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NHMRC Chronic Kidney Disease Centre of Research Excellence

Biomarkers in CKD

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Mission

The usefulness of kidney biomarkers to predict progression of CKD has not been validated in Australia.

We are hoping to turn scientific discoveries into better diagnosis and treatments...

Modern world-class research facilities at Translational Research Institute (UQDI) (Gobe and Evans), Univ of Sydney (Endre), Royal Brisbane & Women's Hospital/QIMR (Healy and Wilkinson), UQ Sch Human Movement Studies (Coombes), Logan (Ken-Soon Tan)

Aim

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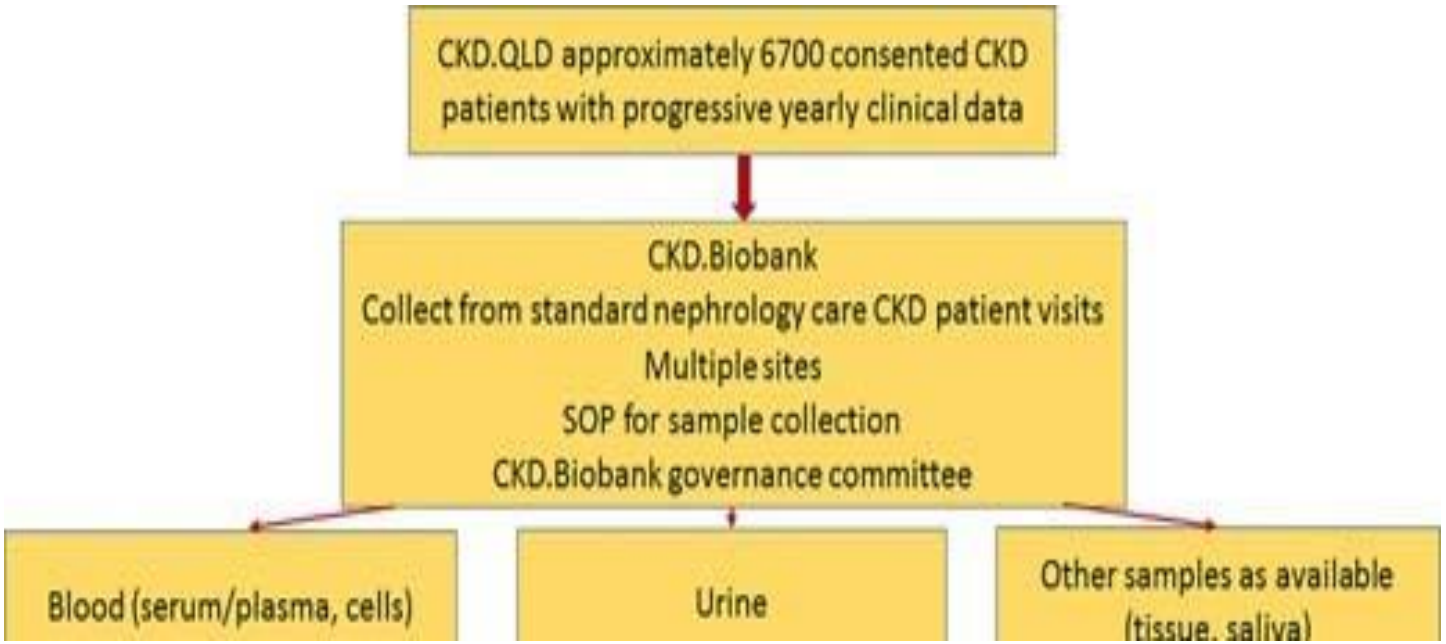
- Largest available CKD cohort in Australia, with over 6,500 registered patients
- Over 3,000 with progressive clinical data for at least 2 years
- Randomly select well-phenotyped subjects with progressing or stable CKD for over 2 years

- Determine utility of measuring renal reserve (how well a kidney can bounce back after injury) and mechanistic kidney damage biomarkers for diagnosis at baseline and for predicting CKD progression over 2 years.

CKD Biobank

- Access to quality bio-specimens and clinical data from CKD patients and matched healthy controls
- Received HREC approval in March 2016 and Site Specific Approvals (SSA) for Logan and RBWH in July/August 2017



Candidate Discovery

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Medicinal chemistry

Korenkova et al., Med chem 2015, 5:2
http://dx.doi.org/10.4172/2161-0444.1000249

Research Article Open Access

Urinary Biomarkers for Detection of Early and Advanced Chronic Kidney Disease - A Pilot Study

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Abstract

Chronic kidney disease (CKD) is a significant and costly public health problem with increasing prevalence in most societies and the need for improved diagnosis. The aim of this study was to demonstrate how it is possible to decipher a combination of markers from a compendium of differentially-expressed proteins using available statistical tools when more than two study groups are involved. Screening for potential urinary biomarker profile stratifying early and later stages of CKD were performed. Sixteen patients with defined CKD staging were selected and compared with ten healthy individuals. Urinary proteins were quantified using theiTRAQ method and analysed with ProteinPilot, GenEx and Meta Core software. Four proteins (out of 194) (apolipoprotein D; protein AMBP; zinc-alpha-2-glycoprotein; and kininogen 1) were identified as critical for CKD stage separation. In conclusion, this preliminary work provides evidence that several unique urinary proteins are involved in early and later stages of CKD and suggests that a selected combination of biomarkers could be used to profile patients into different CKD stages. Further validation studies are now needed.

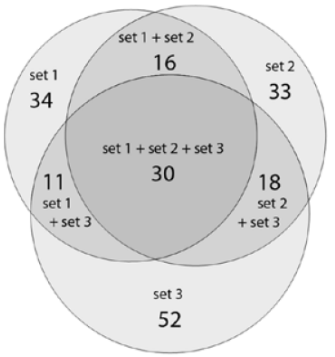

Figure 1: Proteins identified in the three technical replicates using iTRAQ.

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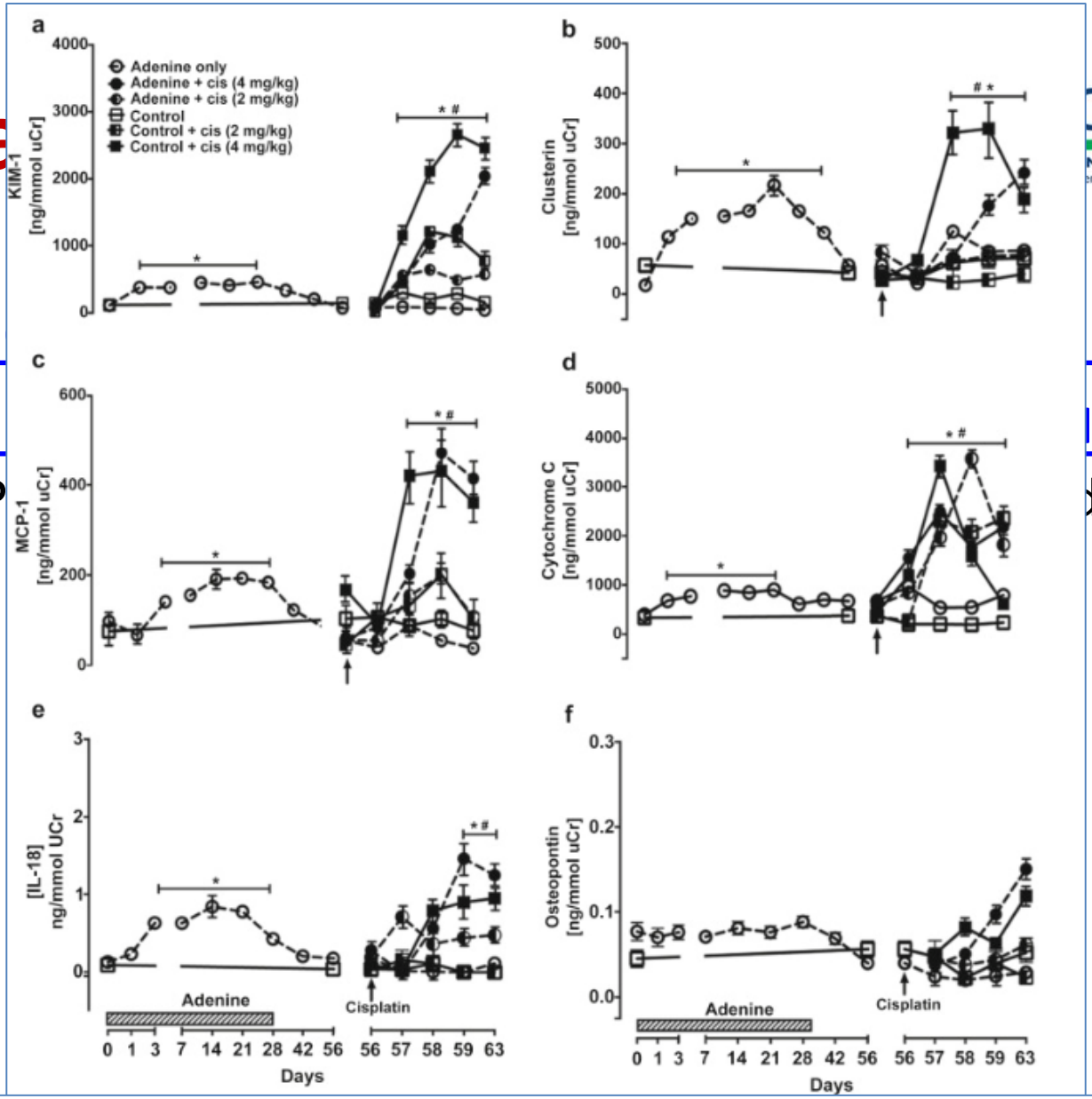

Demonstrated that altered profiles of functional and damage biomarkers were sensitive as indicators of subclinical CKD

NHMRC Project Grant

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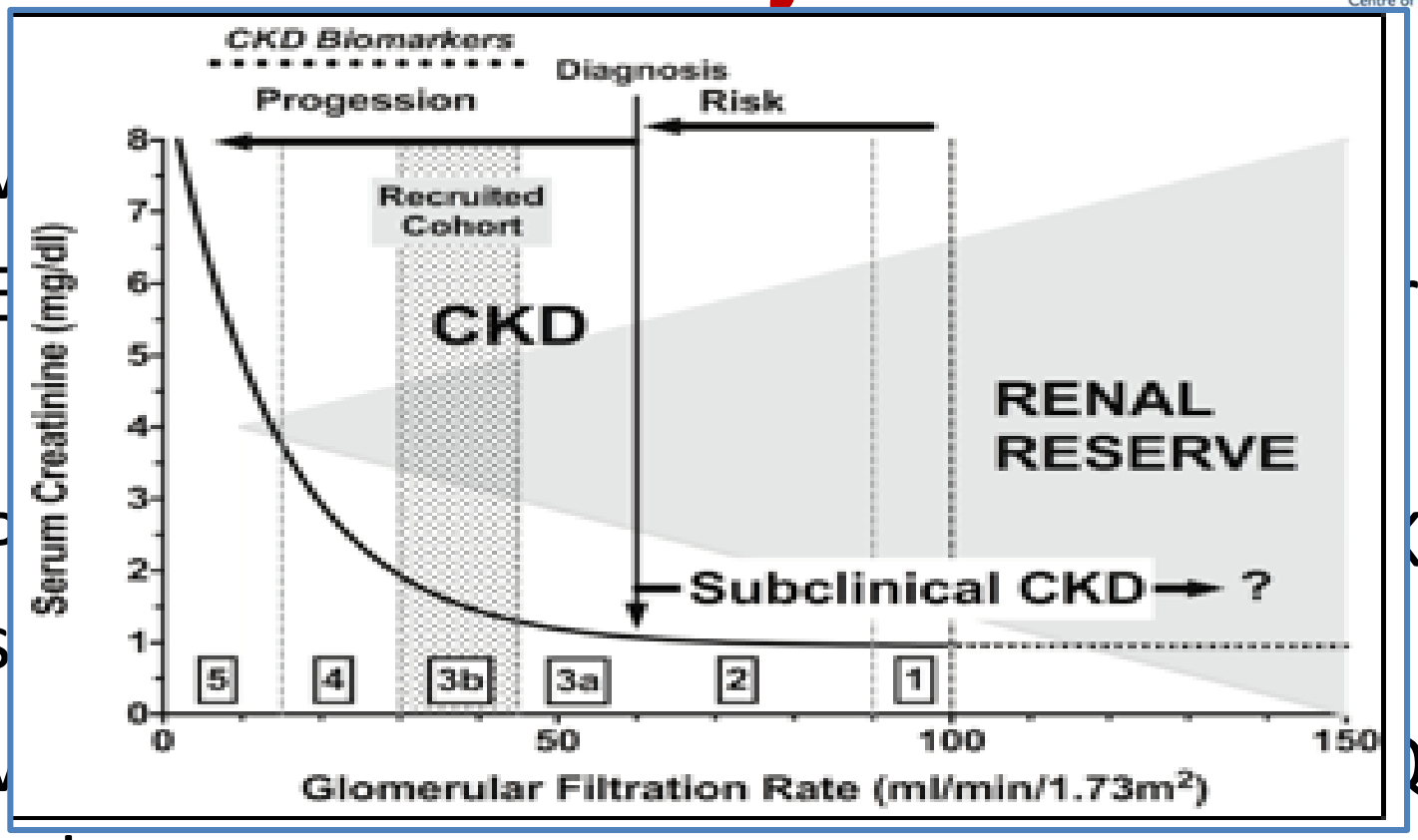

Using SCr as preferred biomarker (and GFR), almost 2/3 of a person's renal reserve may be lost before initial diagnosis. Improve diagnosis in subclinical CKD.

aCQuiRE Study

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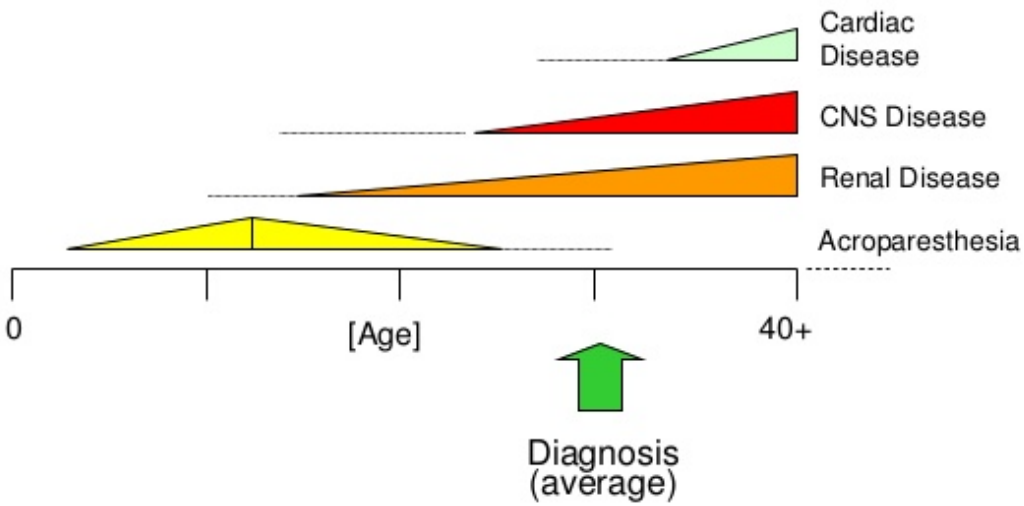
Fabry Disease Progression



Genetic disorder; Progressive multi-organ failure, but most especially kidney failure.

aCQuiRE Study

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- CIs Hoy, Mallett; PhD student Owens
- Screen 1,500 CKD pts on dialysis & 1,500 with pre-terminal CKD, with novel blood spot technology
- Benefit is potential for enzyme replacement therapy, supported by Australia's PBS, which might delay symptom development.
- Families of Fabry Disease subjects will be offered screening, referral, treatment, (genetic program, Dr Charles Denaro, RBWH).
- This is an undertaking with truly preventive potential.

Tiwi Community biosamples – a national treasure

- Hoy, Gobe, Mott
- Chronic disease profiles and chronic disease deaths in the Tiwi community:
  a ten year follow-up.
- Transfer from Menzies School of Health Research to NHMRC CKD.CRE Biobank, Brisbane
- Truly enormous potential

HDR students – benefits of CRE training

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Evan Owens
PhD student, CRE
PhD scholarship
CKD biomarkers;
DROP CKD project

Rob Ellis
MD/PhD student
Progression to CKD after kidney cancer nephrectomies
CKD-Tuned project

Summary

- Ethics complete
- Biobank established
- Logan and RBWH samples from patients of the CKD.CRE data base
- Complementary samples identified (Tiwi)
- Projects identified
- HDR students in training
- Publications accomplished or in progress