Thesis Portfolio

Engineering Suicide Gene Approaches to Improve Chemotherapeutic Response in Glioblastoma

(Technical Paper)

Consumer Access in the Field of Medicine

(STS Paper)

An Undergraduate Thesis

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Cancer is one of the leading causes of deaths in the US, and it is estimated that approximately 2 million people will be diagnosed with some form of cancer in 2023. This is not counting the millions of people who already live with cancer and go through many different expensive treatments that have not progressed in decades for many of the cancers. Currently, the leading treatments for cancers are surgery followed by chemotherapy and radiotherapy. These are all costly methods that a lot of times do not lead to a sure result because there are recurrences after a period of time. For this reason, the technical focus of this project is aimed at finding a novel gene therapy approach to targeted treatment of glioblastoma (a form of brain cancer). The STS research paper aims to look into the social factors that affect the cost and accessibility of healthcare.

For the technical portion of my thesis I have been working in a lab that works on different cancers to determine new methods of detection and treatment. Over the last three years I have worked on a project that focuses on glioblastoma, which is the most common brain cancer in adults, and it is uniformly lethal. Existing therapies, such as surgery followed by chemotherapy and radiation, fail to prevent disease recurrence, and new treatment approaches are urgently needed. Suicide genes are a potentially promising approach for glioblastoma wherein viruses are used to transduce tumor cells to express a foreign protein that converts a prodrug into a toxic product, resulting in cell death. The focus of my project is to engineer a suicide gene that cooperates with temozolomide chemotherapy in glioblastoma. Our design is based on herpes simplex virus thymidine kinase (HSVtk), which converts the prodrug ganciclovir to a toxic phosphorylated form. We have created versions of HSVtk fused to PEST sequences (domains rich in proline, glutamate, serine, and threonine that control protein turnover) that we predict will be stabilized by p38, a kinase activated by the stress of temozolomide-mediated DNA damage.

The ability of these next-generation suicide genes to augment the effects of chemotherapy and the molecular mechanism involved was studied in glioblastoma cells using immunoblotting, RT-qPCR, immunofluorescence microscopy, and flow cytometry. The results of this work will allow for post-translational control of a suicide gene with the combination of chemotherapy drugs.

In my STS paper, my main focus is to look into consumer access in the field of medicine from the perspective of the sociology of scientific knowledge STS framework. The sociology of scientific knowledge (SSK) framework focuses on "science as a social activity" specifically the social implications of scientific growth. This is an appropriate framework to use because with new treatments and therapeutic approaches to treat certain diseases there is the concern for the social effects on this. In 2021, 27.2 million people in the US did not have health insurance, which is necessary to help with the costs of medical care. For the thesis my plan is to understand the cost and profit ratios for the pharmaceutical companies as well as the consumer costs with or without insurance. SSK advocates would say that with the growth of scientific knowledge and with advancements in the field it is important to consider the social implications and those that are affected on a personal level such as the consumers of the treatments.

Through my work over the year researching and understanding ethics and how it affects decisions that are made in society I have gained a better understanding of the flaws in the healthcare system in the US. I have a great focus on healthcare and creating things that can cause advancements in the field of healthcare, and I think it is important for me, and others in the field, to understand the impact of their work on the users of their treatment and how it will be accessible for them. It is crucial to think about the use of treatments and how you make sure that the most people can have access to possibly life saving treatments. This is past the simple

discussion of whether something is ethical or not but more getting to whether someone should be able to get treatments or not depending on their financial circumstances.

I would like to thank the professors that got me to this point in my education, and a special acknowledgement to Dr. William Hart and Dr. Matthew Lazzara for teaching me all I know about research.