# Cystinosis Research Foundation

*Lay Abstract Template for Awardees*

Please complete this lay-oriented grant abstract form which will be published on the CRF web site, in CRF Star Facts and in the CRF magazine when we announce your grant award. *Please do not exceed 400 words (no more than 1-1/4 page total).* Please submit this form electronically to nstack@cystinosisresearch.org as a Word document.

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**Principal Investigator (s)**: Ting Miao

**Project Title**: Profiling Dysregulation of Kidney Coenzyme A (CoA) Biosynthesis in Cystinosis

**Objective/Rationale**: Please write a lay-oriented statement of the scientific rationale for this project. Approximately 75-85 words.

Cystinosis, a genetic disorder caused by mutations in the CTNS gene, leads to the accumulation of cystine in the kidneys and other organs. This buildup causes cellular stress and metabolic disturbances. Recent research from our laboratory indicates that cystine transport is crucial for Coenzyme A (CoA) biosynthesis, a vital metabolic process. This project aims to explore how CoA biosynthesis is affected in the kidneys of cystinosis patients, potentially uncovering new treatment strategies. Using Drosophila models, we will investigate the role of CoA biosynthesis in kidney function and overall metabolic health.

**Project Description**: Please write a brief, lay-oriented description of how you will carry out the project. Approximately 125-135 words.

To carry out this project, we will use Drosophila (fruit flies) to model cystinosis due to their genetic similarities to humans and ease of genetic manipulation. First, we will create Drosophila models with mutations in the CTNS gene to mimic cystinosis. We will then study these models to understand how these mutations affect kidney function and Coenzyme A (CoA) biosynthesis. Advanced metabolomics techniques will be employed to measure metabolite levels in the kidneys, identifying disruptions in metabolic pathways. Additionally, we will use genetic and biochemical methods to assess how changes in CoA biosynthesis impact kidney function and overall metabolic health. By comparing the results with healthy flies, we aim to uncover the specific metabolic alterations caused by cystinosis, potentially leading to novel therapeutic strategies.

**Relevance to the Understanding and/or Treatment of Cystinosis**: Please explain how the project will impact cystinosis treatment or increase our understanding of cystinosis. Approximately 75-80 words.

This project will enhance our understanding of the metabolic disruptions caused by cystinosis, specifically focusing on the role of Coenzyme A (CoA) biosynthesis in kidney function. Recent metabolomics analyses have reported significant alterations in the CoA biosynthesis pathway in individuals with cystinosis, suggesting a link between cystine transport deficiency and CoA imbalance. Given CoA's pivotal role in cellular metabolism, dysregulated CoA biosynthesis may underlie systemic metabolic abnormalities in cystinosis. By uncovering these mechanisms, we may identify new therapeutic targets, potentially leading to more effective treatments and improved outcomes for cystinosis patients.

**Anticipated Outcome**: Please write a lay-oriented description of what you expect to learn/discover. Approximately 75-80 words.

We expect to discover how the disruption of Coenzyme A (CoA) biosynthesis in the kidneys contributes to the symptoms and progression of cystinosis. Using Drosophila as a model, we will investigate: 1) the impact of dCTNS deficiency on kidney CoA biosynthesis; 2) the role of CoA biosynthesis and dCTNS in renal function; and 3)

the influence of kidney CoA biosynthesis on whole-body metabolic homeostasis. This research aims to identify new treatment targets to better manage the metabolic abnormalities in cystinosis, ultimately improving patients' quality of life.