An Interview with Insa Marie Schmidt, MD, MPH, the second-place winner of the 2022 CJASN Trainee of the Year competition.

CJASN Editor-in-Chief Rajnish Mehrotra interviewed Insa Marie Schmidt on the findings from her CJASN article, “Circulating Plasma Biomarkers in Biopsy-Confirmed Kidney Disease,” as well as her outlook on the field and advice for trainees. Listen now!

Insa Marie Schmidt, MD, MPH, received her MD degree from Hanover Medical School in Germany and her MPH degree from Harvard University. She has a broad range of interests in quantitative and qualitative clinical research. Her projects focus on associations of chronic kidney and cardiovascular disease, the development of novel biomarkers for kidney pathology and prognosis, and the environmental and social determinants of kidney health and disease. She recently joined the Nephrology faculty at the Boston University School of Medicine as an Assistant Professor of Medicine.

RM: Can you introduce yourself to the CJASN audience?

IS: My name is Insa Schmidt and I am an assistant professor at Boston University and Boston Medical Center. And before I joined BU’s School of Medicine as faculty, I did a postdoctoral fellowship here, and the work published in CJASN we’re talking about today results from this time.

RM: Nice! What sparked your interest in biomarkers and kidney disease?

IS: My passion for biomarker research dates back almost to medical school and then clinical training, where I became aware of current limitations to diagnose and treat kidney diseases and realized the importance of discovery and testing of novel diagnostics to advance patient care. And I believe that biomarker studies in nephrology really is an area of medicine where scientific advances to increase diagnostic and prognostic precision are much needed.

RM: What is the gap in knowledge that you hoped to bridge with your work with regards to biomarkers?

IS: The main markers we currently use to diagnose and stage CKD is we know eGFR and proteinuria provide reasonable risk prediction for kidney disease outcomes, but they have limitations as they do not capture histopathologic correlates of the underlying disease or yield specific information about individual prognoses. And so with this work, we hoped to discover new plasma proteins or protein signatures that would be associated with histopathologic lesions and prognosis in human kidney disease to enhance clinical phenotyping of CKD.
RM: So, what did you find with your work?

IS: In this study, we used the Olink proteomics platform, and we measured 225 plasma proteins in 549 participants of the Boston Kidney Biopsy Cohort. We identified several biomarkers associated with kidney disease histopathology and prognosis.

So, for example, we found that the top-performing markers positively associated with acute tubular injury and interstitial fibrosis and tubular atrophy were kidney injury molecule-1, also known as KIM-1, and then V-set and immunoglobulin domain-containing protein 2 (VISG2), which has not been studied previously in the setting of CKD.

Across the 30 proteins that were associated with a higher risk of kidney disease progression, we observed the strongest association with Placental Growth Factor, a member of the VEGF family that has been studied in preeclampsia. Interestingly, among the 35 markers associated with death, we found five biomarkers that had an inverse association with death. Here, the top-performing marker was stem cell factor, or SCF. Low levels of SCF have also been reported to be associated with mortality in previous studies.

So, many of the markers identified in our study have not been reported previously and may represent important avenues for future research including mechanistic and physiology studies.

RM: Interesting! Let’s just take a step back: how does your work fit into this larger body of work that has been done with biomarkers?

IS: I would say, most studies to date haven’t been performed in cohorts with biopsy-confirmed kidney disease. And we measured our proteomics panel in a cohort study of patients with CKD and semiquantitative assessment by two kidney pathologists. I believe this is an important contribution to the ongoing quest for the identification of noninvasive estimates of kidney pathology and prognosis.

RM: Right, that makes a lot of sense. I think what you have done is clearly a meaningful advance in our knowledge. What are the next steps in your research? And more broadly, the field of biomarkers in kidney disease, where do you think the field is headed?

IS: I am very interested in expanding our proteomics approach in the Boston Kidney Cohort to also encompass several thousand proteins and combine this with metabolomics and spatial transcriptomics so that we could identify regulatory pathways and relationships across cell types in CKD tissue. And then more broadly, I think the field of biomarker studies will benefit from more mechanistic studies to better understand the underlying biology of markers we have identified in studies to date. Additionally, the combination of multiple types of data, for example, exposomics or data on allostatic load with biomarkers, will also provide interesting new insights in causes of CKD, I believe.
RM: Yes, this is very important. Congratulations again for being selected to be the prize recipient this year! What words of advice or wisdom do you have for people that are contemplating or just starting their research training with a focus on kidney diseases?

IS: I think being persistent will certainly help to overcome many obstacles. But foremost, I would say, identify a research topic that you feel truly passionate about. From biomarkers to social epidemiology, kidney research has so much to offer, and I believe we always do best when we love what we do.