

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): Bruno Gasnier

Project Title: A critical role for cystinosin during mammalian embryonic development

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

Cystinosis occurs when a specific gene, responsible for a protein called cystinosin, is not working properly. This protein is essential for moving an amino acid called cystine out of a cell structure called the lysosome. In our earlier studies with mice, we found a surprising connection between cystinosin and another lysosomal protein. When both genes are inactivated, the development of embryos is severely impaired, showing a new role for cystinosin. We have figured out that this role involves providing nutrients to the developing embryo, but we still do not understand how cystinosin is involved. This research aims to answer that question.

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

In our previous work, we found that both cystinosin and its genetic partner are crucial for the nutrition of mammalian embryos in the early stages before the placenta starts working. This nutrition process relies on a special tissue called the yolk sac. The yolk sac breaks down proteins from the mother to produce amino acids and other nutrients needed for the growing embryo. When both cystinosin and its partner are missing, this early nutrition process is seriously affected and a wide range of amino acids is affected. However, we are still trying to understand how these two proteins work together. Why do they compensate for each other when just one is missing? How do they cooperate in this process?

To figure this out, we will test how cystinosin and its partner affect specific biochemical pathways suggested by a technique called metabolomics. We will use various scientific approaches to examine the candidate pathways. Additionally, we will try to fix the faulty pathways by treating the mice with drugs.

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.

Our study may uncover new insights into cystinosis. On one hand, similarities between the yolk sac and the kidney (the first main target of cystinosis) could help us understand common disease mechanisms in these tissues. On the other hand, the interplay between cystinosin and its partner might suggest unexpected ideas about how metabolism is affected in cystinosis and how other genes influence the severity of the disease.

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

This research will reveal new roles of cystinosin in the body. Understanding how it works with another lysosomal protein and identifying the biochemical pathway in which they cooperate will give us a broader understanding of the physiological function of cystinosin. This fundamental knowledge could lead to fresh ideas about the disease mechanisms.