Thesis Portfolio

Developing EGFR-Targeted Nanoliposomal Therapeutics in Head and Neck Squamous Cell Carcinoma
(Technical Report)

Public Trust in Gene Therapies: A Sociotechnical Analysis to Investigate How Best to Approach Patient Education
(STS Research Paper)

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By Patrick James Beck

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Technical Team Members:
Sally Greenberg
Abhishek Karkar
An Smith

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The 20th century saw an exponential increase in life expectancy for the average American. Much of that increase can be attributed to the improved capacity of modern medicine to manage and even cure a wide variety of diseases. However, as medicine's scope of disease treatment has increased, so has the complexity of the treatments themselves, bringing under focus the topic of delivery. Optimizing the delivery of pharmacological agents inside the human body can be quite challenging. Many drugs can show success in laboratory testing, but fail to successfully transition into humans due to a variety of pharmacological and physiological factors. Even if the biological delivery challenges are overcome, effectively educating lay patients about these complex drugs to properly elicit informed consent remains a difficulty for medical professionals. Through all of the many technical and social challenges involved with delivery in medicine, the overarching question arises: what are the factors that impact the effectiveness and use of medical treatments?

Head and Neck Squamous Cell Carcinoma (HNSCC) is the 7th most common cancer worldwide, but only one HNSCC-targeted therapy exists to treat it: Cetuximab. Cetuximab has shown promise at times, but the patient outcomes vary significantly, highlighting the need to develop more effective and consistent HNSCC treatment options. One new therapeutic that has shown promise in cancer treatment is the ceramide nanoliposome (CNL). The CNL is a cancer cell death-inducing drug currently in Phase I clinical trials for multiple cancers. The Kester Lab at the University of Virginia has already identified a synergistic cell death effect between CNL and Erlotinib or Gefitinib, two FDA-approved drugs with the same molecular target as Cetuximab. The purpose of this study was to fully investigate the combination of CNL and Erlotinib, Gefitinib, or Cetuximab and prepare these combinations for use in living-organism HNSCC trials. Through successive cell viability experiments, synergy was confirmed between

CNL and Erlotinib or Gefitinib, while no synergy was found between CNL and Cetuximab. To improve bloodstream retention time and host immune system shielding, Erlotinib and Gefitinib were successfully encapsulated inside their own lipid nanoparticle delivery vehicles. Optimization of the delivery vehicle compositions to maximize the drug payloads was in progress until this study was interrupted by the Covid-19 pandemic. The procedure to attach Cetuximab to the CNL particle surface to serve as a molecular targeting mechanism was developed, but never attempted or optimized due to the institution of remote learning. This study characterized a novel combinatorial effect between CNL and Erlotinib or Gefitinib and laid the groundwork for future targeted delivery systems to combat HNSCC.

Gene therapies are considered by many to be the next revolutionary tool in a physician's arsenal, and attitudes within the medical research community have been incredibly optimistic. However, a patient death during an early gene therapy clinical trial served to remind medical professionals and patients alike that gene therapies have not existed long enough for their risks and long-term effects to be fully explored. As gene therapies become a more mainstream treatment in the near future, medical professionals will need to understand factors that impact gene therapy education to help patients confidently provide their informed consent. This study explored how different social, cultural, and political factors could influence public trust in gene therapies to directly suggest strategies to optimize patient education. Aspects of society, cultural groups, and politics were researched to determine their impact on the public's beliefs and perceptions of gene therapies and genetic technologies. Learning about medical treatments was found to occur long before a patient is face-to-face with a physician. As such, suggestions for gene therapy education initiatives outside of healthcare facilities were provided. Significant changes to traditional genetic technology communication methods, such as public conferences

and conventions, were suggested. Additionally, it was recommended that building a foundation of trust with America's youth would be critical, as they are likely be influenced the most by future gene therapies. Finally, it was encouraged that those responsible for gene therapy education exercise empathy and possess diverse perspectives to optimally connect with those they interact with. With this study, progress has been made toward establishing protocols to best educate patients about gene therapies.

Both of the above studies were successful. While the technical project was not fully completed, two new drug delivery platforms were developed to target HNSCC. This project provided a foundation for future studies to continue to explore the above novel synergistic drug combinations. The STS research project provided some of the field's first research into social, cultural, and political factors that may influence public trust and gene therapy education. Future studies will need to research the command structure and coordination necessary to implement the recommendations provided by this study. As a whole, this thesis successfully explored how engineering design and public perception can impact the effectiveness and use of medical treatments.