PROOF

Centre of | Centre d' **EXCELLENCE**

Biomarqueurs – Solutions en soins de santé.

Biomarker solutions for health care.

The Centre of Excellence for Prevention of Organ Failure (PROOF Centre) is a not-for-profit organization that develops high value biomarker-based blood tests to better manage patients with heart, lung and kidney disease, by harnessing the power of clinical, molecular and computational science.

www.proofcentre.ca

Blood tests for better manangement of chronic kidney disease

The PROOF Centre is developing biomarkers to predict the risk of rapid chronic kidney disease (CKD) progression and identify patients with recovered kidney function. CKD affects 51 million people North America and is currently managed primarily on the basis of symptom burden. Our markers will allow for individualized treatment and support the development of new therapies for chronic kidney disease.

FIGURE 1. CKD programs at a glance.

CKD progression	A proteo-genomic panel for predicting risk of rapid chronic kidney disease progression	Discovery AUC 0.80
Recovered Kidney Function	A 10-protein panel to identify kidney failure patients who have recovered from treatment	Replication AUC 0.81

FIGURE 2. Biomarker discovery process, CKD.
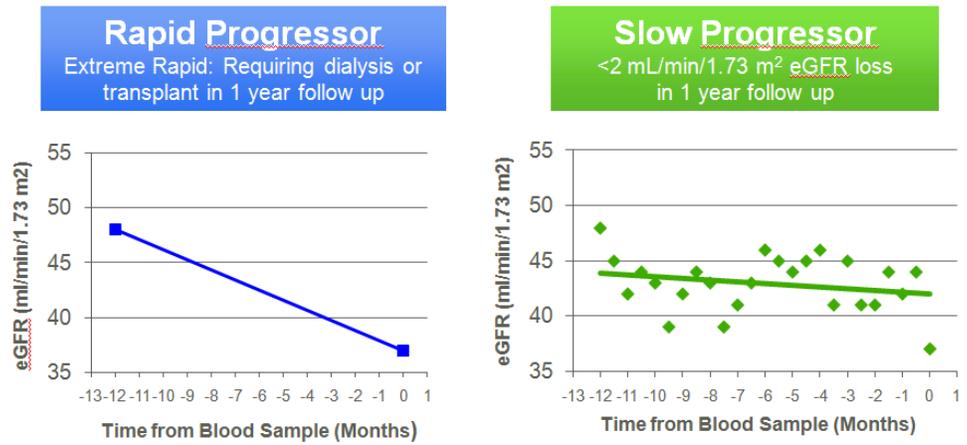

Providence
HEALTH CARE
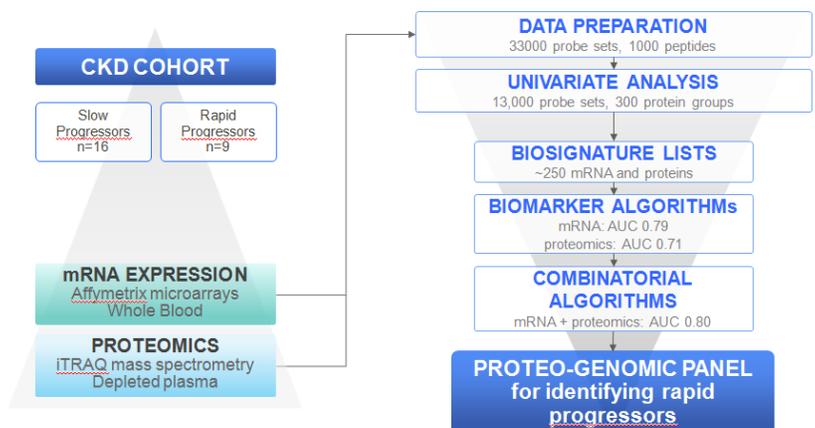
How you want to be treated.

UBC

a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA

FIGURE 3. Rapid versus slow chronic kidney disease progression. Adult CKD patients who were not on dialysis and had estimated glomerular filtration rate (eGFR) <25mL/min/1.73m2 were recruited at St. Paul's Hospital. Blood samples were collected at recruitment and outcomes were tracked for over 12 months..

Rapid Progressor
Extreme Rapid: Requiring dialysis or transplant in 1 year follow up

Slow Progressor
<2 mL/min/1.73 m² eGFR loss in 1 year follow up

Using Affymetrix microarrays and iTRAQ mass spectrometry to measure gene and protein expression, respectively, we have identified a combinatorial panel of genomic and proteomic biomarkers that can identify patients with rapid CKD progression. We are now replicating these markers in an external cohort.

FIGURE 4. A proteo-genomic panel of 16 proteins and 73 mRNA markers distinguish extreme rapid from slow CKD progression (right, principle components analysis plot) with an area under the receiver operating characteristics curve (AUC) of 0.80, 88% sensitivity and 56% specificity (left).

AUC	Sensitivity	Specificity
0.79	0.81	0.44
0.71	0.82	0.44
0.80	0.88	0.56

Slow
Extreme Rapid
Non-Extreme Rapid
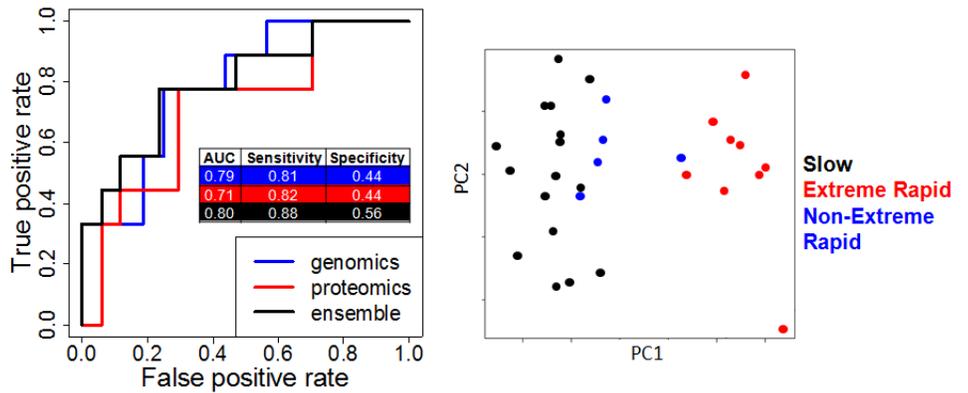
Using mass spectrometry, we have also replicated a panel of 10 proteins that identifies patients with recovered kidney function.

FIGURE 5. Discovery and replication performances of a 10-protein panel for recovered kidney function..

Discovery AUC=0.97
Replication AUC=0.81
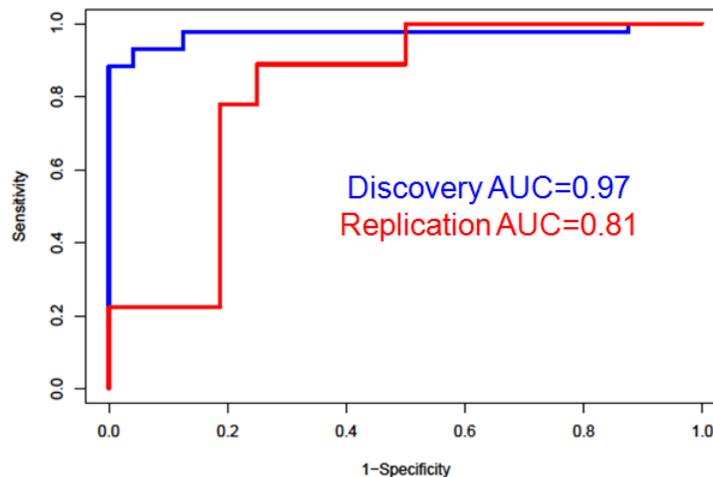
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