Chronic kidney disease (CKD) affects 2 million (M) Canadians, 50 M patients in the US, and 45 M patients in the 7 major markets, and places a significant burden on patients, their families, and health-care systems. Progression of CKD to end-stage renal disease (ESRD) results in patients requiring renal replacement therapy through dialysis and/or organ transplantation, which is highly resource-intensive and burdensome. While aggressive management of blood pressure and proteinuria can slow the progression of CKD to ESRD, physicians currently have limited ability to assess the risk of rapid CKD progression. The PROOF Centre is developing panels of genomic and proteomic markers of CKD severity that will distinguish patients with stable disease from those with rapidly progressive disease using a simple blood draw. Detection of rapidly progressive CKD would allow physicians to identify the patients most likely to benefit from aggressive therapy and follow-up, and delay progression to ESRD.

Biomarker panels arising from this program may also be used to support the discovery and development of newer, safer drugs that modulate CKD progression. The multiple medications CKD patients take to manage their underlying disease and symptoms are not

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**Unmet need:** A blood test that will distinguish CKD patients with stable disease from those with rapidly progressive disease.

**Chronic kidney disease (CKD) affects ~2 million (M) Canadians, 50 M patients in the US, and 45 M patients in the 7 major markets, and places a significant burden on patients, their families, and health-care systems. Progression of CKD to end-stage renal disease (ESRD) results in patients requiring renal replacement therapy through dialysis and/or organ transplantation, which is highly resource-intensive and burdensome. While aggressive management of blood pressure and proteinuria can slow the progression of CKD to ESRD, physicians currently have limited ability to assess the risk of rapid CKD progression. The PROOF Centre is developing panels of genomic and proteomic markers of CKD severity that will distinguish patients with stable disease from those with rapidly progressive disease using a simple blood draw. Detection of rapidly progressive CKD would allow physicians to identify the patients most likely to benefit from aggressive therapy and follow-up, and delay progression to ESRD.**

**Biomarker panels arising from this program may also be used to support the discovery and development of newer, safer drugs that modulate CKD progression. The multiple medications CKD patients take to manage their underlying disease and symptoms are not**
commonly associated with adverse drug effects arising from impaired renal function and/or drug-drug interactions. Prognostic biomarkers for CKD therefore speak to the therapeutic market’s need for products to slow down the progression of CKD.

Program team: Solid partnerships.
The CKD program is a collaboration between the PROOF Centre team and Dr. Adeera Levin (UBC Professor of Medicine, Division of Nephrology; Director, Kidney Function Clinic; Director, Education and Research, St. Paul’s Hospital), who leads a team of nephrologists and clinical statisticians.

The program leverages the rich history of renal research at St. Paul’s Hospital as well as the provincial PROMIS database, through which CKD patient data is linked to clinical outcomes. The program will build on the existing CanPREDICT cohort, a pan-Canadian cohort of more than 2,600 CKD patients for the validation phase.

Progress and projected milestones:
We are on a journey to discover and develop biomarker panels of CKD progression.

In order to identify biomarkers of CKD progression, the program team recruited a cohort of 84 patients with low kidney function known to have rapidly progressive or slowly progressive CKD. Demographic and clinical data was collected, and patient blood samples were utilized for genomic and proteomic biomarker discovery via Affymetrix Human Gene ST 1.0 microarrays and ABI iTRAQ mass spectrometry, respectively.

Currently, we are identifying genomic and proteomic biomarkers that distinguish patients with rapidly progressing CKD from those with slowly progressing disease. We are assessing the discriminatory power of separate genomic and proteomic panels as well as panels that combine genomic and proteomic biomarkers, with and without supplemental clinical variables (e.g., blood pressure, urine protein levels etc), into a prognostic algorithm.

Alongside our biomarker discovery efforts, we have identified multiple potential validation cohorts, and are planning a biomarker validation study for 2012 that will leverage the existing patient cohort recruited through the CanPREDICT study. These efforts will yield validated biomarker panels suitable for further development into clinical diagnostics. They may also support new drug development in new pharmaceutical companies by identifying new drug targets for CKD therapy.

Contact us to learn more or to find out how you can get involved.
The PROOF Centre is based at St. Paul’s Hospital (Institute for Heart + Lung Health) in Vancouver, Canada, and is hosted by the University of British Columbia. Our objective is to improve the health of Canadians, while decreasing the financial burden on our healthcare system by preventing disease and improving health.

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