ISSN: 2161-0681
Volume-12
Journal of Clinical & Experimental Pathology

Title: Ophthalmic and genetics profiles of cystinosis in Tunisian patients

Latifa Chkioua

University of pharmacy Monastir, Tunisia

Received: August 18, 2022; Accepted: August 20, 2022; Published: September 25, 2022

Ocular cystinosis is a rare autosomal recessive disorder characterized by intralysosomal cystine accumulation in renal, ophthalmic (cornea, conjunctiva), and other organ abnormalities. Patients with ocular cystinosis are mostly asymptomatic and typically experience mild photophobia due to cystine crystals in the cornea observed accidently during a routine ocular examination. The ocular cystinosis is associated with different mutations in CTNS gene. Cysteamine therapy mostly corrects the organ abnormalities.

In the present study, In silico analysis on the functional and structural impact of the reported mutations helps to provide comprehensive insight into molecular mechanisms of cystinosin synthesis, function, and interaction with the lipid bilayer and to better understand the related clinical manifestations observed in eight Tunisian patients.

The studied patients were found to have cystine crystal limited anterior corneal stroma and the conjunctiva associated with retinal crystals accumulation. CTNS gene sequencing disclosed 7 mutations: three missense mutations (G308R, p.Q88K, and p.S139Y); one duplication (C.829dup), one framshift mutation (p.G258f), one splice site mutation (c.681+7delC) and a large deletion (20327-bp deletion). Crystallographic structure analysis suggests that the novel mutation p.S139Y is buried in a first transmembrane helix closed to the lipid bilayer polar region, introducing a difference in hydrophobicity which could affect the hydrophobic interactions with the membrane lipids. The second novel mutation p.Q88K which is located in the lysosomal lumen close to the lipid membrane polar head region, introduced a basic amino acid in a region which tolerate only uncharged residue. The third missense mutation introduces a positive change in nonpolar tail region of the phospholipid bilayer membrane affecting the folding and stability of the protein in the lipid bilayer. Our data demonstrate that impaired transport of cystine out of lysosomes is the most common, which is obviously associated with the mutations of transmembrane domains of cystinosine resulting from a total loss of its activity.

In this and our previous study, the finding data demonstrate that the mutational spectrum of the Tunisian patients is particular and different from patients in other countries, probably due to on one hand, the heterogeneous origins of the population and on the other hand due to the still high proportion of marriages between first cousins.

Biography

I am a research professor at the Faculty of Pharmacy of Monastir, University of Monastir. I have completed my postgraduation at the age of 26 years. I obtained my Master's degree in Molecular and Cellular Biology at the Faculty of Sciences of Sfax, University of Sfax, then the Doctorate degree on pharmaceutic sciences at the Faculty of Pharmacy of Monastir.