Thesis Project Portfolio

Optimizing a Gas and Liquid Gradient Bioreactor to Mimic Tumor Microenvironment

Researching Physicians' Priorities and Treatment of Mental Illness in Hypothyroidism

An Undergraduate Thesis

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Sociotechnical Synthesis

Mental and physical health are inherently connected: "…people living with physical health conditions experience depression and anxiety at twice the rate of the general population. Co-existing mental and physical conditions can diminish quality of life and lead to longer illness duration and worse health outcomes" (*The Relationship between Mental Health, Mental Illness and Chronic Physical Conditions*, n.d.). Despite the availability of drugs and therapies for various diseases, many of them are not completely cured yet. Unfortunately, in some cases, the research aimed at enhancing treatment options is not carried out efficiently or at all. As a biomedical engineer, my approach to patient care is holistic, and I aim to systematically observe symptoms to gain a better understanding of the research paths that are necessary. Determining areas where resources should be prioritized in medical research can expedite the development of more effective drugs and devices. This, in turn, can decrease mortality rates and improve the quality of life for patients while addressing both physical and mental health concerns.

Cancer has proven to be a major health issue globally, currently ranking as the second leading cause of death worldwide (Nagai & Kim, 2017). In the United States alone, cancer is projected to claim the lives of 609,820 individuals in 2023 (Siegel et al., 2023). While lifestyle changes may mitigate the risk factors associated with cancer, preventing cancer altogether is impossible. Thus, effective treatments and therapeutics are essential in reducing mortality rates. However, the success rate of translating cancer research into clinical success is strikingly low, with oncology clinical trials experiencing the highest failure rate among therapeutic areas (Begley & Ellis, 2012). Inaccuracies of the *in vitro* studies, which are studies performed outside of a living organism (e.g., in a test tube), and used in drug development, contribute significantly to this failure. Current *in vitro* tumor models lack physiological relevance and are unable to capture all aspects of the complex tumor microenvironment (TME) (Katt et al., 2016). Moreover,

the translation of research to clinical practice is painfully slow, with an average of 4-8 years of research required before clinical trials can commence (Zhang et al., 2020). My technological project improves and quickens *in vitro* research on anti-cancer therapeutics through the development of a dual gas and solute gradient bioreactor that can more accurately simulate the TME. My capstone team 3D printed a device that creates an oxygen concentration gradient, similar to those found in tumors, in which there exist regions that experience resistance to standard anti-cancer therapeutics such as radiotherapy and chemotherapy (Byrne et al., 2014). Utilizing an Arduino Uno and stepper motor pumps, we created an external pumping mechanism that generates a solute gradient within the device, orthogonal to the oxygen gradient. The resulting bioreactor is a device that simulates the dynamic TME, is biocompatible for cancer cell cultures, and has a transparent imaging window to be used for real time cell imagine via microscopy.

Hypothyroidism, or an underactive thyroid, occurs when the thyroid gland fails to produce and release enough vital thyroid hormones into the bloodstream. About 5% of the general population is affected by this condition, with a further estimated 5% being undiagnosed. Its symptoms include weight gain fatigue, poor concentration, depression, impaired memory, and menstrual irregularities (Chiovato et al., 2019). Orally administered levothyroxine (LT4) taken daily has been considered the standard of care for treatment of hypothyroidism for many years (Jonklaas et al., 2014). However, the adequacy of LT4 monotherapy treatment for all patients is being questioned as a substantial proportion of patients have persistent complaints despite consistent treatment (Chaker et al., 2017). The insufficient relief of symptoms, particularly those related to mental well-being, motivated me to explore further into the current treatment and provider care for hypothyroidism patients. My thesis combines an analysis of academic journal

articles and research studies done on hypothyroidism treatment with a dissection of literature discussing systematic contributions to physician complacency as a way to investigate why physicians place more importance on treating physical symptoms than on psychological symptoms in hypothyroidism patients. Through my research, I found that there is an over-reliance on the biomedical model of healthcare and a general lack of knowledge and resources concerning hypothyroidism and mental health. With these newfound answers, I was able to provide recommendations for future research into new diagnostic processes and hypothyroidism in general that could lead to the development of fully successful treatments.

Working on both my technical project and my thesis simultaneously provided me with a unique perspective on the interconnectedness of physical and mental health concerns in patients. Both projects highlight the need for more accurate and relevant research models. The insights into the challenges faced by physicians in addressing both physical and psychological symptoms in their patients that my thesis provided helped inform the design and development of my bioreactor as a new research *and* diagnostic device. This research continued to emphasize the importance of taking a holistic approach to patient care and played a large role in the work done on my technical biomedical engineering project. Overall, working on the two projects concurrently changed my entire outlook on how to responsibly practice engineering.

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