# 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)**: Liang Feng

**Project Title**: Probing protein mutagenesis and modulation in cystinosis

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

Lysosomal membrane transport proteins play a crucial role in maintaining cystine homeostasis within lysosomes. The dysfunction or dysregulation of these proteins is the underlying cause of cystinosis. The biophysical properties of these transport proteins are key to their function. Understanding how alterations in these proteins affect their biophysical properties is vital for elucidating the molecular basis of cystinosis. This knowledge is fundamental for developing targeted, mechanism-based therapies.

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

The functions of lysosomal membrane transport proteins are tightly linked to their fundamental biophysical properties. To assess the impact of alterations in these key proteins in cystinosis, we will develop and implement robust assays designed to efficiently measure their critical biophysical properties. These measurements will provide crucial insights into the modulation of these proteins' function. Additionally, we aim to develop highly selective methods to modulate the activity of these transport proteins based on our molecular understanding. This approach may potentially lead to the development of novel therapeutic strategies for treating cystinosis.

**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.

Defective lysosomal membrane transport is the cause of cystinosis. Understanding the molecular mechanisms by which alterations in key membrane transport proteins involved in cystinosis affect their function will provide crucial insights into the underlying causes of cystinosis. This knowledge will enhance our ability to assess the risk of cystinosis and guide the development of novel therapeutic strategies specifically aimed at mitigating the detrimental effects of defective membrane transport proteins.

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

The proposed research will provide new approaches to better understand the fundamental properties of key membrane transport proteins in cystinosis, uncover how alterations in these proteins' biophysical properties affect their function, and explore new ways to modulate their activity for potential therapeutic purposes. These studies will deepen our understanding of lysosomal membrane transport and the underlying causes of cystinosis, ultimately aiding in the development of novel, selective therapeutic strategies to treat cystinosis.