

Title and Aims	Populations studied*	Biomarkers studied*	Outcomes
<p>Tubular injury biomarkers of and progression in established CKD</p> <p>Aim: To determine if levels of tubular injury biomarkers (NGAL, L-FABP, KIM-1, and NAG) are associated with subsequent loss of renal function, independent of known clinical risk factors for CKD progression in patients with established CKD</p>	ARIC, CRIC, NIDDK American Indian Study	Urinary L-FABP, NGAL, NAG, KIM-1	CKD Progression
<p>Assessing combinations of injury and filtration biomarkers for adverse outcomes in CKD</p> <p>Aims: To determine if combinations of blood filtration markers and urine tubular injury markers explain more of the observed variability in cardiovascular events, all-cause mortality and CKD progression than either type of biomarkers alone, independent of known clinical risk factors.</p>	CRIC	Urine tubular injury biomarkers (L-FABP, NGAL, NAG, KIM-1) and blood filtration markers (B2M, BTP)	Cardiovascular events, all-cause mortality and CKD progression
<p>Normal ranges and biological variability of CKD biomarkers</p> <p>Aims:</p> <ol style="list-style-type: none"> 1) To determine reference values of CKD biomarkers in healthy individuals 2) To determine the short-term biological variability of CKD biomarkers in healthy individuals and in those with CKD 	Healthy adult volunteers recruited from the community Adult patients with eGFR 15 to 60 ml/min/1.73m ² or > 1gm proteinuria	Urinary KIM-1 Urinary NGAL Plasma KIM-1 Plasma creatinine and cystatin C	Reference ranges in healthy individuals Short-term biological variability
<p>Prediction of Outcomes in CKD with Blood Biomarkers</p> <p>Aims: To evaluate blood biomarkers for their prediction of CKD outcomes</p>	ARIC, NHANES NIDDK American Indian Study, AASK, MDRD, CRIC	BTP, B2M (compared to creatinine and cystatin C), FGF-23, vitamin D, vitamin D binding protein	Primary : ESRD and all-cause mortality; Secondary (where available): cardiovascular (CVD) mortality , non-fatal CVD events, heart failure, AKI, and progressive CKD
<p>CKD Blood Biomarker Discovery</p> <p>Aims: To identify and verify novel blood biomarkers where altered levels precede or follow rapid CKD progression using state-of-the-art proteomic methods</p>	CRIC	de novo proteomic discovery	CKD Progression defined as slope >5 ml/min/1.73m ² /year; total decline of at least 30 ml/min/1.73m ² ; follow-up of at least 3 years

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<p>Prediction of Outcomes in CKD with Longitudinal Change in Blood Biomarkers</p> <p>Aims: To examine the longitudinal (one and two year) change in BTP, B2M, creatinine and cystatin C, alone and in combination, for enhanced risk prediction of ESRD, cardiovascular disease and mortality</p>	MDRD, AASK	BTP, B2M (compared to creatinine and cystatin C)	<p>Primary: ESRD, mortality;</p> <p>Secondary: CVD mortality and CKD progression defined in these clinical trials as a 50% reduction in measured GFR</p>
<p>Novel Blood Biomarkers for Chronic Kidney Disease: Verification and Validation of Initial Discovery Results</p> <p>Aims:</p> <ol style="list-style-type: none"> To identify existing assays or to develop assays which could be used for faster and more precise measurement of these novel biomarkers. To verify and validate candidate blood markers identified in the discovery phase. 	ARIC, AASK	Most promising markers that have been identified in the de novo proteomics discovery phase (CKD Blood Biomarker Discovery protocol)	CKD Progression
<p>Cross-Species Targeted Marker Discovery (CSTD)</p> <p>Aims:</p> <ol style="list-style-type: none"> To screen kidney tissue damage markers, identified by cross-species (mouse-human) transcriptional profiling in human and murine kidney disease, using a step-wise approach of western blot and/or ELISA (or other suitable) methodology, in urine of non-renal controls, 'non-progressive' and 'rapidly progressive' CKD cases. To advance prescreened candidate biomarkers for CKD progression to early and late BioCon validation protocols 	Mount Sinai Clinical Cohort	Complement C3 fragments (C3a, iC3b and C5b-9), IGF-binding protein 3 (IGFBP3), Dickkopf 3 (DKK3)	CKD association, CKD progression
<p>Biomarker Discovery and Analysis by Methods Appropriate to Urine Sample Storage</p> <p>Aims:</p> <ol style="list-style-type: none"> To perform proteomic analyses of NIDDK American Indian Study samples after long storage at -20°C. Compare proteomes to samples from the same individuals that have been stored at -80° C. To identify markers of early stage CKD in persons with type 2 diabetes mellitus. 	NIDDK American Indian Study	Promising urine proteome markers identified in discovery analysis.	<p>Differences in promising markers identified in samples stored at different temperatures.</p> <p>Progression to macroalbuminuria, reduced GFR, ESRD, and death.</p>

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<p>Development of IPP2K and Bradykinin Assays</p> <p>Aim: To develop and optimize a quantitative mass spectrometry assay for urine IPP2K and plasma bradykinin.</p>	Joslin clinic cohort	Urine IPP2K and plasma bradykinin peptides	Renal function decline in type 1 diabetes
<p>Markers of Early Diabetic Kidney Disease</p> <p>Aim: To identify markers of early stage CKD in persons with diabetes mellitus.</p>	NHS, RASS, NIDDK American Indian Study	Urine MCP-1, Hecpidin, IPP2K, uromodulin, transferrin, albumin, and plasma bradykinin peptides	Changes in kidney histology and morphometry over 5 years (NHS and RASS). Cross-sectional associations of histology and morphometry (NIDDK American Indian Study)
<p>Biomarkers of Interstitial Kidney Pathology</p> <p>Aim: To test combinations of biomarkers for detection of interstitial inflammation or fibrosis in lupus and other glomerular diseases.</p>	Ohio State University, Cincinnati Children's Hospital, and the Brigham and Women's cohorts	Osteopontin, hemopexin, endothelial protein C receptor, urine MCP-1, serum creatinine, proteinuria	Interstitial inflammation or fibrosis identified on kidney biopsy
<p>Markers of Early Lupus Nephritis</p> <p>Aim: To identify markers of early stage CKD in persons with lupus nephritis and diabetes mellitus.</p>	Ohio SLE Study, Children's Lupus Cohort, NHS, RASS	Urine MCP-1, Hecpidin, transferrin, uromodulin, LFABP, IPP2K and plasma bradykinin peptides	Lupus Nephritis: Incident CKD Diabetes Mellitus: Changes in kidney histology and morphometry over 5 years
<p>Plasma Proteome Biomarkers of Chronic Kidney Disease Progression in Type 1 Diabetes</p> <p>Aim: To study the plasma proteome to identify candidate biomarkers of CKD progression in subjects with type 1 diabetes.</p>	DCCT/EDIC	Plasma proteome	Progression to advanced CKD, as defined by eGFR < 30ml/min/1.73m ² with or without associated albuminuria

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Plasma KIM-1 and Chronic Kidney Disease Aims: 1) To test plasma KIM-1 as a predictor of CKD progression 2) To test plasma KIM-1 as a predictor of cardiovascular disease events	CRIC	Plasma KIM-1	CKD progression, Atherosclerotic disease events, Congestive heart failure events

Abbreviations*AASK:** African-American Study of Kidney Disease and Hypertension**ARIC:** Atherosclerosis Risk in Communities Study**BTP:** beta-trace protein**B2M:** beta-2 microglobulin**CRIC:** Chronic Renal Insufficiency Cohort Study**DCCT:** Diabetes Control and Complications Trial**EDIC:** Epidemiology of Diabetes Interventions and Complications**FGF-23:** fibroblast growth factor 23**IGF:** insulin-like growth factor**IPP2K:** inositol pentakisphosphate 2-kinase**KIM-1:** kidney injury molecule-1**L-FABP:** liver fatty acid binding protein**MCP-1:** monocyte chemoattractant protein-1**MDRD:** Modification of Diet in Renal Disease Study**NAG:** N-acetyl- β -D-glucosaminidase**NGAL:** neutrophil gelatinase associated lipocalin**NHS:** Natural History Study**RASS:** Renin Angiotensin System Study**SLE:** Systemic Lupus Erythematosus