Ocular Surface

- Cornea
- Limbus
- Conjunctivica
- Area 1.3cm²
- Nearly adult size at birth
- Anterior aspect: 11-12 mm (horiz.) 9-11 mm (vert.)
- Posterior aspect: ~11.7 mm (horiz. and vert.)
- Thickness: 0.5 mm (centre), 0.7-1 mm (periph.)
- Steepest in center, flatter in periphery
- Radius of curvature: 7.8 mm (ant.)
  6.2-6.8 mm (post)
- Refractive power: 43D
  (ant. Surf + 49D; post. Surf -6D)
- Refractive index: 1.376
- Water content 78%
FIGURE 9: (Top) Three-dimensional representation of a prolate cornea with hypothetical reflected photokera-
toscope rings (R₁ through R₅). The normal cornea is prolate, defined as an increasing radius of curvature from the center (r₁) to the periphery (r₅). (Bottom) Cross-sectional representation of the same prolate cornea. The radii of curvature (r₁ to r₅) are drawn relative to the reflected rings (R₁ to R₅). The prolate corneas’ radii of curvature are longer (and, therefore, greater in magnitude) toward the periphery (r₅) than toward the center (r₁).
Spherical aberration

- In total spherical object peripheral parallel rays of light refract more and focus in front of ideal image point.
- Effects - blurred vision

- Spherical aberration is minimized by aspheric (prolate) shapes of eye surfaces - due to peripheral flattening
Power: \( N2-N1 \) / \( R \)

**Radius of Curvature and Refractive Power**

- Air-tear = 7.7 mm = +43.6 D
- Tear-cornea = 7.7 mm = +5.3 D
- Cornea-aqueous = 6.9 mm = −5.8 D
- Total central power = 43.1 D

**Central thickness**

- 540 \( \mu \)m

**Peripheral thickness**

- 700 \( \mu \)m

**Central radius**

- Anterior 7.7 mm
- Posterior 6.5 mm

**Refractive Index**

- Air 1.000
- Tear 1.336
- Cornea 1.376
- Aqueous 1.336
Refractive Power calculation

\[ P = \left( N_2 - N_l \right)/R \]

- **P**: Power of corneal surface (Diopters)
- **Nl**: Refractive Index of 1st medium (air = 1.000)
- **N2**: Refractive Index of 2nd medium (tear film = 1.336)
- **R**: Radius of Curvature in metres (anterior surface)

\[ P = (1.336 - 1.00)/0.0077 = .336/.0077 = 43.6 \text{ D} \]

\[ D = 1/\text{focal length in meters} \]
Functions of the Cornea

• Refract light
  - 80% of the refracting power of the eye occurs in the cornea; 20% in the lens

• Protection
  - to be discussed
Histology of the cornea, showing the epithelium (1), epithelial basement membrane (2), Bowman’s layer* (3), stroma (4), Descemet’s membrane** (5), and endothelium (6). Normally, no blood vessels (avascular).

* ALL, anterior limiting lamina  
** PLL, posterior limiting lamina
Neural Innervation of The Cornea

Confocal Imaging in vivo
Fig. 1.2A Confocal biomicroscopy of the human cornea. 

A, Superficial layer of the corneal epithelium.
B, Basal cell layer of the corneal epithelium.
C, Subepithelial nerve plexus.
D, Shallow layer of the stroma, containing polygonal keratocytes and straight, branching nerve fibers.
E, Deep layer of the stroma, containing keratocytes and stout nonbranching nerve fibers.
F, Endothelium, comprising hexagonal endothelial cells of uniform size.
Neural Innervation of The Cornea

- Sensory: derived from ciliary nerves (end-branches of the ophthalmic division of the 5th cranial nerve—CN V or Trigeminal)
- Sympathetic: (adrenergic) from superior cervical ganglion
- Parasympathetic: (from ciliary ganglion) rats, cats but not shown for humans
- Penetrate anterior 2/3 cornea
- Plexi: subepithelial (stromal), basal epithelial and epithelial
- Lose myelin sheath (enhances transparency), retain Schwann cells until they enter epithelium
The trigeminal nerve is responsible for sensation in the face and motor functions such as biting and chewing; it is the largest of the cranial nerves. Its name derives from the fact that each of the two nerves has three major branches: the ophthalmic nerve (V1), the maxillary nerve (V2), and the mandibular nerve (V3). The ophthalmic and maxillary nerves are purely sensory, whereas the mandibular nerve supplies motor as well as sensory functions.
From: Muller et al., Exp Eye Res 76:521, 2003
Neural Innervation of The Cornea

Mouse genetically modified to express a green fluorescent protein in its sensory nerves

Stromal nerve enveloped by keratocyte

Only beaded fibers bifurcate and turn 90 degrees
Basal nerve fiber density plotted against increasing age (n=85 subjects, age range 18–87 years).

Neural Innervation of The Cornea

Sensory (trigeminal)

Neuropeptides:
- Substance P
- Calcitonin gene related peptide (CGRP)
- Pituitary adenylyl cyclase activating peptide (PACAP)
- Galanin
- Excitatory amino acids (glutamate, aspartate)?

Density highest in central cornea

Sense pressure (pain), temperature and pH

Protective: induce reflex tearing/blanking

Neurotrophic: support normal epithelial turnover promote wound healing
Neural Innervation of The Cornea

Sympathetic (superior cervical ganglion)

Neurochemicals: norepinephrine, serotonin, neuropeptide Y

Modulate ion transport in epithelium

Neurotrophic: support epithelial proliferation
Glucose
Most diffuses from aqueous humor
Uptake via glucose transporters (GLUTs)
Large stores of glycogen in epithelium
Metabolism:
  - normal oxygen via glycolysis/Krebs/OxPhos
  - low oxygen (overnight lid closure; some contact lenses) to lactate via pyruvate or hexose monophosphate shunt or sorbitol pathway

Oxygen
From atmosphere via tears

Other nutrients (amino acids etc..) via aqueous humor
ATP – adenosine triphosphate

energy from catabolism or photosynthesis

energy available for cellular work and for chemical synthesis
• **Glucose**
  Most diffuses from aqueous humor (5mM...similar to blood)
  Uptake via GLUT transporters
  Large stores of glycogen in epithelium
  Metabolism:
  - normal oxygen via glycolysis/Krebs/OxPhos
  - low oxygen (overnight lid closure; some contact lenses) to lactate via pyruvate
  or hexose monophosphate shunt
  or sorbitol pathway

• **Oxygen**
  From atmosphere via tears

• **Other nutrients** (amino acids etc..) via aqueous humor
Glycolysis
- occurs in the cytoplasm
- converts glucose to pyruvate

Net gain = 2 ATP and 2 NADH
Nutrition

- **Glucose**
  - Most diffuses from aqueous humor
  - Uptake via GLUT transporters
  - Large stores of glycogen in epithelium
  - Metabolism:
    - normal oxygen via glycolysis/Krebs/OxPhos
    - low oxygen (overnight lid closure; some contact lenses) to lactate via pyruvate or hexose monophosphate shunt or sorbitol pathway

- **Oxygen**
  - From atmosphere via tears

- **Other nutrients** (amino acids etc.) via aqueous humor
Mitochondrion

Matrix contains enzymes required for the Kreb’s cycle and the breakdown of fatty acids.

Inner membrane contains enzymes that carry out oxidative phosphorylation and ATP synthesis (electron transport chain).

Outer membrane contains enzymes for lipid metabolism.
Krebs cycle generates:
• 1 GTP (= 1 ATP)
• 3 NADH
• 1 FADH$_2$
Nutrition

- **Glucose**
  - Most diffuses from aqueous humor
  - Uptake via glucose transporters (GLUTs)
  - Large stores of glycogen in epithelium
  - Metabolism: - normal oxygen via glycolysis/Krebs/OxPhos
    - low oxygen (overnight lid closure; some contact lenses) to lactate via pyruvate or hexose monophosphate shunt or sorbitol pathway

- **Oxygen**
  - From atmosphere via tears

- **Other nutrients (amino acids etc..) via aqueous humor**
**Electron Transport Chain – oxidative phosphorylation**

- Electrons from NADH and FADH$_2$ transferred to carriers of the electron transport chain (cytochromes).
- Electron movement down the chain releases energy which drives H$^+$ ion movement into intermembrane space.
- Resulting pH and voltage gradient drives H$^+$ ions back into matrix and activates ATP synthase (oxidative phosphorylation).
ATP from Glucose Metabolism

Glycolysis:
- 2 ATP
- 2 NADH
- 2 Pyruvate

2 Pyruvate to 2 CoA:
- 2 NADH

Citric Acid Cycle:
- 2 GTP (= 2 ATP)
- 6 NADH
- 2 FADH$_2$

\[
\begin{align*}
4 \text{ ATP} & \quad + \quad 10 \text{ NADH} \\
& \quad + \quad 2 \text{ FADH}_2 \\
& = 38 \text{ ATP}
\end{align*}
\]
**Nutrition**

- **Glucose**
  - Most diffuses from aqueous humor
  - Uptake via GLUT transporters
  - Large stores of glycogen in epithelium
  - Metabolism:
    - normal oxygen via glycolysis/Krebs/OxPhos
    - low oxygen (overnight lid closure; some contact lenses) to lactate via pyruvate or hexose monophosphate shunt or sorbitol pathway

- **Oxygen**
  - From atmosphere via tears

- **Other nutrients (amino acids etc..) via aqueous humor**
**Anaerobic Metabolism**

- Occurs when oxygen lacking
- Occurs during lid closure, contact lens wear
- Glucose metabolised by glycolysis, generates 2 ATP and pyruvate which is converted to lactic acid by lactate dehydrogenase
Lactate diffuses out of cell or when oxygen returns converted back to pyruvate
**Glucose**
- Most diffuses from aqueous humor
- Large stores of glycogen in epithelium
- Metabolism:
  - normal oxygen via glycolysis/Krebs/OxPhos
  - low oxygen to lactate via pyruvate or hexose monophosphate shunt (pentose phosphate pathway) or sorbitol pathway

**Oxygen**
- From atmosphere via tears; more oxygen in tears than in aqueous humor

**Other** (amino acids etc..) diffuse from aqueous humor
Tear Film (Redfern)

Structures Involved in Tear Production:

- Lacrimal gland
- Meibomian glands
- Goblet cells (Conjunctiva)

Tear film:
- Lipid Layer (Meibomian glands)
- Aqueous Layer (Lacrimal glands)
- Mucin Layer (Epithelial cells)
Tear Film (Redfern)

- 7 um thick and 6.5 ul volume
- 3 layers:
  - superficial lipid layer (0.1 um)
  - aqueous layer (7 um)
  - mucin layer (0.02-0.05 um)
- 98% water
- Function:
  - Lubricant
  - Source of nutrients for corneal epithelium
  - Source of regulatory factors
Proposed model of tear film.

JP McCulley and W. Shine, 1997
Proposed model of tear film.

JP McCulley and W. Shine, 1997
Glycocalyx
Corneal Epithelium

- Precorneal tear film
- Squamous cells
- Wing cells
- Basal cells
- Basement membrane
- Bowman’s layer

(superficial)

(ALL)
Cell-Cell Interactions

- Cells are held tightly together and firmly down to the stroma, so form a barrier
- Layers are rich in certain junctions
- Superficial cells: tight junctions (zonula occludens)
- Wing cells: desmosomes (macula adherens)
- Basal cells: desmosomes
- Gap junctions (Wing and Basal) for cell communication
### Table 1.2 Characteristics of various types of corneal epithelial cells

| Superficial cells | Flat       | Microvilli Microplicae | 2–4 layers | 40–60 µm in diameter 4–6 µm thick at the nucleus 2 µm thick at the periphery | Entire surface | Desmosomes Tight junctional complexes (zonula occludens) | Sparse | + | + | ? |
| Wing cells | Winglike processes | 2–3 layers | 2–3 layers | 18–20 µm high 8–10 µm in diameter Flat at posterior surface | Apical surface | Desmosomes Gap junctions Hemidesmosomes (zonula adherens) | More than superficial cells Large numbers of glycogen granules Prominent mitochondria and Golgi apparatus | +++ | + | + |
| Basal cells | Columnar | Mono layer | 18–20 µm high 8–10 µm in diameter Flat at posterior surface | 2–3 layers | 14–20 µm in diameter Flat at posterior surface | Apical surface | Desmosomes Gap junctions Hemidesmosomes (zonula adherens) | More than superficial cells Large numbers of glycogen granules Prominent mitochondria and Golgi apparatus | +++ | + | + |
**Fig. 1.5** Intercellular junctions in the corneal epithelium. **A–D**, Transmission electron micrographs of the human corneal epithelium. Scale bar, 50 nm. **E–H**, Immunofluorescence micrographs of the rat corneal epithelium stained with antibodies to the indicated proteins. Scale bar, 50 μm. **I–L**, Schematic representation of the intercellular junctions in corneal epithelium. GJ, gap junction; TJ, tight junction; DS, desmosome; AJ, adherens junction; Cx43, connexin 43; Oc, occludin; Dsg 1+2, desmogleins 1 and 2; E-cad, E-cadherin; c-AMP, cyclic adenosine monophosphate; Cld, claudin; zo-1 and -2, zonula occludens-1 and -2; 7H6, 7H6 antigen; AF, actin filament; Dsc, desmocollin; DP I/II, desmoplakin I or II; PG, plakoglobin; KF, keratin filament; α- and β-ctn, α- and β-catenin; P120, P120 catenin.

Junctions affect intercellular space
Adjacent cell membranes

Ocludin

Intercellular space

Tight junctions strands

Interlocking junctional proteins

E/M

Zonula occludens

Fascia occludens

Macula occludens
Corneal Epithelium (Mouse)
Desmosome

membranes of adjacent cells

intermediate filaments

intracellular attachment plaque

desmocollin and desmoglein
Cell-Stroma Interactions

Blistering: autoimmune antibodies
Figure 2. (A) Illustration of an epidermal HD and its components seen by electron microscopy. Afib= anchoring fibril; Afil= anchoring filament; BM= basal plasma membrane; Col= dermal collagen fiber; IP= inner plaque; KF= keratin filaments; LD= lamina densa; LL= lamina lucida; SBDP= sub-basal dense plate. (B) Electron micrograph of mouse corneal epithelial HDs (arrows). Many of the features identified in panel A are evident. Bar= 200nm.
Epithelial cells

Basal lamina

Collagen fibrils

Scanning electron micrograph of a basal lamina in the cornea of a chick embryo
Corneal Epithelium
Microvilli

- Amorphous, densely staining region
- Plus ends of actin filaments
- Plasma membrane
- Lateral sidearms (myosin-I, calmodulin)
- Cross-links (villin, fimbrin)
Cytoskeleton
Cytoskeleton

Microtubules: ~24 nm OD
Intermediate filaments: ~10 nm OD
Microfilaments: ~7 nm OD
Microtubules

Figure 1

Microtubule Helical Structure

- Alpha-Tubulin
- Beta-Tubulin
- Heterodimers
- Protofilament

Dendrite
Dendritic Spine/Synaptic Receptor
Nucleus
Membrane
Axon

Microtubule

Microtubule Associated Protein

Dynein
Kinesin
cargo

- end
microtubule
+ end
Actin Filaments

(A) myosin-I

(B) myosin-II

(C) myosin-I

vesicle

plasma membrane

a-actinin
Actin filament
Vinculin
Talin

Plasma membrane
Integulin
Extracellular matrix
Actin Filaments

- Stress fiber
- Cell cortex
- Filopodium
- Contractile bundle
- Gel-like network
- Tight parallel bundle

100 nm
Actin Filaments
Intermediate Filaments

INTERMEDIATE FILAMENTS

25 nm

25 μm
## Intermediate Filaments

### Table 16–1 Major Types of Intermediate Filament Proteins in Vertebrate Cells

<table>
<thead>
<tr>
<th>Type of IF</th>
<th>Component Polypeptides (mass in daltons)</th>
<th>Cellular Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuclear lamins</td>
<td>lamins A, B, and C (65,000–75,000)</td>
<td>nuclear lamina of eucaryotic cells</td>
</tr>
<tr>
<td>Vimentinlike proteins</td>
<td>vimentin (54,000)</td>
<td>many cells of mesenchymal origin, often expressed transiently during development</td>
</tr>
<tr>
<td></td>
<td>desmin (53,000)</td>
<td>muscle</td>
</tr>
<tr>
<td></td>
<td>glial fibrillary acidic protein (50,000)</td>
<td>glial cells (astrocytes and Schwann cells)</td>
</tr>
<tr>
<td></td>
<td>peripherin (66,000)</td>
<td>neurons</td>
</tr>
<tr>
<td>Keratins</td>
<td>type I (acidic) (40,000–70,000)</td>
<td>epithelial cells and their derivatives (e.g., hair and nails)</td>
</tr>
<tr>
<td></td>
<td>type II (neutral/basic) (40,000–70,000)</td>
<td></td>
</tr>
<tr>
<td>Neuronal intermediate filaments</td>
<td>neurofilament proteins NF-L, NF-M, and NF-H (60,000–130,000)</td>
<td>neurons</td>
</tr>
</tbody>
</table>

K3, K12, K4, K13, K1, K10

Type I

Type II
Intermediate Filaments

- Structural
- Mechanical support for plasma membrane (desmosome) and nuclear membrane
- Don’t participate in motility

Figure 16-19 Molecular Biology of the Cell 5/e (© Garland Science 2008)
Corneal Epithelium – biochemistry

- High level of acetylcholine
- Enzymes for detoxifying drugs/chemicals
- Active transport system for Na\(^+\) and Cl\(^-\) regulated by sympathetic neurons
- Na\(^+\)-H\(^+\) exchanger and lactate-H\(^+\) cotransporter to help maintain pH
- Aldehyde dehydrogenase 3 and transketolase – Corneal crystallins that help maintain cellular transparency ????
Aquaporins 1, 3 and 5 are also in corneal epithelium for outward water movement (anterior direction)

**Figure 4-31** Model of ion transport, ion channels, and sympathetic neural control of chloride channels in the corneal epithelium. The Na⁺-K⁺ pump in the basolateral membrane maintains the Na⁺ gradient for Na⁺-Cl⁻ cotransport. Chloride diffuses down its chemical gradient through apical channels, which are opened by cyclic adenosine monophosphate (cAMP). AC, Adenylate cyclase; ATP, adenosine triphosphate; β, β-adrenergic receptor; NE, norepinephrine. (Based on models proposed in Candia OA: Invest Ophthalmol Vis Sci 31[suppl]:440, 1990; and Klyce SD: J Physiol 321:49, 1981.)
Corneal Epithelium - biochemistry

Tears: Sodium pumped
Stroma

Tears: Cl⁻ transported
Stroma

Transepithelial potential: 25 mV

0 mV

Figure 4-32 Model of ion transport in the corneal epithelium. The epithelium is shown as a single cell layer because the cell layers of the epithelium function as a single transporting epithelium. The Na⁺-K⁺ pump in the basolateral membrane maintains the Na⁺ gradient for Na⁺-K⁺-2Cl⁻ cotransport. Chloride diffuses down its chemical gradient through apical channels. Chloride channels are regulated by sympathetic nerves via a cyclic adenosine monophosphate (cAMP)-mediated pathway. The large potassium channel is regulated by cholinergic stimulation via a cyclic guanosine monophosphate (cGMP)-mediated pathway. This channel also opens in response to decreased extracellular osmolarity and decreased intracellular pH. Intracellular pH is regulated by lactate-H⁺ cotransport and Na⁺-H⁺ exchange. AC, Adenylate cyclase; Ach, acetylcholine; ATP, adenosine triphosphate; β, β-adrenergic receptor; G, heterotrimeric G protein; GC, guanylate cyclase; GTP, guanosine triphosphate; Lac, lactate; M, muscarinic receptor; NE, norepinephrine.
Corneal Epithelium – biochemistry

• High level of acetylcholine and related enzymes, function unknown
• Enzymes for detoxifying drugs/chemicals
• Active transport system for Na\(^+\) and Cl\(^-\) regulated by sympathetic neurons
• Na\(^+\)-H\(^+\) exchanger and lactate-H\(^+\) cotransporter to help maintain pH and eliminate lactate
• Aldehyde dehydrogenase 3 and transketolase – Corneal crystallins that help maintain cellular transparency ???? Cell cycle regulation
Epithelial Turnover

- Keeps the barrier in good condition, eliminates microbes
- Thoft & Friend X, Y, Z hypothesis
- Stem cells - limbus and central cornea (?)

![Diagram showing the processes of cell proliferation, movement, and loss in epithelial turnover.](attachment:image.png)

- $X = \text{proliferation of basal cells}$
- $Y = \text{centripetal movement of cells}$
- $Z = \text{cell loss from the surface}$

$X + Y = Z$
Epithelial Turnover
Epithelial Turnover

- High capacity for self-renewal, last life time of organism
- Long cell cycle time
- Undergo asymmetric cell division

![Diagram showing stem cell dividing into new stem cell and transient amplifying cell]
Evidence that limbal basal cells are stem cells

- Higher proliferative capacity than central corneal cells
- Long cell cycle time
- If absent cornea resurfaced by conjunctival cells
- Do not express K3/K12
- Have different expression of variety of proteins
- Exist in location that could create microenvironment suitable for maintaining “stemness”
Limbal Area

Palisades of Vogt
- RP = rete pegs
- IP = interpalisades (dermal papillae)

rete = an elaborate network of blood vessels or nerve cells
Fig. 1. Concept of limbal location of corneal stem cells and transient amplifying cells. Stem cells (white) are exclusively located in the basal limbal epithelium at the bottom of the epithelial papillae forming the palisades of Vogt. Transient amplifying cells occur in the basal epithelia of limbus and peripheral cornea. Post-mitotic and terminally differentiated cells make up the suprabasal and superficial layers.
Figure 3 Asymmetric cell division of CESCs in the niche

eTAC = early transiently amplified cell
Epithelial steady-state migration patterns

5-7 day turnover cycle
LETTERS

Oligopotent stem cells are distributed throughout the mammalian ocular surface

François Majo, Ariane Rochat, Michael Nicolas, Georges Abou Jaouédé & Yann Barrandon
Protection Against Infection

- Barrier resists penetration/attachment
- Turnover eliminates infected cells in outer layers
- APCs cells detect pathogens and activate immune response
- Secretion of cationic antimicrobial peptides
Antigen Presenting Cells

FIGURE 1 A-L: IF and IVCM images of dendritic cells in human corneas: Keratoconus (A-D): APCs with bright bodies and short dendrites; (A) IF of epithelial HLA-DR+ dendritic cells, (B) IF of epithelial Langerhans cells (Langerin+), (C) IF of stromal dendritic cells (DC-SIGN+), (D) IVCM of APCs in the basal epithelial layer; Status postherpes-keratitis (E-H): APCs with longer interdigitating dendrites; (E) IF of epithelial HLA-DR+ dendritic cells, (F) IF of epithelial Langerhans cells (Langerin+), (G) IF of stromal dendritic cells (DC-SIGN+), (H) IVCM of APCs in the basal epithelial layer; Tx failure (I-L): APCs with longer interdigitating dendrites; (I) IF of epithelial HLA-DR+ dendritic cells, (J) IF of epithelial Langerhans cells (Langerin+), (K) IF of stromal dendritic cells (DC-SIGN+), (L) IVCM of APCs in the basal epithelial layer; (IF magnification 400 ×, IVCM magnification 200 ×).
Fig. 5. DC phenotype in normal and inflamed corneas. A conceptual model for BM-derived cells in the normal versus inflamed cornea shows MHC class II B7 mature CD11c DC in the stromal periphery and Ia– B7– immature or precursor DC in the corneal center. Similarly, the epithelium contains MHC class II but B7– LC in the periphery and MHC class II–B7– LC in the epithelial center. In addition, the posterior stroma contains a population of macrophages. The inflamed cornea becomes endowed with significantly more mature DC and macrophages in the center.
Cationic Antimicrobial Peptides

12-50 aa peptides
+ve charge due to excess of arg, lys, his
Produced by most living organisms
Effective against Gram +ve/-ve, fungi and some Viruses
Have effects on mammalian cell function
Cationic Antimicrobial Peptides - mode of action

- Effective against Gram +ve/-ve bacteria, fungi and some enveloped viruses
- Act by forming pores in microbial cell membranes that disturbs metabolism and may lead to lysis, or can block virions attaching to target cells
CAPs produced by corneal epithelial cells

β-Defensins
  hBD-1
  hBD-2 (during infection/inflammation)
  hBD-3

Cathelicidins
  LL-37

Others
  LEAP
  Thymosin-β4
Other Effects of CAPs
Corneal Epithelium - wound healing

**Lag phase**
- Increased metabolic activity
- Neutrophils arrive to clear debris
- Fibronectin from tear film deposited on wound surface
- Cells flatten
- Hemidesmosomes disassemble

**Healing Phase**
- Migration
- Proliferation
- Adhesion
Corneal Epithelium - wound healing
Epithelial wound healing

- Injury
- Few Hours
- 24 Hours
- 48 Hours
- 4-5 Days
Inflammation within the first 24 hours after epithelial abrasion

IL-22R1

STAT3

IL-17R

IL-22R

CCR6

IL-23R

CXCR2

NK1R

IL-17

IL-22

IL-23

IL-23R

IL-17

IL-22

IL-7R

NK1R

VEGFR1

IL-23R

VEGF

IL-23

CXCL10

IL-17

CCL20

IL-23

CXCL10

Stroma

Keratocytes

Limbal vessels

Sub-basal nerves

Substance P

NK cell

Dendritic cell

Macrophage

γδ T cell

Neutrophil

Platelet

Macrophage

NKp46+, NK1.1+
CD3 -, CD11a++
IL-22 -, CD117 -
IL7R -, NKG2D+
CXCR3+

CD11c+

IL-23+

F4/80+

CD115+

IL-23+ Ly6C+

CD11b+CD11c+

CD80+

GL3+

CCR6+

IL-17+

IL-22+, IL-7R+

CD3+, NK1.1-

Ly6G+

CD11b+

VEGF+

CD41+

CD51+

CXCL4+

CD301+

CD115+

CD206+

CD163+

F4/80+
Corneal Epithelium - functions

Interaction with the tear film provides a smooth surface for refraction which also resists bacterial attachment.

Cell junctions contribute to the formation of a barrier that prevents entry of fluid and noxious substances and resists abrasion.

Cells secrete antimicrobial peptides that destroy or limit the growth of micro-organisms, APCs detect pathogens.

Turnover ensures barrier is maintained in good condition and eliminates micro-organisms.

Rapid epithelial wound healing response ensures quick restoration of barrier and smooth surface for refraction.