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): Sergio D. Catz and Juan Yu

Project Title: Studies of global inflammation in patients with cystinosis

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

The immune system protects the organism from infections but can also cause inflammation, which can be defined as the excessive activation of the immune system. If uncontrolled or dysregulated, the inflammatory response can be deleterious causing cellular and tissue damage. In cystinosis, a lysosomal storage disease caused by a genetic defect of the *CTNS* gene, inflammation is emerging as a causative factor of kidney disease. We previously showed that the cystinotic kidney can release factors that attract inflammatory leukocytes. Uncontrolled white blood cell (leukocyte) activation in cystinosis may lead to tissue damage and cell death. We will study inflammation in cystinosis. Our studies utilize state-of-the-art microscopy approaches to characterize immune white blood cell identity and function in blood from patients with cystinosis.

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

The objective of this research plan is to utilize state-of-the-art inflammatory mediator (cytokine) analysis and omics analysis of pro-inflammatory plasma proteins and lipids, and to apply modern cell-based analysis to characterize the putative inflammatory phenotype in patients with cystinosis. We will also utilize high-dimensional CyTOF (mass cytometry) and muti-marker flow cytometry to identify white blood cell progenitors and subtypes in blood from cystinosis patients. Pro-inflammatory cell subsets from these patients will be used in functional studies.

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.

We anticipate finding elevated numbers of pro-inflammatory immune cell-subtypes in circulation, in cystinotic patients, that positively correlate with inflammatory mediators and kidney disease. We also expect that patients with cystinosis will have increased numbers and dysfunctional white blood cells. The identification of inflammatory cells and markers in blood from cystinosis patients is an step forward toward the discovery of new therapies to treat this devastating disease.

Anticipated Outcome: Please write a lay-oriented description of what you expect to learn/discover. Approximately 75-80 words.
We anticipate that we will discover specific pro-inflammatory markers and white blood cell subtypes to be upregulated in cystinosis. Understanding the different stages of inflammation in cystinosis will help design better therapies to treat this disease.