**A Nano-Enhanced Vaccine for Metastatic Melanoma Immunotherapy**

(Technical Paper)

**The Artificial Divide: How Food Additives Perpetuate Cultural and Socioeconomic Stereotypes in the United States**

(STS Paper)

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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

## Introduction

Two major threats loom over public health: cancer, a well-recognized but unsolved problem, and biased associations between processed food products and certain socioeconomic groups, a latent yet pervasive issue.

The incidence of melanoma cancer is rising faster than that of any other cancer, and nearly 100,000 people will have been diagnosed by the end of 2019 (Miller et al., 2019). This statistic becomes more dire considering data from "Survival Rates for Melanoma" (2016) and "Treatment of Melanoma" (2018) that indicate 5-year survival rates drop by as much as 50% if this cancer becomes metastatic, and surgery alone cannot offer remission. Thus, there is a critical need for cancer therapeutics that treat metastatic melanoma cancers. A challenging element of treatment development is minimizing side effects that degrade a patient's quality of life. There are three prominent approaches to lower toxicity and side effects that utilize targeting and nanomedical techniques: 1) using passive transport of stealthy nano-vesicles containing drug (Dance, 2017), 2) finding a cancer-exclusive target receptor with a highly specific targeting ligand (Suhoski et al., 2007), and 3) identifying a cancer-specific target antigen for immunotherapy (Fan & Moon, 2015). This project aims to develop a therapeutic that uniquely combines all three techniques above in an attempt to maximally treat metastatic melanoma while inflicting minimal side effects. In doing so, this work will address a gap in the treatment available for a disease posing an apparent public health issue.

This paper will also explore a less evident public health problem caused by the differential social construction of health impacts from processed food additives. Historically, embedded racist and xenophobic ideas about minority ethnicities, races, and cultures caused construction of beliefs that certain cultural cuisines are detrimental to health and should be

avoided. Notably, the construction of monosodium glutamate (MSG) as a harmful ingredient led to mass boycotting of Chinese restaurants in late-1960s America (Mosby, 2008). Ideas and fear about this ingredient and, moreover, a distrust in Chinese food establishments became widespread through the majority population. The harmful stereotypes instigated by the social construction of one ingredient motivated this work's research into the embedded social biases and stereotyping that still occur today. Similar biased constructions manifest themselves in many modern food additives, which becomes a problem when groups of people only have access to food products with negative constructions. This ubiquitous social problem is the cause of health disparities and harmful biases, yet the topic is vastly unexplored and unaddressed by the STS community. Thus, this research is vital for its recognition and steps to correction.

On the whole, this paper aims to tackle an infamous disease lacking effective treatment and to expose a subtle social construction of technology that promotes cultural stereotypes.

## Technical Topic

With melanoma as the second most common cancer affecting young adults between 15-29 years old, the need for an effective treatment with few side effects is great (Miller et al., 2019). Many patients do not respond to the available treatments and are left without the option to medically fight their disease. Nanomedical technologies and immunotherapy each offer unique benefits to a cancer treatment's biocompatibility and efficacy, but few researchers have been able to synergize these approaches within a single treatment (Kreuter, 1995). Rosenberg, Yang, & Restifo (2004) describe immunotherapies as using the body's built in mechanisms to overcome a cancer's immunosuppression—the feature of cancer that prevents the body from recognizing and attacking the disease on its own. One promising technique of aiding the natural immune system

is by way of "cancer vaccines" (Klyushnenkova & Alexander, 2012). Cancer vaccines work by taking a nonfunctional piece of a protein that is unique to the cancer's cell surface and injecting that back into the body, out of the tumor microenvironment where the immune cells like dendritic cells can endocytose this peptide as an antigen (Lee et al., 1999). Once this is achieved, the immune cascade has been activated, and an attack on the cancer is mounting.

However, the success of immunotherapy, especially cancer vaccines, faces challenges such as a short half-life of injected peptide antigen. The decreased circulation time means that the body clears the peptide drug before it can have a significant effect, as seen in published clinical trials (Pashenkov et al., 2006; Slingluff et al., 2013; Slingluff et al., 2008). Work on this project in collaboration with the Slingluff Lab began in May 2018 and will continue for this technical capstone. Previous work has used their cancer vaccine, comprised of six melanoma helper peptides, for loading of nanoliposomes, which are nano-sized synthetic vesicles made of lipids and are commonly used for their half-life extension properties (Gabizon, Shmeeda, & Barenholz, 2003). By loading the peptides into nanoliposomes, the half-life can not only be increased to allow for magnification of an immune response (Fan & Moon, 2015), but also allows this work to include the attachment of immunogenic epitope to the vesicle's surface. Adding an immunogen to the surface will allow for greater activation and uptake by dendritic cells, thus enhancing cancer vaccine efficacy.

The timeline for this research will begin with the characterization of the nanoliposomes that have been previously formulated and optimized by the author of this paper. Properties of peptide release kinetics from the nanoparticle cancer vaccine ("nano-vaccine") will be performed through stability studies using the resources in the Kester Lab. Studies of immunogenicity will be evaluated *in vitro* and *in vivo*. Initially, *in vitro* uptake of the nano-vaccine by peripheral

blood mononuclear cells will be performed using the resources of the Slingluff Lab and the UVA Molecular Imaging Core. The first *in vivo* murine study occurred at the beginning of the Fall 2019 Semester to characterize the biodistribution and immune response in the mice. A second *in vivo* murine study will occur in February 2020. This work is funded by the Engineering in Medicine Seed Grant and CIT Grant, and future studies may have supplemental funding from the Slingluff Lab.

In the Spring 2020 Semester, an IND application will be submitted to the FDA for a Phase 0 clinical trial to test the nano-vaccine in a small group of humans with terminal metastatic melanoma. Additionally, bioconjugation of a co-stimulating antigen from CellDex will be attempted to further improve the efficacy of the cancer vaccine for the treatment of metastatic melanoma.

## STS Topic

White adult teachers in the United States shown an association of unhealthy habits with their African American and Hispanic students significantly more than they do for their White students (Priest et al., 2018). While many stereotypes about minority groups are rooted in American society, beliefs that certain groups are unhealthy because of their cuisine or diet is a particularly serious problem. Because of the cognitive bias referred to as the just-world hypothesis, people will tend to believe that people who are in an unfortunate circumstance, such as being in poor health, have brought it upon themselves because of their own choices and behaviors. Thus, when members of groups that eat processed products with food additives at higher rates are stereotyped to be less healthy, society will think that these people are to blame for their own health. Because healthcare providers live within society, a threat to public health is

posed because these stereotypes are likely to increase implicit bias held by physicians that researchers have shown to contribute to the disparity in treatment quality for patients of underserved populations (Paradies, Truong, & Priest, 2013). The causes for higher rates of processed food consumption has been shown to be related to access to food type by a community, but these reasons will largely be black-boxed.

Whether there is truth in the harm of artificial food additives to health or not, there are detrimental social consequences when cultures are isolated from the majority demographic through stereotype labelling. Such effects include embedded biases that forfeit equal opportunity for outcasted individuals to succeed in the job market of mainstream society and for acceptance and patronage of establishments within cultural communities by members of the majority. Thus, the social construction of the health of food additives is a public health and social problem that must be addressed. I will be using the Social Construction of Technology (SCOT) and Actor-Network Theory (ANT) in a combined approach to study this issue.

The Social Construction of Technology is an STS theory whose premises state that the meaning of a technology is by determined by the social groups relevant to the technology. Beyond the consumers and their internal socioeconomic and cultural subgroups, other relevant social groups include the commercial food industries that can be grouped into two categories, brands that promote healthfulness and brands that do not. This theory is necessary to highlight the industries' bombardment of consumers with influential marketing messages, dictating what the general public comes to accept as healthy and unhealthy ingredients under closure and stabilization phase of SCOT. SCOT has been criticized for its unidirectional attribution of influence from social factors to determining the technology and its meaning that is invented. Social context can often be shaped by the technology that groups use, but SCOT does not reflect

this idea. However, for this issue, the of health of food additives is most clearly a social construction.

Actor-Network Theory is a framework that treats human and non-human entities as equal "actors" that have relationships among one another. Identification of these relationships forms the actor-network. ANT is useful for capturing the elements of connection among pre-existing societal biases, food companies and their capitalization on majority attitudes, food packaging materials that perpetuate the social construction, and the various groups of consumers that interact with these products. More complex relations exist between the aforementioned actors—the arrow of causality is not singular or unidirectional; rather, it is a network of multifaceted interactions. Thus, SCOT cannot fully explain the problem that exists because of food additives. ANT is criticized for equally weighting human factors with those that are non-human. However, this feature of the framework will prove beneficial for this analysis. The equal weight will allow emphasis to be place on how, separately, each actor is not necessarily the root of the problem, but the relationship joining two actors creates a new, distinct entity that may be a contributor to the issue.

## Research Question and Methods

My research question asks how sugar-alternative sweetening additives and texture-enhancing agents in processed foods perpetuate cultural stereotypes in the United States.

One method that will be employed is historical case study analysis on social attitudes surrounding MSG and the "Chinese restaurant syndrome" that took hold of popular belief in the 1960s. Discourse analysis will be performed on digital and physical advertisements and campaigns as well as on the packaging of products. Key words and phrases will be searched for

in the product labeling, such as “organic,” “natural,” and messages indicating no artificial food additives in the product. Network analysis will be used to analyze the hierarchical structures present among healthy versus unhealthy commercial food companies, their consumers, and other actors. Documentary research methods will be applied broadly to gather evidence regarding food availability and consumption by region and group demographic, as well as information about food-sweetening additives and the public attitudes surrounding them. Additionally, the policies surrounding the acceptance of a food additive in products as safe or generally regarded as safe by entities like the FDA will be explored using policy analysis.

## Conclusion

The deliverable of the technical portion of this product will include an animal-tested nanosized vaccine drug with immunogenic properties in humans containing melanoma and metastatic melanomas. Specifically, this work aims to achieving a consistent and standard encapsulation range for all of the peptides for a thorough therapeutic characterization as well as evidence of success in cell lines and live mice. Further, this study aims to establish a protocol for the bioconjugation of DEC-205 to the surface of the nanoliposome to enhance dendritic cell uptake and overall vaccine efficacy. The STS portion of this paper aims to deliver an argument highlighting the problem that the social construction of food additives poses to certain cultural groups, especially in terms of their access to equal health care. I hope to deliver an awareness to precede and inspire a social movement to change the social construction of food additives associated with racial-ethnic and socioeconomic minority groups.

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