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Correction of the Cystinotic Phenotype in Cultured Cells by an Aminoglycoside.

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Aminoglycoside antibiotics suppress nonsense mutations leading to expression of full-length transcripts in the presence of premature termination codons. Fibroblasts derived from cystinosis patients with either homozygous deletion of a 57 kb portion of the CTNS cystine transport gene, homozygous for a 5-base deletion (545 del TCCTT), or heterozygous for a premature termination codon (753 G→A, W138X) and a splice-site mutation (IVS11 +2 T→C), were exposed to gentamycin at a concentration of 300 μg/mL for 15 days. The cells were then harvested and the intracellular cystine content measured by a cystine binding protein assay. At nine days of incubation, cells heterozygous for the premature stop codon and a splice-site mutation demonstrated 43% of the cystine content (0.65 ±0.38 nmol cystine/10^6 vs. 1.51 ±0.10 nmol/10^6 cells) of control cells incubated under identical conditions but not exposed to gentamycin ($p < .01$). Cells displaying the 57 kb deletion demonstrated no decline in cystine content (101% of control), and cells displaying the 5-base deletion demonstrated increased cystine (199% of control). No cystine depletion by gentamycin was seen at intervals less than nine days, but depletion was maintained through 15 days in the responsive line. Aminoglycosides are nephrotoxic, and cystinosis exerts its major pathological effect on the kidney, nevertheless, these results are intriguing, and suggest the need for further investigation of this category of compounds in altering gene expression in patients with premature stop codons resulting in lysosomal cystine storage.