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TOKAT GAZİOSMANPAŞA UNIVERSITY

GRADUATE SCHOOL INSTİTUTE

ANALYSİS OF ARPC1B GENE EXPRESSİON İN PTERYGİUM

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Master Thesis

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ETHICAL CONTRACT

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(17/6/2021)

MUSTAFA AHMED
ABDULLAH AL-BAYATI

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ABSTRACT

Analysis of ARPC1B gene expression in pterygium

MUSTAFA AHMED,Master Thesis

TOKAT GAZİOSMANPAŞA UNIVERSITY, TOKAT,2021

Pterygium, or flesh growth in the eye, is a common eye illness that causes the conjunctiva on the cornea to expand out of control. The most common cause of epithelial tissue abnormalities is long-term UV radiation exposure from the sun. Although the precise etiology of the pterygium disease is unknown, additional elements such as dry weather, dust, and a vaporization of the tear film, and other genetic factors, Despite the fact that the exact cause of pterygium illness is uncertain, there seems to be a correlation between outdoor work and the illness's development.

Subunit 1B of the Actin Related Protein 2/3 Complex the name of the ARPC1B gene. The human Arp2/3 protein complex has seven subunits, and this gene codes for one of them. Sensory rhodopsin-2 protein is a component that belongs to the SOP2 family.

The goal of this research was to see how the ARPC1B gene affected pterygium illness. Tissue was extracted during surgery with the subjects' agreement and consent. We employed the technique expression of ARPC1B gene by extracting cDNA synthesis from group of tissues levels assessed by Real-Time PCR, and the diagnosis of pterygium was validated (polymerase chain reaction).

According to the findings of qRT-PCR, there was no discernible change. in ARPC1B gene levels of expression in pterygium and normal conjunctival tissues ($p>0.005$).

Keywords: ARPC1B, Pterygium, qRT-PCR

ÖZET

Pterjiyumda ARPC1B gen ekspresyonunun analizi MUSTAFA AHMED, Yüksek Lisans Tezi TOKAT GAZİOSMANPAŞA ÜNİVERSİTESİ, TOKAT, 2021

Pterjium veya gözde et büyümesi, korneadaki konjonktivanın kontrolden çıkmasına neden olan yaygın bir göz hastalığıdır. Epitel doku anormalliklerinin en yaygın nedeni güneşten gelen UV radyasyonuna uzun süre maruz kalmaktır. Pterjium hastalığının kesin etiyolojisi bilinmemekle birlikte, kuru hava, toz, gözyaşı filminin hızlı buharlaşması gibi diğer faktörler ve diğer genetik faktörler ıle bırlıkte pterjiyum hastalığının olusumunda bu etmenlerın bağlantı olduğu görülmektedir.

Aktin İlişkili Protein 2/3 Kompleks Alt Birim 1B, ARPC1B geninin adıdır. İnsan Arp2 / 3 protein kompleksinin yedi alt birimi vardır ve bu gen bunlardan birini kodlar. Duyusal rodopsin-2 proteini, SOP2 ailesine ait bir bileşendir.

Bu araştırmanın amacı, ARPC1B geninin pterjiyum hastalığını nasıl etkilediğini görmektir hastaların onayı ile ameliyat sırasında doku çıkarıldı. Real-Time PCR ile değerlendirilen bir grup doku seviyesinden cDNA sentezlenecek ARPC1B geninin teknik ekspresyonunu kullanıldı ve pterjiyum tanısı doğrulandı (polimeraz zincir reaksiyonu).

qRT-PCR bulgularına göre pterjium ve normal konjonktival dokularda ARPC1B gen ekspresyon düzeylerinde anlamlı farklılık olmadıgı tespıt edıldı ($p>0.005$).

Anahtar Kelimeler: ARPC1B, Pterygium ,qRT-PCR

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ABBREVIATION AND SYMBOL LIST

ACTB	Actin
ALDH3A1	Aldehyde Dehydrogenase 3 Family Member A1
ARP3	Actin-related protein 3
ARPC1	Actin-related protein 2/3 complex subunit
ARPC1A	Actin Related Protein 2/3 Complex Subunit 1A
ARPC1B	Actin Related Protein 2/3 Complex Subunit 1B
ARPC5A	Actin-related protein 2/3 complex subunit 5A
ARPC5B	Actin-related protein 2/3 complex subunit 5A
BaP	benzo (a) pyrene
BPDE	Benzo [A] Pyrene Diol-Epoxide
cAMP	Cyclic adenosine monophosphate
Cav-1	Caveolin-1
CD8+	HIV suppressor cell count
cDNA	complementary deoxyribonucleic acid
COX2	Cyclooxygenase 2
CTGF	connective tissue growth factor
CTL	cytotoxic T-lymphocyte
CYP1A1	Cytochrome P450, family 1, subfamily A, polypeptide 1
DNA	Deoxyribonucleic Acid
dNTP	deoxyribonucleoside triphosphate
EGF	epidermal growth factor
ELISA	enzyme-linked immunosorbent assay
EMT	epithelial–mesenchymal transition
GHRH	growth-hormone-releasing hormone
GHRH-R	growth-hormone-releasing hormone receptor
GLUT1	glucose transporter 1
GSTM1	Glutathione S-transferase Mu 1
HPV	Human papilloma virus

HSV	Herpes Simplex Virus
IL-1	interleukin-1
IL-4	interleukin-4
IL-6	interleukin-6
IL-8	interleukin-8
MAP	mitogen-activated protein
MMP-10	Matrix Metallopeptidase 10
MMP-2	Matrix Metallopeptidase 2
MMP-9	Matrix Metallopeptidase 9
mRNA	Messenger Ribonucleic Acid
NADP	Nicotinamide adenine dinucleotide phosphate
OSCC	Oral Squamous Cell Carcinoma
OSSN	Ocular surface squamous neoplasia
PCNA	Proliferating cell nuclear antigen
PCR	polymerase chain reaction
PEDF	Pigment epithelium-derived factor
qRT-PCR	Quantitative Real-Time Polymerase Chain Reaction
RNA	Ribo-Nucleic acid
Rnase	ribonuclease
ROS	reactive oxygen species
SNP	Single nucleotide polymorphism
SOP2	sensory rhodopsin-2
SPSS	statistical package for social science
TGF-B	Transforming Growth Factor Beta
TIMP-1	Metallopeptidase-1
TCR	T-cell receptor
UTR	untranslated region

UV-A	Ultraviolet A
UV-B	Ultraviolet B
UV-C	Ultraviolet C
UVR	ultraviolet radiation
VEGF	vascular endothelial growth factor
WASP	Wiskott–Aldrich Syndrome protein

1- INTRODUCTION

Pterygium is frequent eye diseases (Carlos et al;2018). The growth of fibrovascular tissue along the surface of the cornea distinguishes it. The pathophysiology of the pterygium disease is complex and still being researched. (2017, Mologen et al.) The most prevalent cause is long-term exposure to UV radiation from the sun (Farhad et al;2018). Other variables, including as dry weather, dust, and other hereditary variables, also has a function in it (Kyei et al,2016; Carlos et al,2018).

Pterygium is usually asymptomatic although mixed humidity beneath the ocular surface may induce dry eye symptoms such as burning, itching, and lacrimation. Advanced pterygium inside the optical zone reduces sharp-sightedness and requires surgery. (Mologen et al;2017). Although the actual origin of pterygium sickness is unknown, there seems to be a relation between the sickness and outdoor employment (Desheng et al;2013). Until now, there hasn't been a national, population-based study of pterygium occurrence throughout the world, and it seems that a national, pooled estimate based on the worldwide population would be valuable.

Actin Related Protein 2/3 Complex Subunit 1B is encoded by the ARPC1B gene. This gene codes for one of the seven subunits of the human Arp2/3 protein complex. Sensory rhodopsin-2 protein, a member of the SOP2 family, is the name of this component. Because these two proteins are so similar, they may both function as the p41 component of the human Arp2/3 complex, which has been related to cell actin polymerization control. (RefSeq, 2011).

It's probable that the p41 subunit aids in the construction and upkeep of the Arp2/3 complex structure. Various variations of the p41 subunit may match the complex's activities to different types of cells. Because it is a substrate and activator of Aurora kinase A this protein has a function in centrosomal homeostasis (RefSeq, 2011).

Platelet abnormalities with Eosinophilia, Immune-Mediated Disease, and Combined lymph cell and B cell Immunodeficiency are some of the diseases linked to the ARPC1B gene. (RefSeq, 2011).

One of the major causes resulting in pterygium development is thought to be cell cycle disruption, indeed abnormal cell cycle kinetics can cause cellular proliferation and contribute to apoptosis escape.

Patients with mutations in the ARPC1B component of Arp2/3 show signs of immunodeficiency and immunological dysregulation, including recurrent viral infections and a low CD8+ T cell count. We show here that a lack of ARPC1B results in a loss of CTL cytotoxicity, with the defect happening on two levels. Across immunological synapse infections, ARPC1B is necessary for the development of lamellipodia, cell movement, and actin remodeling.

Second, ARPC1B is necessary for the preservation of TCR, CD8, and GLUT1 membrane proteins in CTL plasma membranes, since recycling via the retromer and WASH complexes is hampered in the absence of ARPC1B. (RefSeq, 2011).

The retromer complex identifies cargo proteins that are localized in specific areas of the endosomal membrane, where tubules transport cargo proteins to the right destination, and the WASH complex is a 500 kDa complex that comprises WASH1, FAM21, and SWIP and other proteins (Derivery et al;2009).

ARPC1B have a role in the formation and The ARP2/3 complex, which is involved in actin branching from a filament, is maintained. They speculated that ARPC1B loss in T cells might result in cytoskeleton and functional abnormalities.

Six patients with associated early-onset sickness, severe infections, autoimmune symptoms, and thrombocytopenia had biallelic mutation ARPC1B which is identified by RefSeq, Immunological characteristics included T-cell lymphopenia, a low number of T cells, and hyper-immunoglobulin E. (RefSeq, 2011).

Actin Related Protein 2/3 Complex Subunit 1B have a role in platelet dysfunction, in which a large number of platelets causes hard tissue sclerosis in the eye, and we know that pterygium disease is the formation of triangular tissue on the cornea.

The goal of this study is to look at the influence of the ARPC1B gene on pterygium disease. According to the literature there is no study has been done on the ARPC1B gene and the formation of pterygium tissue, the work that will be done is groundbreaking in Turkey and throughout the globe.

2-GENERAL INFORMATION

Pterygium is a noncancerous conjunctival tumor that is benign. localized in front of the sclera. In certain situations, it may cause vision impairment and become inflamed, resulting in redness and agitation in the affected region. Additionally, certain eye malignancies, such as ocular surface squamous neoplasia, may develop from pterygium (Ting et al;2013).

The name "pterygium" derives from the Latin form of a-Pterygion"-"pterygos" and meaning "wing" (Hovanesian, 2012).

It is separated into three distinct parts: the apex, the neck, and the body. The body of the pterygium is an elevated triangular component with its base toward the canthus, the neck contains the head invades the cornea, and the limbus is superficial. and forms the apex of the triangle (Chinyelu, 2019).

Pterygium is a degenerative disorder caused by benign conjunctival development that is characterized by fibro vascularization, conjunctival invasion, and collagen elastic degradation. However, since active cell growth occurs with low apoptosis, several investigations have shown that pterygium has several characteristics with malignancies. Pterygium causes vision problems by blocking the visual axis and causing considerable astigmatism (Helen et al; 2019).

Pterygium is a highly common fibrovascular disease in people who live close to the equator, often referred to as the "pterygium zone" (Ting et al; 2013). At these tropical locales, prevalence might be as high as 22%, with fewer than 2% in latitudes above 40°. (Algahtani, 2013; Gingereke et al,2018).

Pterygium mostly affects persons who are exposed to more sunlight; it has been proven that males are twice as likely as women to get the condition, which might be due to the fact that males in certain nations spend more time outdoors than women. (Ting et al; 2013).

Human papillomavirus infection, which is frequent in some populations, is another key environmental component. (Di Girolamo, 2012).

Familial occurrence of pterygium, on the other hand, suggests that genetic factors have a function in pterygium pathogenesis (Ting et al; 2013).

Even with this knowledge, the cause of pterygium illness is unknown. In recent years, investigations using molecular genetic research methods on patient tissue samples have revealed vital new insights on disease pathogeneses. It confirmed the effect of UV radiation it also added viral infections, epigenetic disorders, immunological and antiapoptotic Angiogenic and lymphangiogenic processes stimuli, growth factors, extracellular matrix remodeling, Extracellular matrix modulators are dysregulated. and epithelial changes within the mesenchymal transition (Perra et al, 2006; Cárdenas-Cantú et al, 2016).

Modifications to the inflammatory cascade and cholesterol metabolism have also been identified as potential pathogenic causes. However, most of those characteristics are linked to the disease's progression rather than its beginning. A number of these variables have also been linked to UV light exposure, either directly or indirectly. (Cárdenas-Cantú et al;2016).

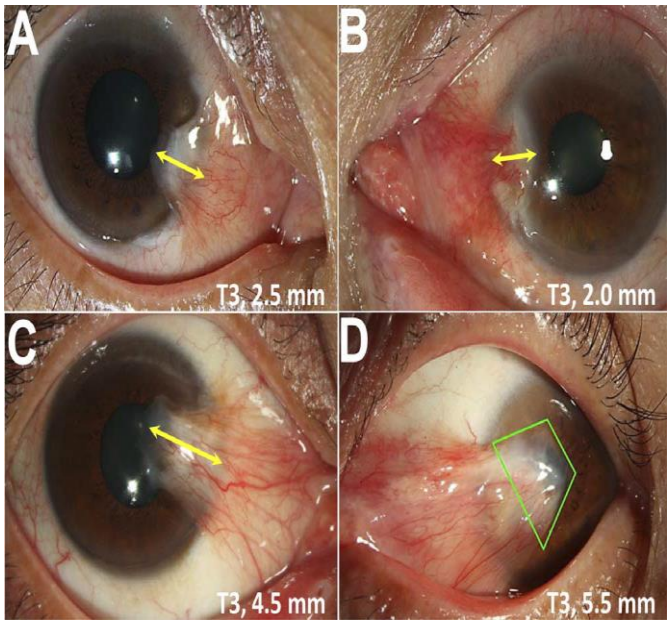

Figure 2.1: Chu et al;2016 primary pterygium of grade T3

2.1. Epidemiology

Race, age, social class, profession, and educational background have all been mentioned as risk factors (Otulana,2013; Helen et al,2019).

According to a big North American research, pterygium disease is 2.5 to three times more common in black people than in white people which is approximately twice as prevalent among people who work outdoors but just one fifth (0.2) as prevalent among those who wear sunglasses all the time outdoors. (Chimdia,2019).

As previously said (UV) light exposure might not be the sole factor connected with the evolution of pterygium. Dust and sand may participate to the happening of pterygium.

This might be explained by the fact that tears normally run inwards, taking any dust particles or fine foreign bodies with them (sandy dust is coarser than fine dust), triggering an inflammatory reaction and the formation of pterygium (Sun et al, 2013; Tano et al,2013).

Pterygium may be prevented with educational programs that alter these possible exposures. Other studies have identified as independent risk factors for pterygium, older age, male sex, lower educational level, rural habitation, and nonsmoking (Tano et al,2013; Helen et al,2019).

Pterygium is believed to be present in 3% of Australians, 23% of blacks in the United States, 15% of Tibetans in China, 18% of Mongolians in China, 30% of Japanese, and 7% of Singaporean Chinese and Indians. (Ang et al,2012).

2.1.2. Etiology and pathogenesis

In recent years, raised Transcript factor levels, cAMP response element binding protein, cytochrome P450 1A1 protein, phospholipase D, and aquaporin-1 and -3 have all been identified as risk factors. (Zhou et al;2016).

During the healing phase following photoactive keratectomy, some growth factors such as metalloproteinase enzyme and cytokines were discovered in the cornea. These

biological components produced by leukocytes are thought to have a crucial function in the genesis of pterygia. UV also activates the signaling pathway in pterygium epithelial cells that allows them to produce growth factors and cytokines. Inflammatory mediator release has been linked to both acute and chronic problems in atopic patients (Shayegan et al; 2016).

Pterygium prevalence and its distribution notably higher in those living in coastal villages than those living in mountainous regions and plains (Liu et al; 2013).

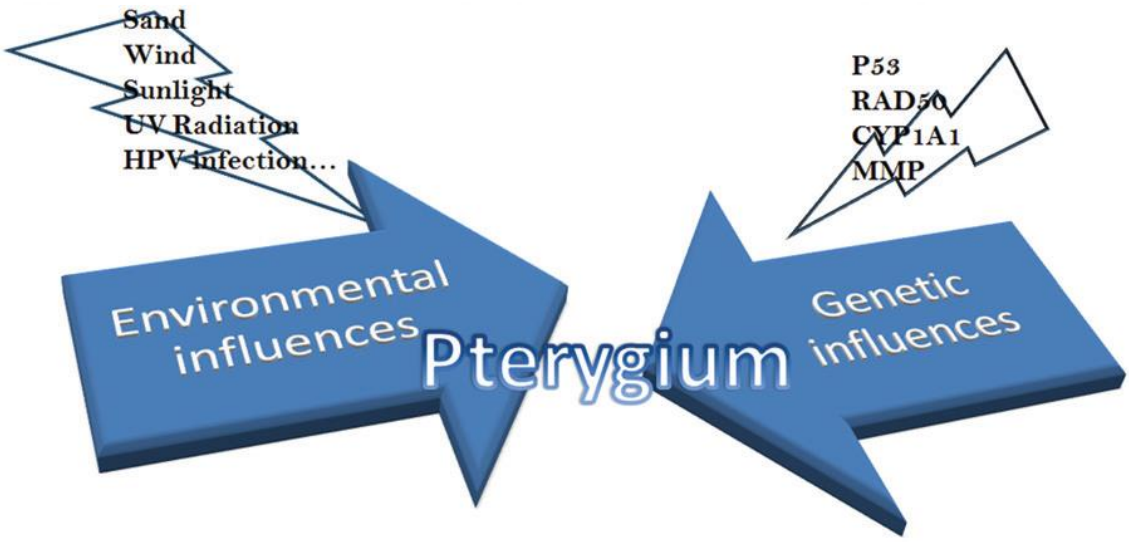

Figure 2.2: liu et al;2013 Pterygium pathogenesis is affected by the interaction of environmental and genetic variables.

2.2. Factors Affecting Pterygium Formation

2.2.1. The role of ultraviolet rays (UVrays)

The relationship between UV radiation exposure and the development of pterygium is as ophthalmulosis. UV rays are nonionizing radiation's shorter wavelengths (wavelength 100–400 nm) lying below the spectrum. UVA (400–320 nm), UVB (320–290 nm), and UVC (290–100 nm) are the three bands of ultraviolet radiation (UVR) (Helen et al;2019).

Because of photosensitivity and a rise in melanin levels in the skin responses, UVA, or near UVR, causes browning of the skin. Sunburn produces severe erythema and blistering, and more UVB exposure is linked to a higher likelihood of cancer. UVC is a germicidal agent that may potentially lead to skin cancer (Gingereke et al; 2018).

UV radiation (UVA and UVB) has been linked to a variety of biological consequences, including DNA damage, oxidative stress, activation of cell surface receptors, and activation of intracellular signaling pathways (Zhou et al., 2016). UV-C is antibacterial and may induce skin cancer (Gingereke et al.,2018). UV radiation causes harm to cells and tissues via two pathways :

A) Direct phototoxic effect on cellular DNA

B) Production of reactive oxygen species that damage cellular DNA, proteins and lipids (Sebastia et al,2013 ; Cárdenas-Cantú et al,2016).

UV light causes the creation of active free radicals, which attack and destroy many macromolecules at the molecular level. (Said et al ;2007).

UVR is generally covered and sheltered from the eyes by a number of factors, include normal horizontal alignment of the eyes, orbits, and brows, which reduces ocular exposure to whole-sky irradiation substantially. (zitiert & Walsh, 2009).

Since research has revealed that the cornea acts as a side on lens, focusing light incident on the temporal cornea to the opposite side of the eye, the anatomy of the nose and cheeks prevent this effect from occurring in the opposite direction, that is, light

incident at the nasal limbus isn't of such a peripheral angle to allow a focusing effect unto the opposite side of the eye. (zitiert & Walsh K,2009).

There is a degree it's shown that scattered light can submit to the attention by alternative transversal pathways, thereby damaging the limbal stem cells on the inner side. During this case, a violation of the corneoscleral limbal barrier subsequently ends up in corneal subjunctivization and also the development of pterygium (Mologen et al;2017).

In addition, it's supposed that the radiation is causes mutations in p53 gene, a tumor suppressor growth, that way contributing to the violation of proliferation radio limbal epithelium (Ang et al;2007).

Collagen degradation has also been linked to excessive sunshine exposure. Collagen degeneration, on the other hand, has been ruled out as a cause of pterygium pathogenesis (Gingereke et al;2018).

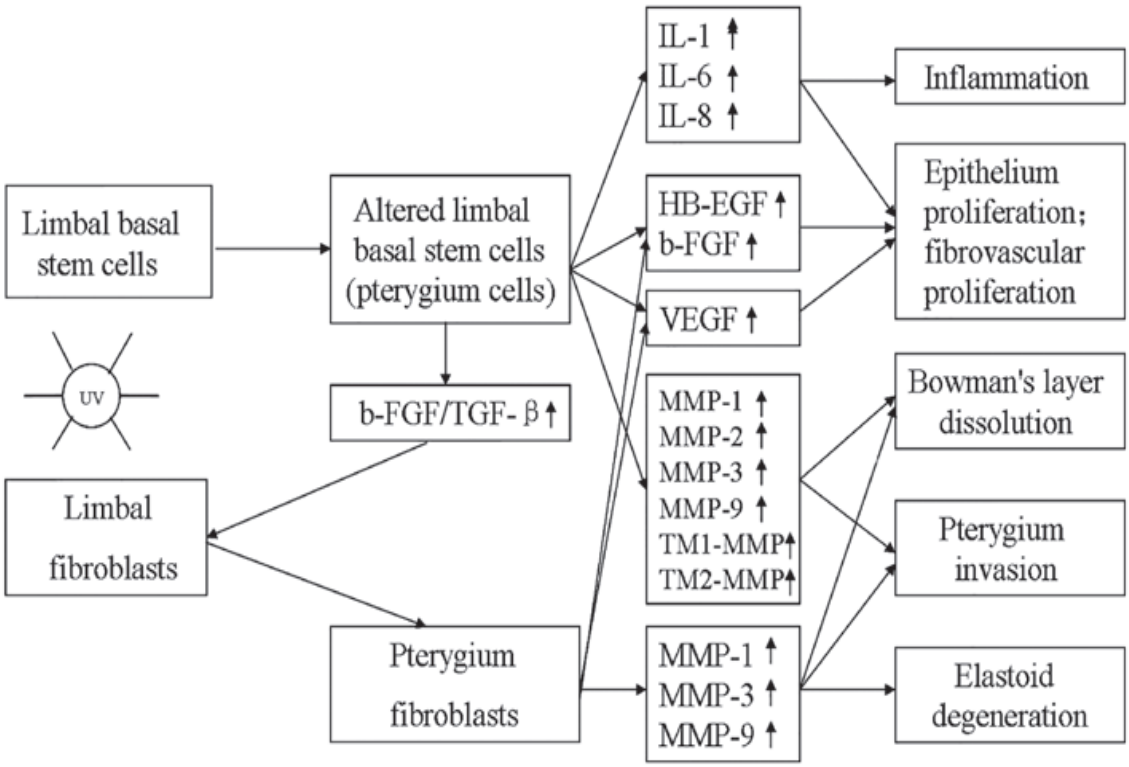

Figure 2.3: Zhou et al;2016 Ultraviolet Radiation's Role in Pterygium

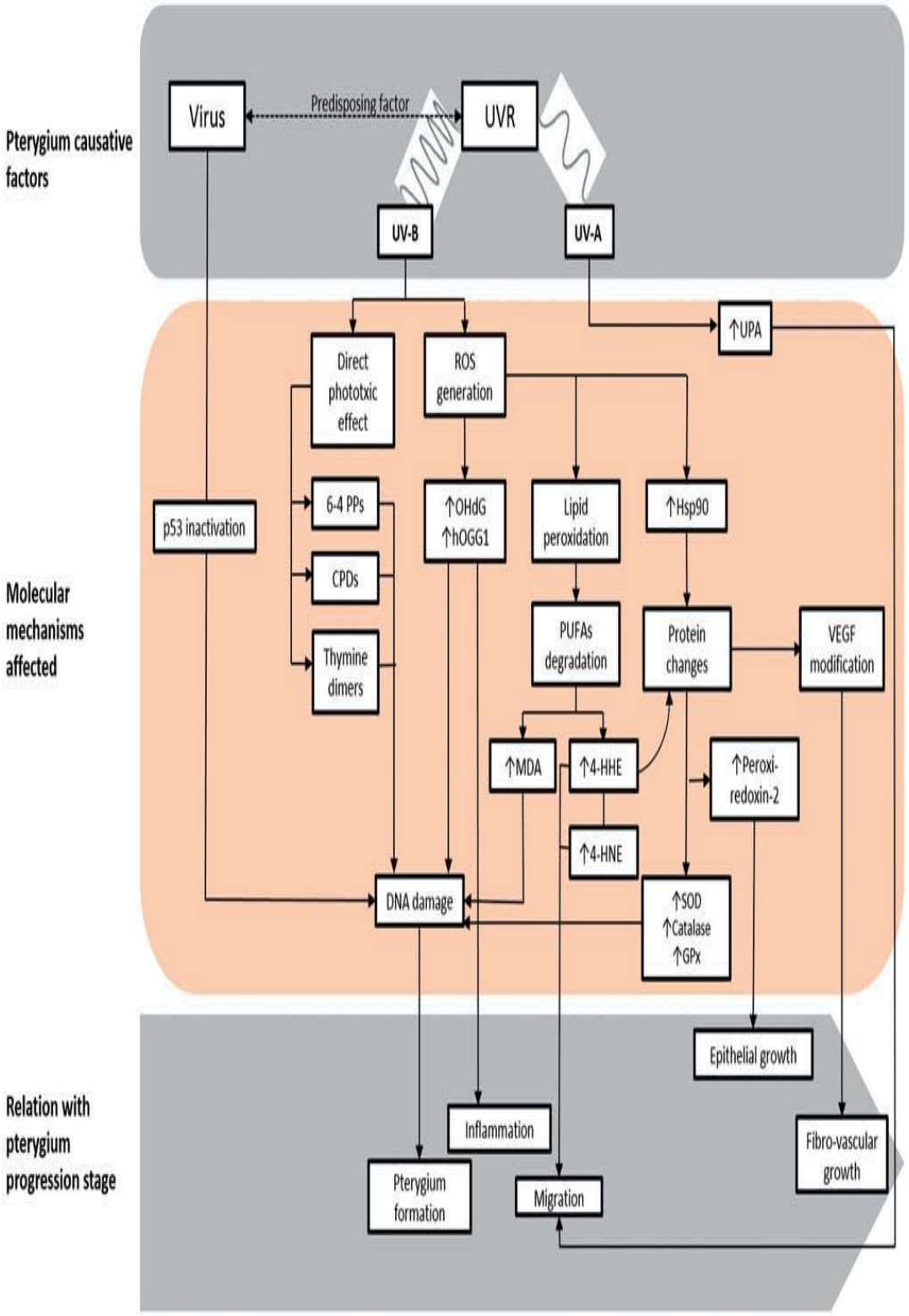

Figure 2.4: Cárdenas-Cantú et al.,2016 The major causes of pterygium, the molecular pathways involved, and their relationship to the stage of pterygium progression

2.2.2. The role of P53 gene

P53 is a tumor suppressor gene that prevents genomic changes by inhibiting the cell cycle. It's a crucial cell stress regulator that regulates the cell cycle as well as DNA repair and synthesis, cell differentiation, and apoptosis., as well as integrating signals from a variety of cellular stressors. However, additional variables like as acetylation and phosphorylation levels, among others, have a role (Mologen et al;2017).

It is noted that the level of p53 expression in pterygium differs between layers of the epithelium, it's more expressed in the basal cells compared with to more surface layers (Mologen et al,2017).

P53 is overexpressed and may be shown immunohistochemically (Yangwuyue et al,2013). The main genetic joint marker of human neoplastic development is p53 mutations. Instead of degenerative dysfunction, pterygium is classified as a neoplastic-like growth condition (Chui et al,2011; Ting et al,2013).

Immunohistochemistry reveals aberrant amounts of p53 expression in pterygium specimens. SNP markers are useful for detecting complicated relationships between genes and illnesses (Laing et al,2011; Yangwuyue et al,2013).

The most pertinent indicators for tumor susceptibility are p53 codon 72 polymorphisms. The existence of aberrant p53 protein production and a codon 72 polymorphism indicate that p53 gene mutation may have function in pterygium growth (Liu et al,2012; Ting et al,2013).

The causes of the p53 mutation were investigated further. Environmental pollutant benzo(a)pyrene (BaP) has been shown to cause p53 mutations. BaP's ultimate metabolite, BaP 7,8-diol 9,10-epoxide (BPDE), has the potential to attack deoxyguanosine and create the BPDE-N2-dG adduct, which triggers the p53 gene mutation (Yangwuyue et al;2013).

The formation of BPDE-like DNA adducts in pterygium samples has been associated to cytochrome P450 1A1 (CYP1A1) polymorphisms. (Tung et al,2010; Ting et al,2013), as a result, a CYP1A1 polymorphism is linked to pterygia and may be used as a predictor of pterygium susceptibility.

2.2.3. The role of Oxidative stress

The generation of reactive oxygen species (ROS) generated by ultraviolet light has been postulated as a beginning point for pterygium formation. (Sonja et al,2013; Gingereke et al,2018).

The Stocker line, a zone of enhanced iron deposition along a pterygium's advancing boundary, has further shown the importance of ROS in pterygium growth. In pterygium tissues, researchers observed the expression of certain proteins that are hypothesized to protect against oxidative stress-induced apoptosis (Kim et al,2014; Helen et al,2018).

ALDH3A1, protein disulfide isomerase and peroxiredoxin II were shown to be highly elevated in pterygium and in frequent pterygium in several investigations. Peroxiredoxin I and II were both shown to be elevated in pterygium in a prior research (Kim et al,2014; Chinyelu,2018).

As a result, topical antioxidant therapy might be used as a first-line treatment for pterygium lesions in the future.

2.2.4. The Role of Viruses

Studies have shown a significant incidence of oncogenic human papillomaviruses (HPVs) in tissue samples, indicating that HPV play a role in pterygium growth and occurrence. (Type 18 was the most frequent genotype, followed by type 16, with types 58 and 59 being less prevalent) (Chong et al,2014; Chimdia et al,2018).

The relationship between HPV infection and pterygium has been studied in many research, although the findings have been equivocal. According to Rodrigues et al. (2008), 58.3 percent of Brazilian pterygium samples were positive for HPV DNA, compared to 9.5 percent of control samples groups.

According to another research (Sjo et al;2007), 4.44 percent of Danish pterygium samples are HPV positive, all of them are type 6.61. Another research found that (Hisao et al;2010) looked at another batch of pterygium samples from Taiwan and discovered

that just two of the 65 samples were positive for Human papillomavirus (Hisao et al;2010).

The absence of HPV DNA in pterygium, at least in certain populations, refutes the idea that HPV is involved in pterygium production. HPV may not be essential for pterygium formation or function alone, but it may play a synergistic role in the multi-stage process of its development. (Hsiao et al,2010; Di Girolamo,2012).

Regardless of this that no agreement has been reached, it seems that the genetic background of populations may be a significant impact in these disparities (Piras et al;2003) The researchers looked for HPV on pterygia from two distinct geographical regions and discovered that Human papillomavirus might have a pathogenesis role in pterygium occurrence (Ting et al;2013).

Furthermore, Di Girolamo conducted 34 research on HPV in pterygium and ocular surface squamous neoplasia, with the results indicating that Human papillomavirus is not essential for the start of either disease but may be a co-factor in susceptible hosts (Di Girolamo, 2011).

Yangwuyue et al. investigated the prevalence of Human Papillomavirus and HSV (Herpes Simplex Virus) in pterygium and discovered a probable viral collaboration that affects the pterygium's clinical profile (Yangwuyue et al;2013).

2.2.5. The Role of heredity

Although previous reports suggest that exposure to sunlight is the most important factor in in the prevalence of pterygium, studies on pterygium occurrence and recurrence have found that heredity is the most important factor in pterygium development, and that sunlight is only a triggering factor for pterygium development (Anguria et al,2014; Helen et al,2018).

For pterygium to develop, it must be passed on through the generations. Family history, which suggests heredity (Carmichael,2001), was linked to the development of pterygiums (Anguria et al;2012), regardless of the use of standard eye medications or the presence of an unstable tear film (Anguria et al;2012).

Pterygium incidence was connected with having confirmed pterygium-affected relatives, which implicates heredity (Islam & Wagoner, 2001), therefore validating familial occurrence of pterygium (Anguria et al;2012).

The chance of genetic disorders occurring in an extended family rises when cousins reproduce (Jaouad et al;2009) The relationship of traditional eye care with pterygium is due to the practice of first-degree cousin marriage, and the usage of traditional medicines implicate genetics in the incidence of pterygium (Anguria et al;2012).

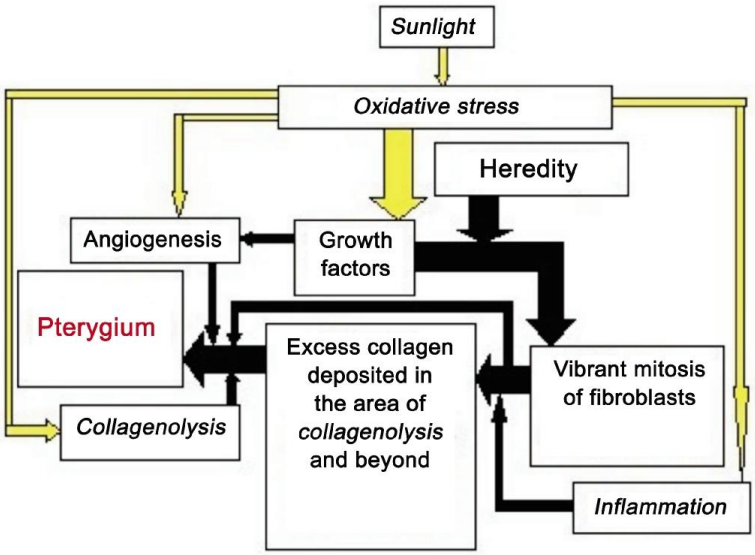

Figure 2.5: Model of pterygium development

2.2.6. Growth factors and cytokine's role in pterygium

The production of several cytokines, growth factors, and growth factor receptors may be stimulated by UVR genetically caused stress. (Chimdia et al;2018), the presence of these components in pterygium has been discovered using immunohistochemistry and ELISA methods (Helen et al;2018).

UVR-inducible cytokines include the interleukin-1 system, the interleukin-6 system, and the interleukin-8 system. (Epidermal growth factor) (EGF) and heparin-binding EGF, (vascular endothelial growth factor) (VEGF), basic fibroblast growth factor, platelet derived growth factor, and transforming growth factor are all implicated in pterygium (Chinyelu,2018).

However, some growth factors were expressed in some controls as well as in cases, indicating that overexpression of angiogenic growth factors isn't the cause of vibrant fibroblast mitosis or the occurrence of pterygium; rather, upregulation of fibro genic growth factors is likely to be the cause of pterygium growth and occurrence. it also shown that VEGF levels is higher in pterygium epithelium compared to normal conjunctiva using immunohistochemistry (Nolan et al;2004).

2.3. Regulation and induction of apoptosis in pterygium

When comparing the pterygium to the normal conjunctiva, abnormal apoptosis was discovered. Furthermore, multiple investigations found the expression of several apoptosis-related genes or proteins varied between pterygium and normal conjunctiva, indicating that apoptosis plays a role in the genesis of pterygium (Hong,2016).

Instead of a gain in proliferative capacity, pterygium is hypothesized to develop as a consequence of improper cellular apoptotic regulation (Zi-Xun,2016). As a result, the modulation of the apoptosis of pterygium epithelial cells seems to be important in pterygium pathogenesis.

MicroRNAs (miRNAs), a class of endogenous, short (20–25 nt) noncoding RNAs that bind to the 30 untranslated regions (UTR) of mRNA transcripts to trigger mRNA degradation or translational inhibition of target mRNAs, play a key role in posttranscriptional protein synthesis suppression (Na et al;2016). A base-pairing complement between the seed sequence of miRNAs and the 30UTR of their target mRNAs is the major factor of specific recognition. With an estimated 1000 human miRNAs produced by the mammalian genome, miRNAs govern a broad variety of biological activities, including cell development, proliferation, differentiation, death, and apoptosis. Because miRNAs are expected to be responsible for a large number of gene transcripts

They believe that miRNAs are involved in pterygium tissues' aberrant apoptosis (kiezun et al,2012; Zi-Xun etal,2016).

Antagonists of the growth hormone–releasing hormone receptor (GHRH-R) in retinoblastoma cells may stimulate the development of Caspase 3 (Casp3), which induces apoptosis. Clara,2018; Chu et al,2016).

GHRH-R antagonists have been proven in many investigations to alter cell growth and death in cancer cells. (Zarandi and colleagues, 2017; Andrew, 2018).

2.3.1. EMT

epithelial mesenchymal transition is the transformation of epithelial cells into mesenchymal cells. It may be identified in the stages of development, growth, wound healing, and carcinogenesis. EMT may have a role in the pathogenesis of pterygium, according to new study, which may provide light on the origins of pterygium fibroblasts.

The origin of Pterygium fibroblasts is unknown. They're most likely from limbal epithelium that's gone through EMT, which may be initiated by growth factors like TGF-C or FGF-2,103, 106 or UV radiation, which induces keratinocytes to produce slug and snail transcription factors connected to EMT (Minas,2008; Denis,2008).

EMT may occur locally during fibrosis, according to animal research, which supports the concept that limbal epithelial cells give rise to pterygium fibroblasts through EMT. The fact that the mesenchymal marker vimentin is expressed in corneal epithelial cells during wound healing adds to the notion (Minas,2008; Denis,2008; Nick,2008)

Animal studies showing the recruitment of bone marrow-derived fibroblasts to active fibrosis at cancer implantation sites and excisional wounds, as well as the discovery of bone marrow-derived progenitor cells in normal corneal stroma in mice and humans, support the latter theory. (Minas, Denis, and Nick, 2008).

Some reports claimed the development of a pterygium-like change in which C-catenin and lymphoid-enhancer-factor-1 are present inside the nucleus, cytokeratin 14 and B-smooth muscle actin are present in the epithelium, and snail and slug transcription factors are present in the nuclei (Nick,2008).

2.3.2. Pterygium cell proliferation, migration, and angiogenesis

considering that sort of unregulated cell growth that isn't harmful (Chui et al;2011). factors that affect cell proliferation including inflammatory, fibrosis, Proliferation, angiogenesis, and the extracellular matrix. disintegration are all characteristics of pterygium, a common ocular surface condition (Demurtas et al;2011).

Pterygium is not a tumor, despite the fact that it is a neoplastic-like development disease. Pterygium, on the other hand, needs local angiogenesis and cell migration, which is identical to cancer metastasis. The most prevalent cause of mortality in cancer patients is neoplastic cell metastasis in an organ other than the one where they originated (Yachida et al;2010).

Genes involved with cell proliferation, like mutant p53and PCNA, have been shown to be abnormally expressed in pterygium samples (Liang et al; 2011).

Angiogenesis, as evaluated by micro vessel density, is highly associated with the number of labrocytes tryptase positive cells in pterygium tissues, according to a prior research (Ribatti et al;2007).

The MAP kinase signaling pathway is known to be always active in cancer cells and is critical for cell proliferation (De luca et al,2012; Del Barco et al,2012) In pterygium, members of the MAP kinase signaling pathway, including as FGF2 and c-Myc, are improperly expressed (Detorakis et al,2010; Cui et al,2011).

In pterygia tissues, interleukin-4 (IL-4) levels are raised transcriptionally, which may trigger the induction of osteoblast specific factor which is associated to the cell cycle, connective tissue growth and function, cell shape and cell division are all factors to consider. MAP kinase/ERK kinase1 inhibitors, on the other hand, decrease the induction effects of IL-4, showing that the MAP kinase pathway is implicated in the genesis and development of pterygium (Kuo et al;2010).

Within the pterygium groups, genes involved in angiogenesis and cell migration are expressed differently. In pterygium samples, MMP-2, MMP-9, MMP-10, and their activator LCN2 are all highly expressed, whereas TIMP1 (TIMP metallopeptidase inhibitor 1) gene expression is reduced. (Tung et al;2010).

Furthermore, the gene for angiogenesis is expressed substantially greater in the pterygium than in normal ocular tissues (Detorakis et al;2010).

Although the treatment findings do not seem to be definitive, anti-angiogenic/anti-vascular endothelial growth factor treatment has been designed to cause Regression of blood vessels and hence postpone pterygium progression.6 (Bahar et al,2008).

Table 2.1: Cárdenas-Cantú et al; 2016 The function of overexpressed inflammatory mediators in the pathophysiology of pterygium

Mediator of inflammation	Potential pathogenic role
IL-1	Other mediators and extracellular matrix modulators are upregulated.
IL-6	Angiogenesis, cell differentiation, tissue invasion, and inflammation are all aided by this substance.
IL-8	Angiogenesis, cell differentiation, tissue invasion, and inflammation are all aided by this compound.
TNFa	Angiogenesis, cell differentiation, tissue invasion, and additional inflammation are aided by this substance.
COX2	Further inflammatory cascades
Phospholipase D	Further inflammation and cellular differentiation
Cystatin C	Regulation of extracellular matrix modulators

2.4. ARPCIB

The ARPC1B gene is a Protein Coding gene that codes for Actin Related Protein 2/3 Complex Subunit 1B. human Arp2/3 protein has seven subunits, and this gene codes for one of them. The SOP2 family of subunits includes sensory rhodopsin-2protein. (RefSeq. 2011).

The similarity of these 2 proteins implies that they may both play a role as the p41 component of the human Arp2/3 complex, which have been linked to cell actin polymerization regulation. It's possible that the p41 subunit has a role in constructing and maintaining the Arp2/3 complex's structure. Various variations of the p41 subunit may match the complex's activities to several kinds of cells. This protein also has s role in centrosomal homeostasis by acting as an Aurora activator and substrate. Diseases linked

to ARPC1B consisting of Platelet Abnormalities with Eosinophilia, Immune-Mediated Inflammatory Disease, and Combined T Cell and B cell Immunodeficiency (RefSeq, 2011).

Patients with mutations in the ARPC1B component of Arp2/3 have lack of immunity and immunological dysregulation signs and symptoms, such as viral infections that reoccur and a down CD8+ lymphocyte count. ARPC1B is necessary for lamellipodia generation, cell movement, and actin remodeling throughout the immune synapse infections, as shown by loss of Actin Related Protein 2/3 Complex Subunit 1B. resulting to loss of CTL cytotoxicity, with the deficiency originating at two separate levels (RefSeq, 2011).

2.4.1. ARPC1B gene and structure

Actin Related Protein 2/3 Complex Subunit is the name of the gene ARPC1B. this gene is localized on the 7th chromosome (7q22.1) and consists of 14 exons, and it has 27127 bp (base pair).

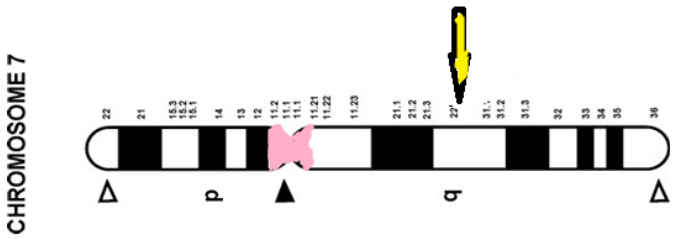

Figure 2.6: ARPC1B gene localization on the 7th chromosome (7q22.1).

The Arp2/3 complex is made up of seven subunits: Arp2, Arp3, Arc-p16, Arc-p20, Arc-p21, Arc-p34, and Arc-p41. (Tyler J et al.,2016). Arc-p41, also known as ARPC1B, is one of these subunits that is thought to have a regulatory function in the complex's formation and maintenance. As indicated by the broad immunological abnormalities identified when this control is disrupted, the exact control of actin

cytoskeleton dynamics is crucial to just about each stage of the immune system's reaction (Swaney & Li,2016).

As a result, it's not unexpected that the molecules that control this crucial activity are connected to immunodeficiency's pathogenesis. A different mutation in this gene was lately discovered in a patient with platelet, neutrophil abnormalities (Kuijpers et al;2017).

ARP2, ARP3, ARPC2, ARPC3, and ARPC4, as well as one molecule each of the ARPC1A and ARPC1B, and ARPC5A and ARPC5B isoform pairs, make up the mammalian Arp2/3 complex. On the human 7th chromosome, ARPC1A and ARPC1B are found together (Laurila et al.,2009). The isoforms they express share 68 percent of their both the amino acid sequence and feature 6 WD40 domain repeats expected to shape a b-propeller fold (UniProt, 2015). (Marko,2017).

ARPC1A has been connected to Oral cancer (Laurila et al.,2009) and has been identified in pancreatic cancer as a regulator of cell migration and invasion (ductal carcinoma) (Laurila et al2009). (Auzair et al;2016).

ARPC1B gene has been discovered as a centrosomal protein taken part in in mitosis, independent of its activity in Arp2/3 (Molli et al.,2010; Julia,2017).

Arp2/3 deficiency causes embryonic death, whereas its suppression inside cells prevents lamellipodia production and migration (Jie, 2017). (Wu et al,2012). There has yet to be documented an inherited human ARPC1B deficiency.

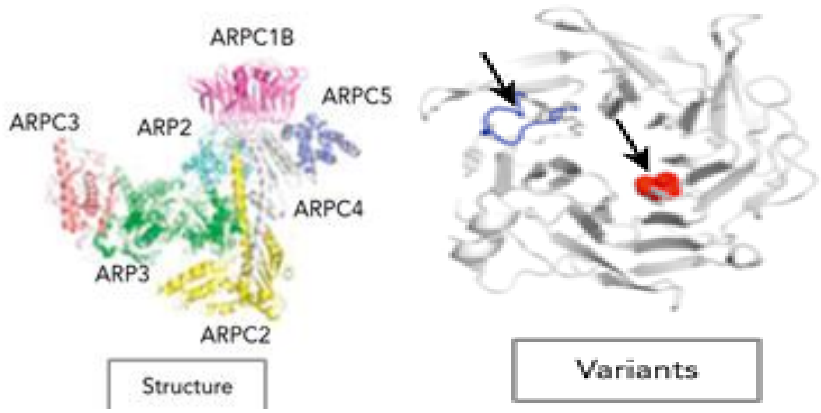

Figure 2.7: Gene structure and Variants

2.4.2. The relationship between ARP 2/3 complex and WASP gene

WASP is known as The Wiskott–Aldrich syndrome protein controls actin polymerization by activating the Arp2/3 complex, which allows new actin filaments to be formed and cross-linked from end to side branch. (Pizarro-Cerda,2017).

WASP, which causes Wiskott–Aldrich syndrome was the first actin-related protein to be identified and researched as a cause primary of immunodeficiency.(Somech et al;2017).

Microthrombocytopenia, eczema, coupled T and B cell immunodeficiency, and a higher prevalence of autoimmune symptoms and cancers characterize WAS, an X-linked immunodeficiency illness with a a unique clinical appearance (Atar et al;2017).

Mutations in the Arp2/3 complex or its activators have yet to be recognized as a cause of immunodeficiency syndromes with WAS-like disorders, owing to the fact that many of these genes are required for healthy development and their loss of function would result in premature death. (Moulding et al;2013).

A different mutation in this gene was lately discovered in a patient with platelet and neutrophil abnormalities (Kuijpers et al;2017).

WASP is one of several nucleation-promoting factors that induce F-actin branching through the actin-related protein 2/3 complex (Arp2/3), which is involved in the process. It is required for cell migration, in addition to cytokinesis (Rotty et al;2013).

Activated WASP binds Arp2/3 in a 2:1 stoichiometry by engaging with the ARP2, ARP3, and ARPC1 subunits, inducing conformational changes that improve actin monomer binding and daughter filament production (Boczkowska et al;2014).

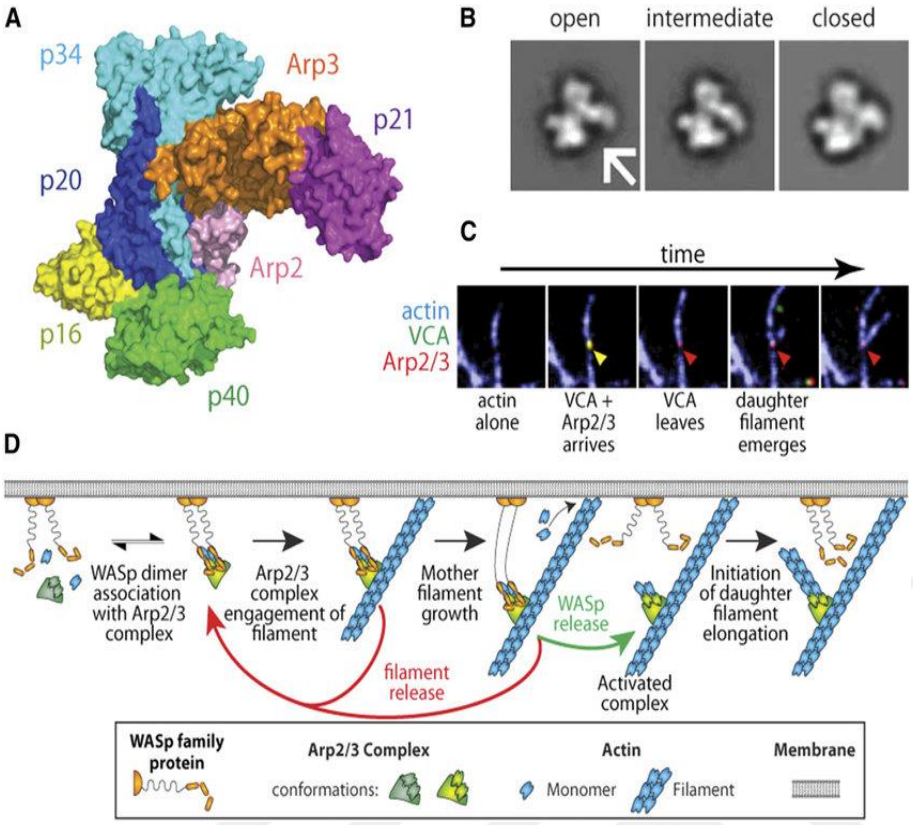

Figure 2.8: WASP stimulates the production of actin branches mediated by the Arp2/3 complex.

3- MATERIALS AND METHODS

3.1. EQUIPMENT

3.1.1. Working Groups

The research was carried out at Tokat Gaziosmanpaşa University's Faculty of Medicine's Eye Diseases Department. There were 27 cases diagnosed with pterygium (18 men, 9 women). They were taken during the procedure in the construction of working groups, with pterygium tissues as the patient group and healthy conjunctival tissues belonging to the same eye of the same patient as the control group. Tokat Gaziosmanpaşa University Faculty of Medicine's Clinical Research Ethics Committee With the project at the Tokat Gaziosmanpaşa University Scientific Research Projects Directorate meeting dated By19-KAEK-024 Project number 2019/110 is being backed up.

3.1.2. Storing Tissues

Tissue taken during surgery with the participants' approval and knowledge The diagnosis of pterygium was confirmed after histological inspection of several of the samples.

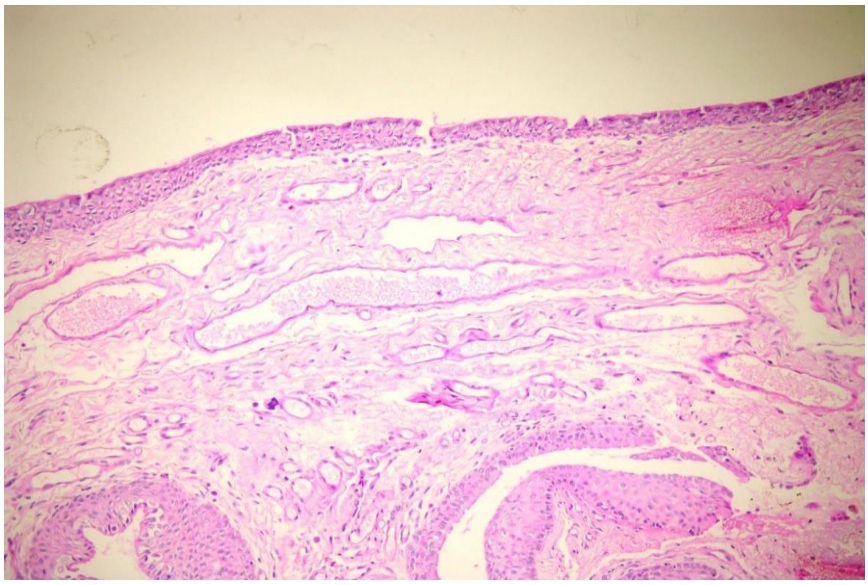

Figure 3.1: Histopathological Image of Pterygium Tissue (HE, X100). On the surface, sections of conjunctival epithelium of dilated vascular structures of different diameters are observed in the subepithelial distances with edema at the bottom.

3.1.3. Devices Used in the Study

Refrigerator (Arcelik, 570 465 MB, Turkey)

Shaker (Ika, Germany)

-20 ° C freezer (Arcelik, 2052DY, Turkey)

-80 ° C Deep Freezer (Nuaire, NU-9483E, USA)

Distilled Water Device (Elga-option Q7, UK)

Oven (Memmert, Germany)

Power Supply (Biorad, 1645070, USA)

Precision Balance (Kern ABT, WB0750631, Germany)

Homogenizer (Next Advance Storme 24, BBY24M-CE, USA)

Magnetic Stirrer (Velp Scientifica, F20520162, Italy)

Microwave (Arcelik, MD554, Turkey)

Autoclave (HMC, HV25, Germany)

Automatic pipettes (Gilson, France)

pH Meter (Hanna Instruments, HI2020W, USA)

Plate (Applied Biosystems, 4346907, England)

Plate adhesive (Applied Biosystems, 201405092, UK)

Qubit 2.0 Fluormeter (Invitrogen by life technologies, Australia)

Real-Time PCR (Appiled Biosystems, UK)

Centrifuge (Hettich, D78532, Germany)

Refrigerated centrifuge (Hettich, Germany)

Vortex (Velp Scientifica, F20220176, Italy).

3.1.4. Chemical Materials Used, Kits and Kit Contents

cDNA synthesis kit (GeneAll, Hyperscript, First strand synthesis kit Catalog # 601-005, Korea)

Reverse Transcriptase Enzyme

10X RTase Reaction Solution

0.1 M DTT

10 mM dNTP mix

RNase Blocker

Oligo (dT) 20

Random hexamer (primary)

Nuclease-free water

Ethanol (Sigma-Aldrich Catalog No: E7023, USA)

Qubit ssDNA Assay Kit (Invitrogen Catalog No: Q10212, USA)

Qubit RNA HS-Assay Kit (Invitrogen Catalog No: Q32852, USA)

RNA isolation kit (Thermo, Catalog No: 12183018A, USA)

Lysis Solution

Washing Solution 1

Washing Solution 2

RNase-free Water

RNaseZap (Thermo Catalog No: AM9780, USA)

Running Solution (ThermoFisher, NP0002, USA)

3.2. METHOD

3.2.1. Protocol for RNA isolation

1-Homogenize pterygium tissue samples in 0.75 ml RiboEx^{TM} LS per 50 ~ 100 mg of tissue using homogenizer.

2-Lyse 0.25 ml the sample in 0.75 ml RiboEx^{TM} LS by pipetting or vortexing.

3-Incubate the homogenate for 5 minutes at room temperature.

4Centrifuge at 12,000 x g for 10 minutes at 4°C and transfer the supernatant to a fresh tube.

5.Add 0.2 ml of chloroform per 0.75 ml of RiboExTM LS. Shake vigorously for 15 seconds, store for 2 minutes at room temperature.

6.Centrifuge at 12,000 x g for 15 minutes at 4°C, then transfer the aqueous phase to a fresh tube.

7.Incubate samples for 10 minutes at room temperature.

8.Centrifuge at 12,000 x g for 10 minutes at 4°C, and discard the supernatant.

9.Add 1ml of 75% ethanol to wash the RNA pellet. The RNA precipitate can be stored in 75% ethanol at 4°C .

10.Centrifuge at 7,500 x g for 5 minutes at 4°C. Carefully discard the supernatant, ethanol, and air-dry the RNA pellet for 5 minutes.

11.Dissolve RNA in DEPC-treated water or in 0.5% SDS solution by incubating for 10 ~ 15 minutes at 56°C.

3.2.2. cDNA Synthesis

Protocol:

To obtain optimum performance with cDNA Synthesis Kit, make sure that RNA samples is not contain PCR inhibitor, reverse transcription inhibitor, RNase activity and genomic DNA. Mix the kit components in a micro tube in the recommended proportions below. Briefly centrifuge the tube to reduce the volume of the contents and remove any air bubbles Place the tube in the freezer until the reverse transcriptase process is complete.

Table 3.1: Reverse transcriptase reaction volume (20 µl)

For 20 µl Reverse Transcriptase Reaction	Volume
10X Reaction Buffer	2 µl
dNTP mix (2.5 mM each)	1 µl
Random hexamer (50 µM)	2 µl
Reverse Transcriptase (200 U/µl)	1 µl
RNase Inhibitor	0.5 µl
RNase free Water	3.5 µl
RNA Template	10 µl

Table 3.2: PCR program applied for cDNA synthesis

RT Steps	**Temp (°C)**	**Time**	**Cycle**
Step 1	25	10 min.	1
Step 2	37	120 min.	1
Step 3	85	5 min.	1
Step 4	4	∞	1

The obtained cDNA samples were frozen at -80 ° C until the Real-Time PCR step.

3.2.3. qRT-PCR step

Real time for expression analysis after cDNA extraction from isolated RNAs**.** At this stage, control and study for the target ARPC1B gene, Beta-actin was used . as the reaction mixtureA.B.T. ™ 2X qPZR SYBR-Green MasterMix (with ROX) (Cat no: Q03-02-01) used.

The reaction mixture was prepared as follows:

Table 3.3: PCR reaction components (20 µl) The reaction cycle was set up on the Applied Biosystems Real Time PCR instrument as follows

A.B.T.™ 2X qPCR SYBRGreen Master Mix (with ROX)	10 µl
1X ROX Dye (50X)	0.4 µl
Forward Primer	1 µl
Reverse Primer	1 µl
Template cDNA	3 µl
Rnase-free Water	4.6 µl

QRT-PCR program implemented

50 ° C 20 sec

95 ° C 10 min

95 ° C

15 sec ←

42 cycles

60 ° C 1 min Melt Curve: 95 ° C 30 sec, 60 ° C 30 sec

4. RESULTS

4.1. Results of Working Group

This research was conducted at the Tokat Gaziosmanpaşa University Faculty of Medicine Medical Biology and Genetics labs and included 27 individuals with pterygium illness.The study group consisted of 18 males and 9 females, age range 43-78 (mean 58 ± 8.43).

The Gender Distribution of Patients Involved in the Research is given in the figure 4.1 below:

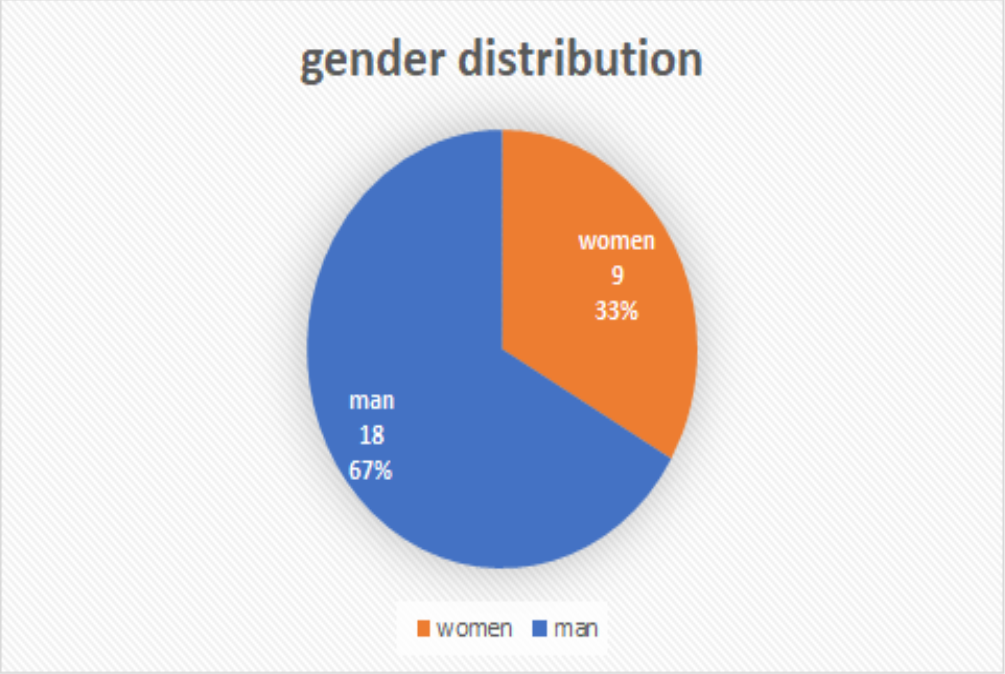

Figure 4.1: The Patients' Gender Representation

4.2. Quantitative Real-Time PCR (QRT-PCR) Analysis Results

4.2.1. QRT-PCR image and evaluation of the ARPC1B gene

SYBR Green based quantitative Real-Time PCR (Polymerase Chain Reaction) method was used to determine the expression level of ARPC1B mRNA expression. For ARPC1B and the gene preferred as a reference (Actin: ACTB), samples of cDNA (1/10: 1/100: 1/1000 and 1/10000) at different concentrations were prepared and serial dilution was made.

In the figures below, the amplification curve and melting peak of ACTB and ARPC1B genes observed as a result of qRT-PCR are given, respectively(Figure 4.2, Figure 4.3, Figure 4.4,Figure 4.5).

Figure 4.2: ARPC1B amplification plot

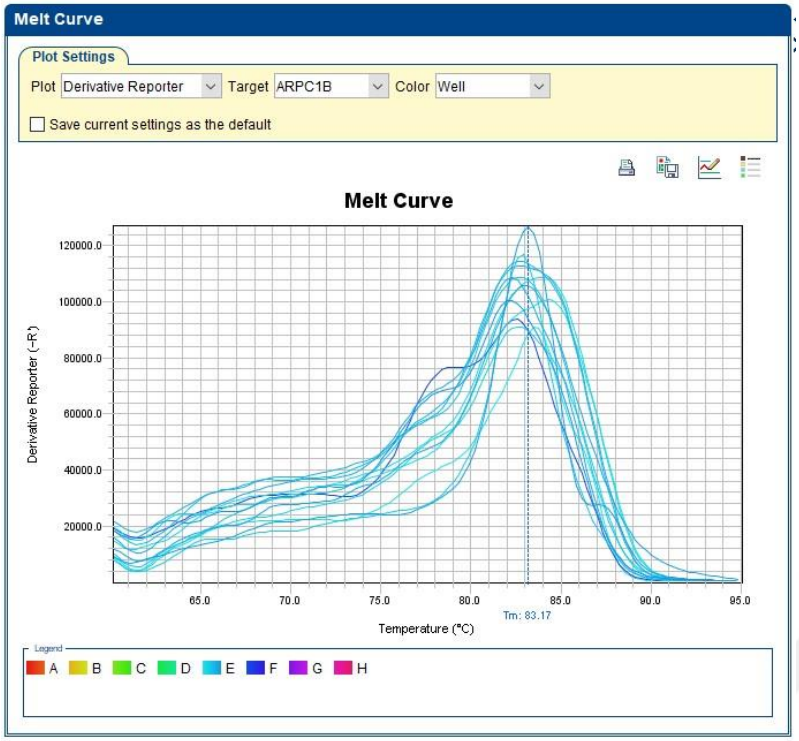

Figure 4.3: ARPC1B melt curve

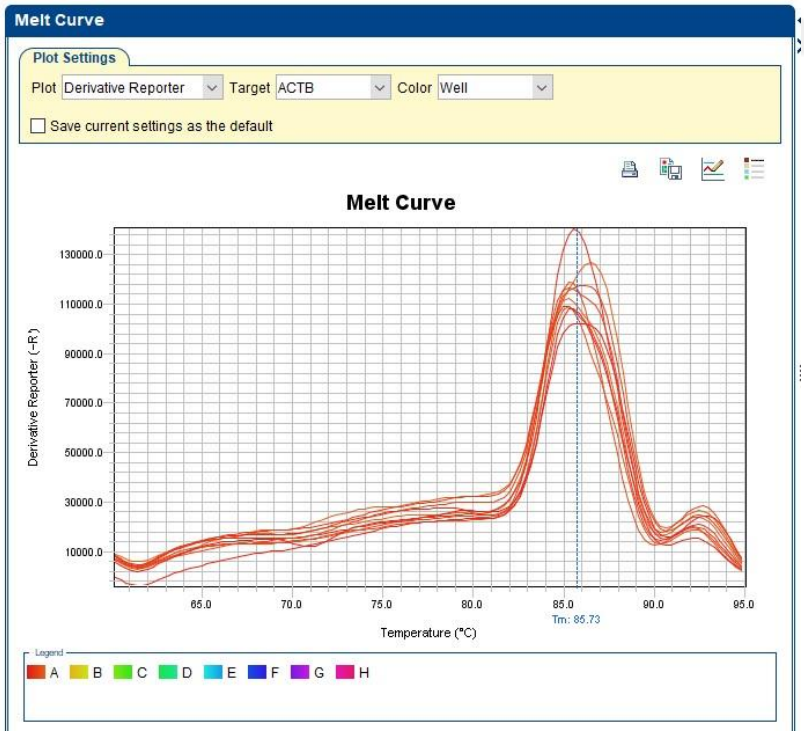

Figure 4.4:ACTB melt curve

Figure 4.5: ACTB amplification plot

4.3. Statistical analysis of qRT-PCR findings of the ARPC1B mRNA gene

QRT-PCR analysis was performed with step one plus software v2.3 for the expression of ARPC1B gene in pterygium and control conjunctiva tissues at the mRNA level. Normalized with ACTB, which is used as housekeeping gene, $2^{-\Delta\Delta Ct}$ formula was used to calculate the floor change. Statistical analysis was performed with the data we obtained. Analysis of the results was made according to the range 0.9 - 1.1. It was accepted that the expression level of the relevant gene decreased in the pterygium tissue compared to the normal conjunctival tissue in values less than 0.9, it did not change when compared with the normal conjunctival tissue in the range of 0.9-1.1, and there was an increase in the expression of the gene in values greater than 1.1 (Schmittgen and Livak., 2008). Statistical analysis of expression data was performed using SPSS 16.0 software. The significance levels of the data was made with Student test analysis If $p \leq 0.05$ was significant, if $p > 0.05$, it was evaluated that there were no difference .

4.3 1. T-Test

TABLE4.1: Statistical analysis of $2^{-\Delta\Delta Ct}$ values of ARPC1B and conjunctival tissues

Analysis results

Expression level of ARPC1B gene in pterygium compared to normal conjunctive tissue

Gene	Tissue	
	Pterygium tissue (N=27)	Normal Conjunctiva (N=27)
ARPC1B (AVG±SEM)	2,514±0,837	
p	0,082	

(2,514±0,837-Foldchange, p=0,082).

According to the findings of qRT-PCR, there was no discernible change. in ARPC1B gene levels of expression in pterygium and normal conjunctival tissues (p>0.005).

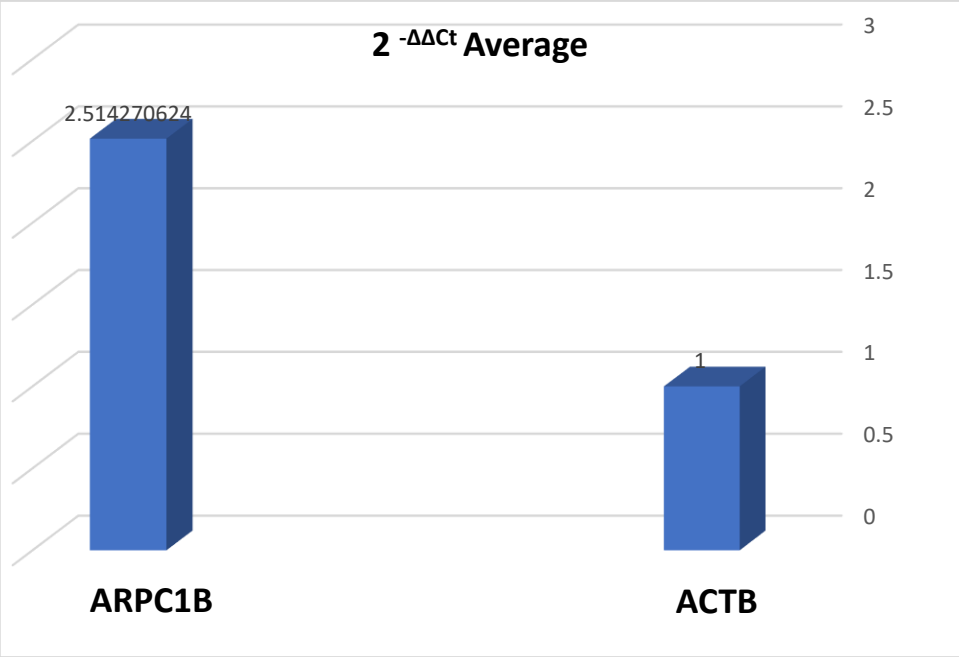

Figure 4.6: Average $2^{-\Delta\Delta Ct}$ values of ARPC1B and ACTB genes

5-DISCUSSION

Pterygium is a degenerative disease that manifests itself as a result of development of triangular tissue on the surface of the eye, conjunctival in the peripheral cornea Proliferation, inflammatory infiltrates, fibrosis, angiogenesis, and the extracellular matrix are all factors that affect cell proliferation. (Demurtas et al;2011).

Pterygium is normally asymptomatic, although it may induce dry eye symptoms including burning, itching, and lacrimation due to mixed humidity on the ocular surface. Advanced pterygium in the optical zone reduces visual acuity and necessitates surgical treatment (Mologen et al;2017).

Recent research suggests EMT (epithelial-mesenchymal transition) might have a function. in the etiology of pterygium, which might explain where pterygium fibroblasts come from (Jeanie,2008).

The pathogenesis of pterygium by p53 gene mutation has been studied extensively. It has been established that they are linked. As a result, excessive cell proliferation in pterygium is more akin to a tumor than to malfunction and a growth condition like neoplasia. (2015, Huang et al.). Pterygium causes vision problems by blocking the visual axis and causing considerable astigmatism (Helen et al;2019).

ARPC1B is required for the formation and maintenance of the ARP2/3 complex, it has a role in actin branching from a filament that already exists. They hypothesized that ARPC1B deficiency could cause cytoskeleton and functional defects in T cells, and they discovered biallelic mutations in ARPC1B in 6 unrelated patients with clinical features of combined immunodeficiency (CID), whose T lymphocytes were not studied but neutrophils and platelets were studied. (Dobbs K et al;2015). They speculated that ARPC1B loss in T cells might result in cytoskeleton and functional abnormalities.

Pancreatic cancer cell lines and primary pancreatic tumors account for 25% of all pancreatic cancer cell lines and tumors. ARPC1B was identified in a region of chromosome 7q22.1 that was amplified according to Laurila et al (2009) study. Amplification resulted in enhanced ARPC1B expression, according to RT-PCR.

ARPC1B silencing slowed However, there was no cell migration. impact on cell proliferation or invasion.

ARPC1B may have a role in platelet dysfunction, in which a large number of platelets causes hard tissue sclerosis in the eye, and we know that pterygium disease is the formation of triangular tissue on the cornea.

The goal of this research was to see how the ARPC1B gene affected pterygium illness.

Platelet Abnormalities with Eosinophilia, Immune-Mediated Inflammatory Disease, and Combined T Cell and B Cell Immunodeficiency are just a few of the conditions that may cause platelet abnormalities. diseases connected to the ARPC1B gene, and elevated ARPC1B has been associated to oral squamous cell carcinoma OSCC (Auzair et al;2016).

According to the findings of qRT-PCR, there was no discernible change. in ARPC1B gene levels of expression in pterygium and normal conjunctival tissues ($p>0.005$).

Several human malignancies have been linked to caveolin-1 and Actin-Related Protein 2/3 Complex, Subunit 1B

Based on their past study (Cheong et al;2009), they identified two candidate genes, Caveolin 1 and Actin-Related Protein 2/3 Complex, Subunit 1B that were found to be differentially expressed in oral squamous cell carcinoma samples. It has been suggested in the literature that these two genes, Caveolin 1 and Actin-Related Protein 2/3 Complex, Subunit 1B are highly involved in (Routray,2014).

A recent research found that over-expression of ARPC1B increases tumorigenicity in breast cancer via causing centrosome amplification (Molli et al;2009). ARPC1B has been Radiation-resistant intraocular choroidal melanoma cells were found to be overexpressed. in addition to breast cancer (Chia et al;2015).

The difference in expression of ARPC1B and Cav-1 between OSCC and normal oral epithelium in the present research suggested that these genes are involved in carcinogenesis. They also discovered that decreased ARPC1B expression was linked to

lymph node metastases and advanced tumor stages in OSCC patients, indicating that the ARPC1B gene may play a role in the aggressive development of OSCC.

Only a few researches have looked at the expression of ARPC1B and its clinical implications different malignancies, such as breast cancer (Molli et al;2009) and intraocular choroidal melanomas (Molli et al;2009) (Lukman et al;2015).

The recent investigation found a link between low ARPC1B protein expression and advanced stage of the illness and lymph node metastases. Methylation of the Arp2/3 complex's member p41- Arc may also cause downregulation of the complex, resulting in loss of expression and the formation of dysplastic morphology.

Furthermore, Zucchini et al. hypothesized that the downregulation of ARPC1B gene in osteosarcoma is one of the causative consequences that leads to metastasis inhibition by reducing dynamic actin disassembly, which is required for a tumor cell movement.

These findings point to ARPC1B's migratory activity in the modulation of focal adhesions and actin filaments, which aids tumor cell metastasis (Chorev et al;2014).

Although deletion of ARPC1B has been linked to a variety of malignancies, the mechanism by which this gene causes OSCC is unknown, and further downstream research is needed to determine its function in oral carcinogenesis.

Increased expression of ARPC1B in OSCC and its link to advanced stage and lymph node metastasis adds to the proof that it plays a role in the genesis and progression of OSCC, the pterygium disease, which is unclear but is a tumor-like tissue, and the molecular basis for pterygium growth, as well as supporting its neoplastic property.

Pterygium is a condition defined by increased basal epithelial cell proliferation, neovascularization, and invasion of the neighboring corneal epithelium; nonetheless, viral infections play an important role.

Pterygium is a frequent eye illness, particularly in the tropics; as a consequence, ophthalmologists operating in hot climates must keep up to speed on current ideas in the understanding of the nature of pterygium as well as current treatment choices in order to achieve better outcomes.

The start and maintenance of pterygium are dependent on hereditary susceptibility. Hereditary factors are more likely to influence the magnitude and seriousness of pterygiums.

Predisposition to pterygium incidence almost certainly follows the polygenic model's multifactorial method of inheritance. Two kinds of genes, one for inhibitory smad proteins and the other for smurf proteins, may be inactive, leading to the development of pterygiums. Pterygium development seems to be dependent on fibro genic growth factors, and pterygium angiogenesis seems to follow fibroblast proliferation, collagen synthesis, and collagen lysis. Pterygium is triggered by sunlight, or maybe reactive oxygen species. Inflammation and collagen damage, which are almost certainly caused by oxidative stress, seem to increase pterygium growth.

Nonetheless, there have been considerable breakthroughs in our knowledge of the nature of pterygium recently, and breakthroughs in therapy have not only continued to lower recurrence rates, but they may also allow alternate methods and treatments to be used instead of surgery.

Current treatments try to reduce the pterygium's recurrence rate after it has been surgically removed. Furthermore, advances in understanding the molecular basis of pterygium pathogenesis, in conjunction with treatments and surgical adjuvants, point to the development of effective pterygium treatments, as well as the prevention and eradication of recurrence following surgery.

The current research reveals that pterygium has an influence on ocular surface characteristics, including direct changes in meibomian gland pattern and tear film.

The results show that the ARPC1B gene has no influence on pterygium illness, and further research is required in the future to establish the effectiveness and see whether there is a link between the ARPC1B gene and pterygium.

More research on the gene ARPC1B should be done in the future, employing various studies with more patients to gain various findings and better understand the influence of the ARPC1B gene on pterygium.

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