What's New in Cystinosis Research?

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The human body has 40 trillion cells, and each cell has compartments called organelles. The nucleus contains DNA, which is organized into 23 pairs of chromosomes—half from each parent. DNA provides instructions for building proteins, and segments coding for specific proteins are called genes. Ribosomes read these genes to assemble proteins, which perform vital functions, including metabolism, structural support, and transport.

Cystinosin is a transporter protein in the lysosome—a recycling center that breaks down old proteins into amino acids. Cystinosin moves cystine out of the lysosome. Mutations in the gene that codes for cystinosin lead to a dysfunctional or absent protein. As a result, cystine accumulates in the lysosome, damaging cells and leading to organ failure.

Cystinosis first affects the kidneys, causing Fanconi's syndrome, where the kidneys fail to reabsorb fluids and nutrients, leading to dehydration, rickets, and renal failure. A kidney transplant treats Fanconi's syndrome but not cystinosis. The disease also impacts the eyes, bones, growth, thyroid, pancreas, muscles, lungs, and nervous system.

Cysteamine helps remove cystine from lysosomes, slowing damage but not curing the disease. A potential cure is gene-modified autologous stem cell transplantation, where a patient's blood stem cells are genetically corrected and transplanted back. In addition to this promising research, the Cystinosis Research Foundation continues to look for better treatments for cystinosis.

Here are some of the areas of research currently under investigation by CRF-funded scientists:

- Injected mRNA therapy developed by Moderna might be used to increase cystinosin production.
- Induced pluripotent stem cells can be transformed into kidney organoids which could eventually be implanted in the kidneys to regenerate healthy kidney tissue.
- The ketogenic diet improves renal and muscle function in mice and rats with cystinosis.
- FDA-approved drugs that target MTORC1 and autophagy could be repurposed for cystinosis.
- CF10 is a longer acting version of cysteamine without the side effects.
- Chaperone drugs developed for cystic fibrosis may be used to prevent cystinosin mutants from being degraded in patients with specific mutations.
- Pepstatin A is a compound that improves bone mass and quality in cystinosis mice.
- Musclin is a muscle-regeneration protein that is reduced in cystinosis and may be a target for improving muscle growth and function.
- Special muscle stem cells, satellite cells, can be generated from skeletal muscle cells and grown into muscle organoids which might be used for muscle disease.
- Respiratory training, tongue exercises, and behavioral feedback may improve swallowing function in patients with dysphagia.