Undergraduate Thesis Prospectus

Sphingolipid Exploration: Understanding the Role of Sphingolipid Metabolism in Cancer

(technical research project in Biomedical Engineering)

The Cost Burden: How the Cancer Community Organizes Against High Medication Costs

(sociotechnical research project)

by

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November 2, 2020

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 cancer treatment options be improved?

Current cancer treatment options leave room for exploration and improvement. In the United States, the number of people living with cancer in 2016 increased to 15.5 million compared to only 3 million in 1971. It is estimated that 20.3 million Americans will be living with cancer by 2026 (Mayer et al., 2017). Because cancer molecular signaling is complex, foolproof treatments are not readily available. For most cancers, conventional cancer treatments can extend life but do not improve quality of life. (Fox Chase Medical Center, 2019). To develop more effective and more accessible cancer treatments, researchers need a better understanding of cancer signaling and networking. Besides better treatments, many cancer patients need better access to care. According to a 2011 forecast, the costs of cancer treatment were expected to rise 27 percent by 2020 (Mariotto et al., 2011). The expense of treatment often burdens cancer patients and their families; in response they and their allies organize to demand less expensive care.

Sphingolipid Exploration: Understanding the Role of Sphingolipid Metabolism in Cancer

How can the characterization and manipulation of bacterial sphingolipids offer insight into their functional role in cancer?

This is a solo Biomedical Engineering capstone project advised by Todd Fox, a faculty member in the Pharmacology department. The goals of this project include characterizing sphingolipid metabolism and manipulating bacterial metabolism to investigate the impact of sphingolipid deficiency on various biochemical markers. Sphingolipids are a class of membrane-bound lipids involved in various cancer signaling pathways (Lahiri & Futerman,

2007). By understanding the impact of sphingolipid metabolism, greater insight may be gained into cancer signaling pathways and possible treatment options.

In the United States, there are estimated to be almost two million newly reported cancer cases and over 500,000 cancer deaths in the year 2020 (Siegal et al., 2020). Various researchers have correlated the dysregulation of sphingolipid metabolism and cancer, but the mechanisms behind sphingolipid dysregulation, including bacterial sphingolipids, are still not fully understood (Furya et al., 2011; Ponnusamy, et al., 2010; Ryland et al., 2011). Therefore, further exploration of sphingolipid metabolism may provide direction for understanding the complexity of cancer signaling pathways and potential treatments, which may then lead to reductions in cancer prevalence.

Previous research and therapeutic solutions involving sphingolipids have dealt with the general class of sphingolipids rather than the division of bacterial sphingolipids. Various studies have explored possible therapeutic options such as modifying current chemotherapeutic approaches with sphingosine kinase inhibitors, but these approaches are not necessarily applicable to the bacterial classification of sphingolipids (Truman et al., 2014). Furthermore, few studies have investigated the impact of bacterial sphingolipid metabolism and its involvement in potential therapeutic treatments. Jang et al. (2018) examined mRNA expression levels of ceramide synthase genes, which impact sphingolipid metabolism, and found statistically significant overexpression of the genes CERS2, CERS5, and CERS6 in colorectal cancer patients. However, the mechanisms impacting the dysregulation of sphingolipids were not fully explained (Jang et al., 2018). Without the exploration of bacterial sphingolipid metabolism, advances cannot be made towards improving the treatment options of cancer patients. Therefore,

this project will explore the mechanisms involved in bacterial sphingolipid metabolism and potential impacts on cancer signaling pathways.

This project includes two broader phases: modeling and testing. The modeling phase will examine the impact of genetic sequences on the development of sphingolipid deficiency in sphingolipid-producing bacterial strains, as well as the impact of sphingolipid deficiency on different biochemical markers through bioinformatics and computational approaches. This will include utilization of the Basic Local Alignment Search Tool (BLAST) and MATLAB to identify genetic points of interest and to launch testing scenarios to generate data that will provide insight into the impact of the manipulation of different genetic parameters. The data collected from the modeling phase will then be tested through laboratory procedures such as cell and bacteria passaging, lipid assays, confocal microscopy. The purpose of the testing phase will be to examine the practicality of genetic modification explored during bioinformatics and computational approaches through the manipulation and creation of sphingolipid-deficient bacteria. If successful, insight will be gained on the functional role of bacterial sphingolipids, which may be applied to better understanding cancer signaling pathways and possible treatment strategies for cancer.

The Cost Burden: How the Cancer Community Organizes against High Medication Costs

In the United States, how have cancer patients and their families organized in response to the burden of high cancer medication costs?

In the United States, the high costs of cancer medication burdens cancer patients and families. Over the 20 years, the costs of cancer medications have increased over tenfold (Kantarjian & Rajkumar, 2015). The consequent financial hardships are greatest on those who

lack the means to cover out-of-pocket expenses (Abelson, 2014). Some patients who need life-saving care cannot afford it. The high costs of cancer care are well documented (Siddiqui & Rajkumar, 2012; Venkat et al., 2012). To combat high costs, patients, their families, and their allies organize. In response to the high costs of cancer medication, cancer patients and their families work to change the coverage system of cancer treatments (Gilligan et al., 2018; Kolker, 2004).

Researchers have investigated how patients and their allies organize to demand more affordable care. Rowland & Bellizzi (2014) investigated the importance of post-treatment programs, such as financial assistance, in the rehabilitation of cancer patients. Such programs can make a big difference. (Rowland & Bellizzi, 2014). Gilligan (2018) investigated movements to reduce the costs of cancer medication. To pay for care, some cancer patients or family members deplete savings, take second mortgages, or sell other property; others apply for Medicaid or seek support from assistance programs or advocacies (Gilligan, 2018). Kolker (2004) studied how breast cancer activists in the early 1990s organized to demand federal subsidies to relieve healthcare expenses (Kolker, 2004). Over the past 10 to 20 years, patients' means of organizing to relieve the burden of healthcare expenses have proliferated (Kolker, 2004). Coalitions of patient advocacies warrant more research attention (Rowland & Bellizzi, 2014).

Participants include cancer patients and their families who demand better cancer medication coverage (Abelson, 2018; Kandarian, 2014). Successful care can make patients "victims of their own success" who must struggle to pay for the treatment they received (Moore, 2018). Some patients' families "struggle to stay afloat" (Sainato, 2019). Some oncology practices strive to offer care at affordable prices (Penn, 2020). The Cancer Support Community, the largest nonprofit cancer support advocacy, promotes quality cancer care and connects cancer

patients with resources, including financial support (Fontana, 2020). The Cancer Support Community recognizes “cancer patients, in particular, who are in treatment are in a vulnerable category” and “provides $50 million in free support and navigation services each year to individuals affected by cancer” to alleviate the financial burden of cancer medication (Fontana, 2020; FreedomPay, 2019). Pharmaceutical companies seek to protect profits by resisting some efforts to control drug prices (Zand, 2018).

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