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التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

MONA MAGHRABY

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جامعة عين شمس

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Polymorphisms of some genes in Egyptian patients with keratoconus

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ABSTRACT

Keratoconus (KC) is a non-inflammatory progressive disorder distinguished by thinning of the corneal tissue and bulging forward into a cone-shaped fashion. Yet its etiology, which is multifactorial, despite intensive research remains elusive. Corneal exposure to reactive oxygen species causing oxidative DNA damage has been reported to be associated with KC and therefore suggesting that DNA base excision repair mechanism (BER) might lie behind the pathogenesis of the disease.

We studied the association of three variants in two BER genes (*XRCC1* and *POLG*) and KC occurrence in a cohort of patients from Egypt. Genotyping of the three variants was performed using PCR and restriction enzymes analyses. We observed that A allele and A/A genotype of the c.1196A>G variant in the *XRCC1* gene were significantly associated with increased KC occurrence while the G allele was associated with decreased KC occurrence. Similarly, the A/A genotype of the c.–1370T>A polymorphism in the *POLG* gene and the A allele were associated with increased occurrence of KC, while T/A genotype and the T allele were accompanied with decreased occurrence of KC. On the other hand, no association was observed between the c.580C>T variant in the *XRCC1* gene and KC occurrence among the studied group of patients.
Our results suggest that c.1196A>G variant of the *XRCC1* and c.–1370T>A variant of the *POLG* gene may be involved in KC pathogenesis and might be considered as a genetic risk factors of the disease.

***Keywords*:** Keratoconus; Base excision repair; *XRCC1*; *POLG*; Genotyping; PCR-RFLP.

List of Abbreviations

AD	Alzheimer's disease
Arg	Arginine
BER	Base excision repair
CAST	Calpastatin
Cdc42	Cell division cycle 42
Cn	Calpain
CO-1	Cytochrome oxidase subunit 1
COL4	Collagen type IV
COL4A3	Collagen (type IV) alpha-3
COL4A4	Collagen (type IV) alpha-4
DOCK9	Dedicator of cytokinase 9
FECD	Fuchs endothelial corneal dystrophy
FFKC	Forme fruste keratoconus
Gln	Glutamine
His	Histidine
IL1	Interlukien-1
ILl-α	Interleukin-1 alpha
IL1-β	Interleukin-1 beta
KC	Keratoconus
LOX	Lysyl oxidase
Lp	Lens-specific calpain
miR-148	microRNA- 148
mtDNA	Mitochondrial DNA
OS	Oxidative stress
PCR	Polymerase chain reaction
PEO	Progressive external ophthalmoplegia
PKP	Penetrating keratoplasty
POAG	Primary open angle glaucoma
POLG	Polymerase gamma
RFLP	Restriction fragment length polymorphism
ROS	Reactive oxygen species
SNP	Single nucleotide polymorphism
SOD1	Superoxide dismutase 1
SSB	Single strand break
UV	Ultra violet rays
UTR	Untranslated region
VSX1	Visual system homeobox 1
XRCC1	X-ray repair cross-complementing group 1