# 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.

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**Principal Investigator (s)**: Ester De Leo and Francesco Emma

**Project Title**: Efficacy and safety of genistein in *Ctns*$^{-/-}$ rats

**Objective/Rationale**:
Cystinosis is a rare disease that still lacks complete and definitive cure. In previous studies, we have shown using cells derived from patients with cystinosis that genistein decreases cystine content and reverts some altered key cellular functions. Subsequently, we have shown that prolonged genistein administration to female cystinotic mice decreases cystine crystal accumulation in the kidneys and protects their function. In order to proceed to testing genistein in human subjects, we need to confirm these results in another model and perform additional experiments to test the safety of the drug.

**Project Description**:
The present study represents the last pre-clinical step of our research on genistein. We will use our recently developed *Ctns*$^{-/-}$ rat model to confirm the beneficial effects of genistein on kidneys. In addition, we will test the effects of genistein on other organs. We will study in particular if genistein reduces the deposition of cystine crystals in the skin because these may represent an important marker of efficacy that can be monitor with noninvasive techniques in patients. Since genistein may have unwanted endocrine effects, in particular on the reproductive system, we will closely monitor the hormonal profiles of treated female and male animals.

**Relevance to the Understanding and/or Treatment of Cystinosis**:
Should results obtained in mice be replicate in rats and toxicity tests be satisfactory, they will provide a strong rationale to perform a clinical study in human subjects. Potentially, genistein could be used in the clinical practice in combination with cysteamine to potentiate its cystine-lowering effect by acting on a different mechanism of cystine clearance.

**Anticipated Outcome**:
We expect to confirm in rats the reduction of cystine crystal deposition that we observed in mice, as well as the protective effects of genistein on the kidneys. Duplicating our results in a second animal model is important, since sometimes responses to drugs are specific to a given animal model. We also expect that the safety profile of genistein will be satisfactory, but until the tests planned in this project are performed, a clinical trial in humans cannot be planned.