Thesis Portfolio

Engineering 3D spatiotemporally dynamic hyaluronic acid hydrogels with heterogeneous mechanics to mimic idiopathic pulmonary fibrosis

(Technical Report)

Identifying social factors that influence sex-specific policy in the regulation of clinical trials

(STS Research Paper)

An Undergraduate Thesis

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Sociotechnical Synthesis

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Clinical trials are a critical step in the approval of emerging therapeutics as they represent the first time that the treatment is tested in human subjects. These first tests in human subjects are crucial for determining the safety and efficacy of treatments before they are released to the market for use by larger markets. The technical and STS research topics are linked in that they both look to fill a need in the clinical trial setting. Through the use of biomaterials, the technical project aims to take important steps in creating an *in vitro* disease model for idiopathic pulmonary fibrosis (IPF), a progressive scarring disease of the lungs which currently has no cure. The STS research paper looks to analyze social factors that influence the outcomes of clinical trials, specifically those that influenced the exclusion of women from clinical trials during the late 20th century.

IPF is the most common and aggressive form of interstitial lung disease and has a median survival of only 3-5 years after diagnosis with most deaths occurring as a result of respiratory failure. Though the disease is devastating, there currently is no cure largely due to the lack of pre-clinical models capable of accurately predicting a therapeutic's performance in the clinical trial setting. The technical project looks to address this need through the use of hydrogels, or water-swollen polymer networks. Hydrogels present multiple advantages as a disease model as there are many features such as mechanical properties which can be tuned to better mimic the natural tissue environment. They also allow for high throughput screening of therapeutics that would not be possible in animal models. This hydrogel model looks to better mimic the

mechanical properties experienced by cells in the native disease environment during IPF progression by introducing heterogeneous mechanics into the hydrogel that model the formation of fibroblastic foci seen *in vivo*. Developing more accurate models capable of recapitulating the environment experienced by cells in the body can lead to advancements in the development of curative treatments of IPF.

Beyond the technical aspects of clinical trials that are crucial to success, social factors may also heavily influence clinical trial outcomes given that they are human trials. The exclusion of various social groups from clinical trials can lead to unexpected outcomes once the drug is released to the larger market as valuable data on drug effects may be lost through such exclusionary action, whether intentional or unintentional. By examining historical policies such as the Kefauver-Harris amendments, the STS research paper identifies social factors that influenced the exclusion of women from clinical trials. The paper then looks to identify lasting effects caused by the past exclusion of women from clinical trials by examining two cases in which the female population experienced adverse effects from drugs that underwent clinical trials under FDA policies that prohibited women from participating in early phase clinical trials.

With improvements in disease models, more therapeutics for diseases such as IPF will be allowed to enter the clinical trial setting. Ensuring the safety and efficacy of these treatments for all populations will be critical for protecting patients and ensuring trust in potentially life-saving medicines.