GENETICS AND GENODERMATOSES

IDENTIFICATION OF FOUR NOVEL XPC MUTATIONS IN TWO XERODERMA PIGMENTOSUM COMPLEMENTATION GROUP C PATIENTS AND FUNCTIONAL STUDY OF XPC Q320X MUTANT

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Xeroderma pigmentosum (XP) is a rare, recessive hereditary disease characterized by sunlight hypersensitivity and high incidence of skin cancer with clinical and genetic heterogeneity. We collected two unrelated Chinese patients showing typical symptoms of XPC without neurologic symptoms. Direct sequencing of XPC gene revealed that patient 1 carried IVS1+1G > A and c.958 C > T mutations, and patient 2 carried c.545_546delTA and c.2257_2258insC mutations. All these four mutations introduced premature terminal codons (PTCs) in XPC gene. The nonsense mutation c.958 C > T yielded truncated mutant Q320X, and we studied its function for global genome repair kinetics. Overexpressed Q320X mutant can localize to site of DNA damage, but it is defective in CPD and 6-4PP repair. Readthrough of PTCs is a new approach to treatment of genetic diseases. We found that aminoglycosides could significantly increase the full length protein expression of Q320X mutant, but NER defects were not rescued in vitro.