

Thesis Project Portfolio

Urinary Extracellular Vesicle Diagnostic Tool Development – Computational Model for Dilution Determination (Technical Report)

The Role of the National Institute of Diabetes and Digestive and Kidney Diseases in Regard to Racial Health Disparities Surrounding Chronic Kidney Disease (STS Research Paper)

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Executive Summary

The motivation of the two projects contained in this portfolio stems from the broad examination of healthcare within the United States, with specific focus towards kidney health and kidney-related diseases. Healthcare within the United States is a highly contentious topic with numerous structural breakdowns evoking a plethora of health disparities for many. Such disparities are presented not only in access to proper medical care but also in prognosis and diagnosis of specific diseases. Investigation into the technical topic began through the Virginia Kidney Technology Development Research Education Program (VA K-TUTOR), an NIH Funded UVa Nephrology training program, whereby cohort members witness clinical cases and conduct associated research in promoting nephrology. The sociotechnical research investigates the available programming, initiatives, and policies in-place with regards to the communities most affected by kidney disease.

The technical project is focused on developing a diagnostic tool to address the apparent disparities within renal healthcare by harnessing the potential of urinary extracellular vesicles. Urinary extracellular vesicles (EVs) are promising new kidney disease biomarkers. EVs are membranous particles containing cell cargo with inherent biological information that are shed into the extracellular space. EVs are not bound to a specific location and can travel throughout the body via biofluids. Despite availability of sensitive instruments for EV analysis, most require processing of EV containing samples. These enrichment methods lead to unclear effects on EV properties, highlighting the need for novel methods using unprocessed samples. Following enrichment, characterization of EVs includes western blot analysis, flow cytometry, particle analysis, and omics approaches. These combined methods require large volumes and long processing times to complete, limiting their use when less volume is available such as existing

biobanks, animal studies, and limited patient samples. Given the lack of non-invasive early detection methods, the overarching project aims to develop a new EV detection tool requiring significantly less volume of unprocessed sample and can be completed without the need for enrichment. A subgoal of the project is to develop a standard method for dilution of samples must be investigated. The development of the computational model was critical in discovering a standard recommended dilution value based on sample integrity and composition. The model was developed from both the basic characterization of EVs through methods including cryogenic electron microscopy (CryoEM), western blot analysis, and nanoparticle tracking analysis (NTA) as well as quantitative analysis of measured sample creatinine levels and associated particle counts obtained using single particle interferometric reflectance imaging sensor (SP-IRIS).

The sociotechnical project is focused on evaluating the current role and responsibilities that the federal government holds with regards to racial health disparities and chronic kidney disease. The National Institutes of Health (NIH) are a set of federal research agencies focused towards the advancement of health and reduction of illness and disability. Of the 27 institutes that compose the NIH, each have specific focus areas towards diseases pertaining to various organ systems and functioning of the human body. One of the most notable diseases of focus is chronic kidney disease (CKD). CKD, a focus area of research for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is a progressive renal disease with no known sustainable cure. Aside from the lack of sustainable treatment and notable cures, CKD also has affected various populations differently presenting underlying racial health disparities that are embedded within historical context. Given the destructive nature of CKD as well as the overarching presence of racial health inequity, the research question of interest is as follows: how has the formal institutionalization of the National Institute of Diabetes and Digestive and

Kidney Diseases (NIDDK) affected racial health disparities present with regards to chronic kidney disease (CKD)? The frameworks used in evaluation of the research question are the theory of technological politics by Langdon Winner and the theory of knowledge as a form of power originally proposed within the works of Michel Foucault. The research investigates the current initiatives of the NIDDK, focusing on the artifacts developed as well as the inherent responsibility the institute holds with regards to health and safety. Investigation is significant as it provides context and accountability of the actions and structure of the NIDDK with regards to current and future necessary initiatives. Furthermore, the results obtained from this research promulgates further investigation into other federal agencies and their associated purpose in promoting public health.

In conducting both projects concurrently, the inequalities present with regards to the status and condition of healthcare services and treatments have been made transparent. The development of a novel diagnostic method in combination with the associated initiatives offered to those affected by the numerous forms of kidney disease has demonstrated apparent gaps within the healthcare system that promote systemic inequality.