Cystinosis Research Foundation

*Lay Abstract Template for Awardees*

Spring 2013 Grants

Please complete this lay-oriented grant abstract form which will be published on the CRF web site and in the CRF Star Facts with announcement of your award. Please do not exceed 350 words total. Please submit this form to us as a Word file.

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**Principal Investigator (s)**: Paul Goodyer

**Project Title**: Novel Genetic Strategies for Cystinosis

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

Although cysteamine therapy has changed the natural history of cystinosis, kidney transplantation is eventually required in every patient and devastating non-renal complications may appear in young adults. One day it may be possible to treat cystinosis patients with their own stem cells after correcting the mutated CTNS gene, but CTNS mutations vary from one patient to another. Here we propose a range of molecular strategies to fix the CTNS gene in ways which address the individual mutations seen in our patients.

**Project Description**: Please write a brief, lay-oriented description of how you will carry out the project. Approximately 125-130 words.

Among French Canadians, a specific mistake in the genetic code tricks each cell into stopping synthesis of cystinosin protein before completion. We will test new drugs that allow the cell to overlook the French Canadian mutation and others like it. For patients in whom the CTNS gene has been deleted, we propose a method to insert the normal gene in an alternative site within the DNA. For those with small errors in the CTNS gene that disturb its normal function, we have devised a third approach that cuts that DNA and then guides the cell’s natural repair system to insert the proper genetic code. All three strategies will be developed using a unique panel of skin cells derived from our patients that harbor the full range of cystinosis mutations.

**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 words.

If we can show that novel drugs allow cells to overlook the common French Canadian mutation, oral therapy might then be attempted to restore activity of the mutated gene in this group of patients. Strategies to edit the CTNS gene in cultured cells assume that similar techniques can be applied for correcting the gene in each patient’s stem cells in the future.

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

New drugs have been developed that allow the cell to overlook mistakes in the genetic code or use the cell’s natural repair mechanisms to fix them. These therapies are being applied to other genetic diseases. In this proposal, we are trying to learn how they might be applied in an individualized way to the specific mutations that cause cystinosis.