A DIAGNOSTIC ASSAY FOR IL-33 AND SST2 AS BIOMARKERS FOR ACUTE KIDNEY DISEASE

GENETIC, SOCIAL, AND ENVIRONMENTAL CONTRIBUTORS TO UNEQUAL OUTCOMES OF KIDNEY DISEASE

An Undergraduate Thesis Portfolio
Presented to the Faculty of the
School of Engineering and Applied Science
In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Biomedical Engineering

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May 9, 2022

SOCIOTECHNICAL SYNTHESIS

The kidney is extremely important as it receives 25% of the body's blood flow, but if this blood flow is interrupted, such as is the case during cardiac surgery, acute kidney injury (AKI) can occur. The technical project aims to create an assay that clinicians can apply at the bedside to diagnose and treat AKI in the early stages, vitally preventing its progression into lifelong chronic kidney disease (CKD). The assay can do so by measuring the concentration of urine biomarkers IL-33 and sST2, which are compounds that can indicate kidney disease. It is important that the technical project prevents the early stages of kidney disease, however, as CKD is a condition that significantly reduces quality of life and causes unequal outcomes across racial boundaries. Therefore, the STS paper considers the various factors that cause racial disparities in CKD, particularly for African Americans, through the lens of Actor-Network Theory. The coupling between the AKI focus of the technical project and CKD focus of the STS paper crucially uncovers options to eliminate complications of kidney disease in both the early and later stages.

AKI can occur in as much as 31.0% of cardiac surgery patients. If the diagnosis and treatment of AKI are prolonged, the kidney experiences greater damage and has a lower chance of recovery. Currently, AKI is diagnosed in one of two ways: first, with a blood or urine test to measure levels of creatinine, or second, by measuring urine output over several hours. However, both these tests are imperfect as they do not directly measure kidney function and are not sensitive. Thus, these tests should not be continued to be applied in the clinic to test for early-stage AKI. Biomarkers IL-33 and sST2 are proteins that regulate the immune system, and prior work has found that they are elevated in kidney disease. By creating a protocol to sensitively

detect these biomarkers in urine samples from cardiac surgery patients, the technical project aims to provide clinicians with a useful tool that is superior to current methods.

It was found that storage conditions of urine–particularly storage time and temperature–do not have statistically significant effects on detectability of either biomarker. However, cycles of repeatedly freezing and thawing urine did worsen detectability of the biomarkers. Lastly, it was found that IL-33 and sST2 were both detectable in cardiac surgery patients' urine samples, however there was no clear threshold that indicated whether a patient had AKI. Regardless, the team proposed the following protocol for optimal detection of IL-33 and sST2: urine samples should be taken 1-hour before testing and stored on ice (4°C). Results would then be available after the approximately 6-hour-long assay is completed.

Despite clinical interventions, AKI can still proceed to long-term CKD, which is riddled with complications that cause a disproportionate burden on the African American community. The STS research paper aims to analyze the various factors that contribute to these disparities and frame them in a way that highlights potential points of intervention. The paper does this through examining data from several cross-sectional, case-control, and population studies. Disparity-producing factors are then grouped into genetic, social, and environmental categories and interconnections are drawn between them based on Latour, Law, and Callon's Actor-Network Theory.

It was found that elevated levels of chronic kidney disease in African Americans are genetically tied to the APOL1 and Thrifty genes. In the clinic, racial correction factors cause underdiagnosis of kidney disease in Black patients, making it tougher for them to receive necessary treatment. Simultaneously, Black patients are less likely to receive a fistula access, which is associated with better CKD outcomes, possibly because of clinician bias. Black patients

are also likely to live in neighborhoods that have both worse access to quality dialysis center and elevated pollution levels, both of which are associated with poorer CKD outcomes. This is because of historical policies that upheld residential segregation such as redlining. This research shows that policy interventions to eliminate factors such as racial correction factors, clinician bias, and historic effects of redlining can lessen CKD disparities.

It is essential to tackle the complications of kidney disease with a two-pronged approach by both attempting to prevent its initial onset and alleviating the disparities associated with the disease once it occurs. The pairing of the technical and STS projects accomplishes this, by highlighting potential solutions for both AKI onset and CKD disparities. In all, the work completed for both projects could potentially lead to better overall outcomes of kidney disease, particularly for African American patients.

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