A Novel Therapeutic Strategy for Nephropathic Cystinosis

Capstone Students: Mariam Badmus, Daniel Gonzalez, Caroline Hu, William Vo
Project Sponsors: Minnie Sarwal, Swastika Sur, Bonnie Crater, Chih-Hung Lai, Tara Sigdel
University of California, San Francisco, USA. University of California, Berkeley, USA.

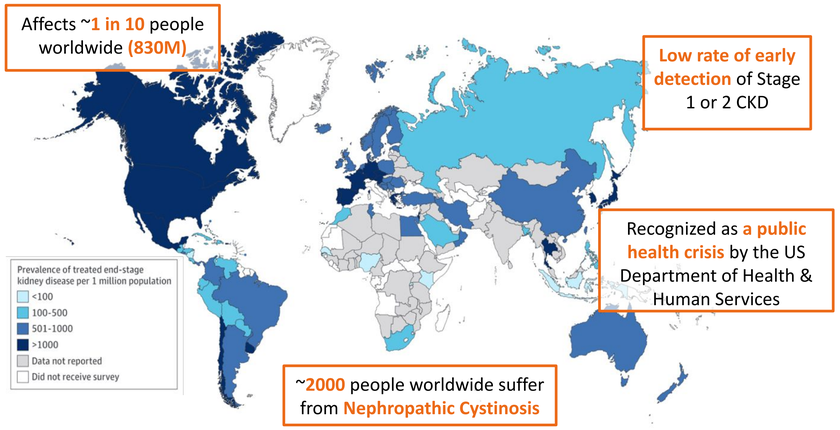
Master of Translational Medicine
UC Berkeley - UC San Francisco

Sarwallab
Translational Research for Personalized Medicine

UCSF
University of California San Francisco

Global Clinical Need

Affects ~**1 in 10** people worldwide **(830M)**

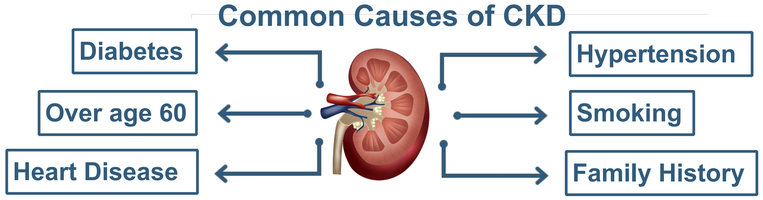


Low rate of early detection of Stage 1 or 2 CKD

Recognized as **a public health crisis** by the US Department of Health & Human Services

~**2000** people worldwide suffer from **Nephropathic Cystinosis**

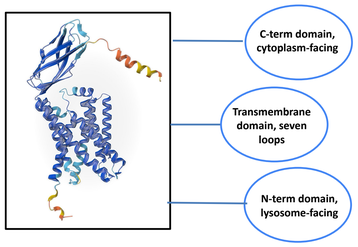
Common Causes of CKD



Orphan Disease Indication

Cystinosin (CTNS) is an amino acid transporter residing in the lysosomal membrane.

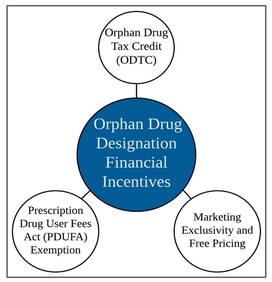
Accumulation of cystine in cell lysosome across all organs. Patients predominantly present with kidney injury.



Current therapies solely address cystine accumulation without targeting the underlying kidney injury. As a result, patient progression to kidney failure is inevitable.

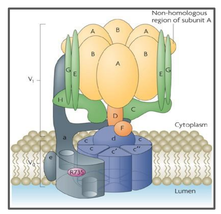
Our Distinctive Edge

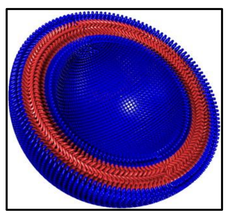
- Access to KOLs in both therapeutics and diagnostics
- Previously established *in vitro* and *in vivo* models of cystinosis (CTNS -/-)
- Access to UCSF SMDC facility
- FDA's Orphan Disease Designation



Our Integrated Solution

- We have identified a small molecule drug (**XTA**) that corrects unaddressed cellular dysfunctions associated with disease progression.
- **XTA** upregulates ATP6V0A1.
- **XTA** does not correct cystine accumulation in the lysosomes.





Stages of Kidney Disease	Improved detection of CKD	
	CKD Kit	Proteinuria
Stage 1	✓	
Stage 2	✓	
Stage 3	✓	✓
Stage 4	✓	✓
Kidney Failure	✓	✓

For patients with nephropathic cystinosis, our combination therapy is a breakthrough treatment that prevents rather than merely delays kidney failure by **addressing both cystine accumulation and underlying cellular dysfunction**. Our robust companion diagnostic enables us to establish a **novel trial endpoint** to detect our therapeutic's ability to rescue kidney injury in early stage CKD patients.

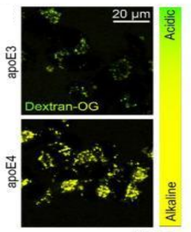
Current Scientific Aims

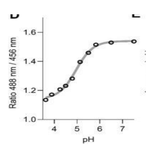
Benchtop Research

Proteomics Study — Sandler-Moore Mass Spectrometry Core Facility

Additional molecular mechanistic insights:
- mTORC1 Pathway
- TGFBeta Signaling
- Mitochondrial Function
- Inflammation
- Vesicular Transport

Lysosomal pH Tracking

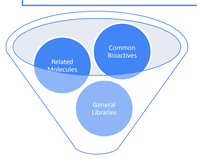




Further optimization is required to prevent death in RPTEC and CTNS KO cell lines.

Library Screening

Small Molecule Discovery Center



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TargetMol® A DRUG SCREENING EXPERT

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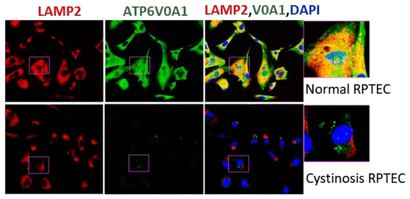
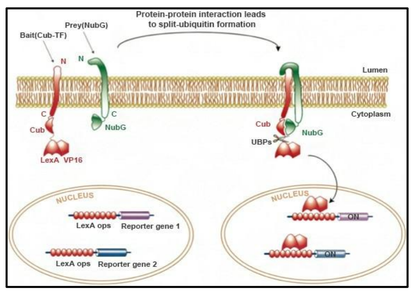
ATP6V0A1 Upregulation

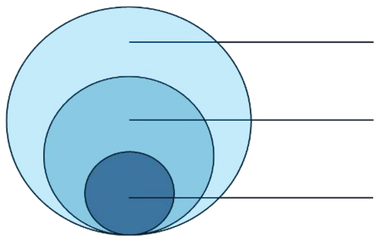


Mechanism Deconvolution



Key Questions:
- What protein-protein interactions does wild-type CTNS participate in?
- Are any of these PPIs disrupted by the clinically-relevant mutations?
- Is this consistent with our findings?

Market Analysis and Competitors



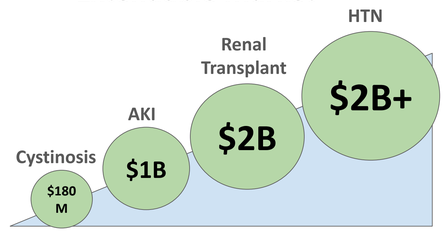
$180M **Total Available Market**
Nephropathic Cystinosis patients Worldwide

$95M **Serviceable Available Market**
Nephropathic Cystinosis patients in North America, Europe and Asia

$53M **Serviceable Obtainable Market**
Nephropathic Cystinosis patients in United States & United Kingdom

FDA-approved drugs for Cystinosis:
- **Cystagon (exp. 2026)**
  - Taken 4 times daily
  - Limited to children 6+ years
  - Costs $10,000 annually
- **Procysbi (exp. 2034)**
  - Taken two times daily
  - Limited to children 1+ years
  - Costs $300,000 annually

Extendable Market



	KIT	NephroCheck*
Test	KIT	NephroCheck*
Intended Use	Native Injury (+Transplant Rejection)	AKI
Estimation	Quantitative (Risk Estimate)	Qualitative (AKI vs No AKI)
Sensitivity Specificity	96% 98%	76% 51%
NPV PPV	99% / 90%	88% / 31%
Sample Type	Urine	Urine
Biomarkers	6 DNA and Protein	2 Proteins
Methodology	ELISA	POC $5,000
Price	$2740 for transplant CMS Native kidney injury TBA	$85
TAT	1 day	20 min in ICU

Project Timeline

	Delivery Mode Optimization Complete	MOA Studies Complete Start Patent Application	NIH Grant Submission	Preclinical Mice Studies Begin	NDA Submission
	February 2025	March 2025	June 2025	July 2025	Late 2025
XTA					
KIT	KIT Biomarker Optimization Complete	Lateral Flow Assay Reader Development		Rapid TAT in Outpatient Setting	Smartphone Version for POC Testing

Conclusion

Operating at the cutting-edge of CKD research, the Sarwal Lab is well equipped to translate their in-vitro validation of XTA to preclinical mouse models. Built upon a robust scientific understanding of the molecular mechanisms of action, drug-drug interactions, polymer chemistry, and kidney injury biomarkers, we are excited to address the unmet clinical need of nephropathic cystinosis. We foresee this novel therapeutic strategy and companion diagnostic serving as a **comprehensive solution for both early detection and treatment for kidney disease.**

Acknowledgements

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