Cystinosis: Back to the Basics

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The human body is made up of 40 trillion cells. Each cell has different compartments called organelles. The most important compartment is the nucleus. The nucleus contains the genetic blueprint of the cell, called DNA, which is wound up tightly into structures called chromosomes. Humans have 23 pairs of chromosomes, half from the mother and half from the father.

DNA is instructions for building proteins. A segment of DNA that codes for one protein is called a gene. Proteins are made up of building blocks called amino acids. The cell has special machinery called ribosomes that read the genes and build proteins. Proteins perform many different functions in the cell. Some proteins catalyze metabolic reactions. Some proteins are important structural components of cells. Some proteins are transporters, and move things in and out of cells and organelles.

There is a gene that codes for a protein called "cystinosin." This protein is a special transporter in the membrane wall of an organelle called the lysosome. Lysosomes are the recycling center for the cell. Lysosomes digest old proteins and break them down into amino acids, which are shipped out of the lysosome into the cell where they can be used to build new proteins. The protein cystinosin moves the amino acid cystine out of the lysosome.

Sometimes there are errors in the DNA, called mutations. When a ribosome is reading the instructions and comes upon an error, it either makes a bad protein or doesn't make any protein at all. In the disease cystinosis, there is a mutation in the DNA that codes for the cystinosin protein. The ribosome makes a bad protein, or sometimes doesn't make a protein at all. This means the lysosome can't get rid of cystine, which accumulates in the recycling center until it causes irreversible damage. This process happens in every cell of the body, resulting in organ damage and failure.

Cystinosis affects the kidneys first, causing Fanconi's syndrome. The kidneys become unable to reabsorb fluids, electrolytes, sugars and proteins that are filtered from the blood, leading to wasting in the urine. This leads to dehydration, failure to thrive, rickets and eventually renal failure. A kidney transplant cures Fanconi's syndrome, but not cystinosis.

Cystinosis affects every organ in the body. It causes corneal crystals, rickets, growth failure, hypothyroidism, diabetes, hypogonadism, infertility in males, muscle wasting, difficulty swallowing, pulmonary dysfunction and neurologic disease.

There is a drug that can help get cystine out of the lysosome. It is called cysteamine, and was discovered by Jerry Schneider in 1976. It goes into the lysosome, binds to the cystine, and helps it get out through a different transporter protein. While cysteamine helps slow organ damage, it is not a cure, and people eventually die from complications of cystinosis.

In order to cure cystinosis, you need to fix the gene. One potential way to do this is gene-mediated autologous stem cell transplantation. Blood stem cells are removed from a person with cystinosis and genetically modified using a virus to insert the correct cystinosin gene into the cells' DNA. These stem cells are then transplanted back into the person with cystinosis. This approach has been successfully used to cure mice with cystinosis mutations. It has also been used to cure other genetic diseases in humans, including X-linked adrenoleukodystrophy, metachromatic leukodystrophy, Wiskott-Aldrich syndrome, SCID and chronic granulomatous disease.