Council (ICC) works to connect minority communities with these systems (Wingo et al., 2005). Finally, studies on four distinct groups of Americans (Native Americans, Alaskan Natives, Pacific Islanders, and Puerto Ricans) show how they focus on culturally-

specific comprehensive cancer control (CCC) for disparities that exist in their communities (Weinberg et al., 2010).

There are three participant categories that play a large role in the alleviation of cancer health inequalities in the U.S.: cancer minority advocacy organizations, the medical professionals who work with them, and minority cancer patients.

Cancer Minority Advocacy Organizations

Cancer minority advocacy organizations serve many purposes, but commonly aim to support minority cancer patients via peer support, strategies to improve treatments, and education about the inequalities that minorities face. The Greensboro Health Disparities Collaborative's (GHDC) agenda is to "empower and facilitate communities in defining and resolving issues related to disparities in health" (GHDC, n.d.). They accomplish this via The Partnership Project and a variety of equity workshops/training.

The African American Breast Cancer Alliance (AABCA) was formed in 1990 by six female African American cancer patients (AABCA, n.d.). In a press release with CBS Minnesota, co-founder and president Reona Berry said that "the AABCA learned facts about black women and breast cancer could not be found in a brochure, so they created one. It is now used nationally and internationally" (Chapman, 2013). This organization has three main programs: education, support, and survivorship which aim to create a safe space where patients and survivors can learn, connect, and survive.

Medical Professionals

Medical professionals carry out the programs envisioned by the cancer minority advocacy organizations in order to enact change. The GHDC partners with the Wesley Long Cancer Center and the Hillman Cancer Center to run the Accountability for Cancer Care

Through Undoing Racism and Equity (ACCURE) program (UNC, n.d.). ACCURE studied the completion of treatments by black and white breast or lung cancer patients and found that black patients were ~6% less likely to complete treatment. To attend to these disparities, the cancer center staff was trained by the Racial Equity Institute (REI) and patients were interviewed to ascertain where the treatment failed. Many black women stated that their diagnoses were not explained and there was a lack of support when complications arose. Afterwards, ACCURE nurses worked with them to "ensure patients understood their treatment options" (Hostetter & Klein, 2018) and began following up with patients if they missed an appointment or treatment milestone.

Minority Cancer Patients

Finally, minority cancer patients are trying to eradicate the health disparities they face. Survivor Ricki Fairley started her own nonprofit organization (Touch: The Black Breast Cancer Alliance) and has said "until we get more Black women to participate in research, we really don't know if the therapies are going to work on our bodies… we have a lot of work to do" (Gilead, 2021). Sheila McGlown is another breast cancer patient who is speaking out about issues she faces as a female minority with cancer. She stated, "I've never known a black woman who has been on a clinical trial until I got on one" (Ciitizen, 2020). Both of these women are working to increase the involvement of people of color in the research for the treatment that will directly affect them.

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