

# 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](mailto:nstack@cystinosisresearch.org) as a Word document.

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**Principal Investigator (s):**

Bruce A. Barshop, MD, PhD, Jon A. Gangoiti, MS

**Project Title:**

Trial of a Hydrolase-Activated Thiol Prodrug in Cystinotic Fibroblasts

**Objective/Rationale:**

The mainstay treatment for cystinosis for more than two decades has been cysteamine. Cysteamine is known to reduce intracellular cystine and its effectiveness has been shown to be related to good compliance. However, there are problems with all available formulations of cysteamine, including stomach upset or ulcers, bad breath and body odor, and these side effects often make it difficult to take the full prescribed dose. There is a drug candidate which is designed to release cysteamine only inside of cells, and we will test if that candidate will reduce the cystine content in cultured skin cells from patients with cystinosis.

**Project Description:**

The prodrug will be added at various concentrations to fibroblasts (cultured skin cells) from patients with cystinosis. After a series of time intervals, the intracellular cystine content of those cells will be measured by tandem mass spectrometry, following our standard lab methods. We also plan to measure the concentrations of the prodrug, LL-244, in the cells and the growth medium, as well as the cysteamine which is released in the medium and inside the cells. We will also attempt to isolate intact lysosomes

**Relevance to the Understanding and/or Treatment of Cystinosis:**

We expect to find that this hydrolase-activated precursor is as effective as cysteamine. We will determine if it is hydrolyzed in the fibroblast, inside the lysosome, or in the medium. We will look for evidence that cysteamine is recycled between the lysosome and cytoplasm.

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

This study would be a useful first step for possible future development of an agent which potentially could eliminate or reduce the troublesome side effects of cysteamine therapy.