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SCIENTIFIC LETTER

Molecular Analysis of the *CTNS* Gene in Indians with Nephropathic Cystinosis

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Abbreviations	
CTNS	Cystinosin
Ser	Serine
Phe	Phenylalanine

To the Editor: Cystinosis is a rare autosomal disorder, caused due to the malfunctioning of *CTNS* (Cystinosin), a lysosomal protein responsible for the transport of cystine from the lysosome to the cytosol. Based on the clinical features, the disease can be classified into infantile, juvenile and ocular cystinosis. Functional analysis of mutations associated with these clinical forms suggests that a defective CTNS transporter leads to the accumulation of cystine and is one of the causes of the pathophysiology [1].

In India, there are now several reports of clinically confirmed cystinosis but these are rarely followed up to identify the molecular basis. Thus, there appears to be a big gap between developing and developed nations in the diagnosis, awareness and treatment of cystinosis. We report here the identification of a mutation in three new Indian cystinosis patients. The age of the patients diagnosed is between 7 to 13 y, two were siblings. Parental consanguinity was noted in both families. Initial diagnosis for cystinosis was based on the presence of cystine crystals in the eyes of probands who were found to be photophobic. Other clinical symptoms associated with these patients were growth retardation, weight loss, Fanconi syndrome, renal failure and hypothyroidism (Table 1).

Amplification and sequencing of all coding exons revealed the presence of a homozygous point mutation p.Ser141Phe in all three patients (Fig.1). Analysis of the DNA of one of the parents of the two siblings revealed the presence of the mutation in heterozygous form. The p.Ser141Phe mutation is located in exon7, trans-membrane domain 1 of *CTNS* transporter and is highly conserved across different species (Fig. 1).

The identified p.Ser141Phe mutation has been reported only in 2 Arab [2], 2 South African [3] and one Indian patient [4]. It is known to cause a severe defect in the functionality of the transporter (2 ± 5.03 % of WT cystinosin activity) and causes infantile cystinosis [5]. Among 5 Indian patients where the mutational basis is so far identified, one patient has the p.Ser270del, while 4 others have the p.Ser141Phe

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Table 1 Clinical, biochemical and mutational details of cystinosis patients analyzed for molecular defects

Sr. no.	Age (years)	Clinical manifestation	Parental consanguinity	Weight (kg)	Height (cm)	Renal status	Treatment	Mutation
P1	7	Growth retardation, Fanconi syndrome, Renal failure, Hypothyroidism, Corneal crystals, Loss of weight, Affected siblings	Yes	8.3	79.2	Creatinine 2.0 mg/dl	Cysteamine	p.Ser141Phe
P2	11	Growth retardation, Fanconi syndrome, Renal failure, Hypothyroidism, Corneal crystals, Loss of weight, Affected siblings	Yes	24.9	116.6	Renal transplant 3 y back. Normal kidney function.	Cysteamine	p.Ser141Phe
P3	13	Growth retardation, Fanconi syndrome, Renal failure, Hypothyroidism, Corneal crystals, Loss of weight	Yes	13.4	85	Creatinine 1.0 mg/dl	Was on Cysteamine treatment (Died)	p.Ser141Phe

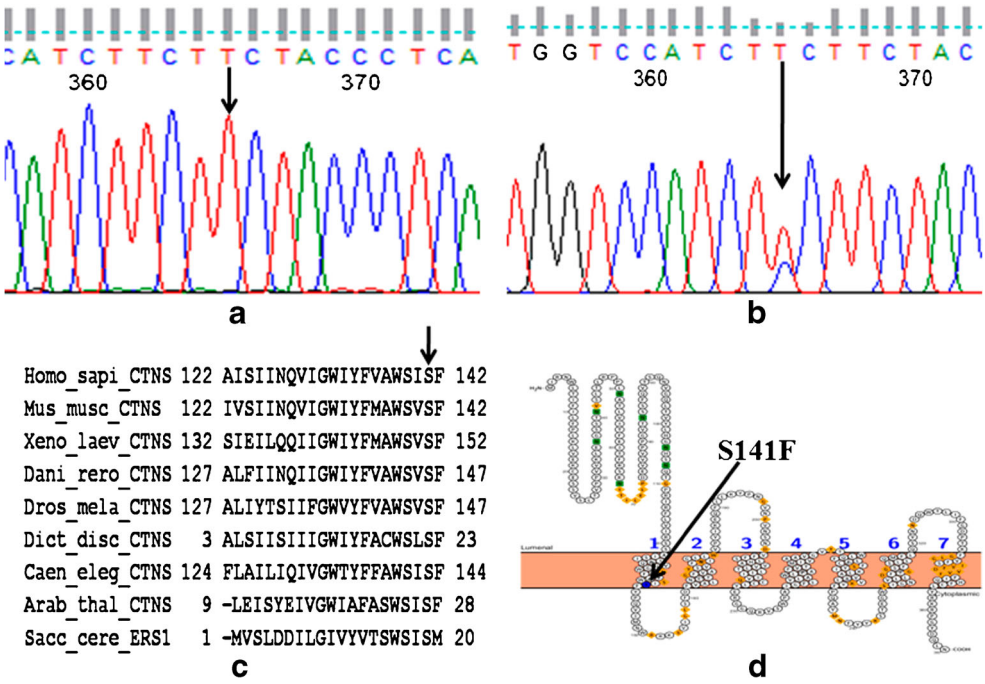

Fig. 1 Molecular basis of cystinosis in probands. Representative sequence chromatogram of *CTNS* (**a**) exon 7 of probands and (**b**) exon 7 of parent (**c**) Multiple sequence alignment for the analysis conservation pattern for the p.Ser141Phe mutation in *CTNS* gene. Causative mutation identified through the sequence analysis of coding regions and respective flanking intronic regions is denoted by an arrow. (**d**) Schematic topological model for the location of p.Ser141Phe mutation in *CTNS* gene

mutation. More patient studies are needed to ascertain if this is a prevalent mutation in Indian cystinotic populations.

Compliance with Ethical Standards

Conflict of Interest None.

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