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.

Principal Investigator (s): Lauren V Albrecht PhD; Renata C Pereira PhD

Project Title: Investigating novel regulators of lysosomes and osteocytes in cystinosis

Objective/Rationale: Please write a lay-oriented statement of the scientific rationale for this project.
This research aims to understand how cellular dysregulation contributes to cystinosis. We focus on understanding the lysosome, a specialized compartment that is essential for regulating the breakdown of proteins. While it is well-established that lysosomes are altered in cystinosis, the molecular consequences and signaling events downstream are not well understood. By addressing this gap in knowledge, our studies aim to uncover new disease processes and molecular targets for therapeutic intervention.

Project Description: Please write a brief, lay-oriented description of how you will carry out the project. Approximately 125-135 words.
We build on previous findings that osteocytes, a type of bone cell, may contribute to bone defects in cystinosis. Additionally, a novel lysosomal pathway, not restored by current treatments, was identified. Specifically, we find that a newly discovered protein tag for lysosomes, MrDegron, is misregulated in bone and kidney of cystinosis patients and disease models. We hypothesize that lysosomal signaling dysregulation plays tissue-specific roles in promoting cystinosis. The research has two aims: 1) Understanding the role of lysosomes in osteocytes, and 2) Investigating a novel methylation-dependent lysosomal pathway essential across tissues. Innovative approaches, including advanced microscopy and proteomics, will be used to gain insights from cultured cells, patient tissues, and murine models. The findings could reveal the fundamental basis of the disease and potential new targets for correcting pathways resistant to current treatments.

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 impact current cystinosis treatments by studying bone and kidney disease where cysteamine treatments are not fully effective. At the completion of these studies, we aim to delineate novel mechanisms of disease to benefit bone disease children and young adults that is not well-understood. Our preliminary data reveals that aberrant lysosomes result in signaling processes that are independent of cystine, which could contribute to the disease processes that are resistant to cysteamine treatments.

Anticipated Outcome: Please write a lay-oriented description of what you expect to learn/discover. Approximately 75-80 words.
We expect to discover how misregulated lysosomes results in altered signaling in cells and tissues. By studying the new molecular signal, MrDegron, that delivers proteins into lysosomes, we expect to elucidate novel biological processes and pathways for designing therapeutics. By studying osteocytes, a bone cell type that was previously ignored in cystinosis and known to regulate kidney-bone crosstalk, these studies could yield new insights in the role of altered organ communication during disease progression or diagnosis.