Corneal Anatomy and Physiology

Subjects: Ophthalmology

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The cornea, known as the window of the eye, is optically transparent, including a special structure that is avascular anatomically. This dome-shaped and specialized tissue is located in the anterior part of the eye. Two major roles of the cornea are protecting the eye from harsh environments, and transmitting over 80% of light to inner portions.

corneal tissue engineering epithelium stroma

1. Introduction

The cornea, which is located in the anterior part of the eye, is a transparent layer and acts as the window of the eye [1][2][3]. The corneal structure contains three transparent layers, and two membranes [2]. The corneal structure transfers light into the eye's environment and protects the eye's structure from mechanical or chemical environmental injuries, UV light, and infection [4]. Corneal dysfunction causes corneal visual loss [5].

Corneal surgery and corneal transplantation are well-known therapies for corneal blindness [5]. According to the World Health Organization (WHO), about 10 million patients globally need healthy corneal donation [1]. Additionally, over 40,000 corneal transplantations are carried out in the United States annually [6]. However, corneal transplantation displayed several drawbacks including shortness of high-quality donor corneas, expensive surgery, and rejected tissue due to the immune system and weakness for long-term transplantation [7]. In addition, because aging diminishes the function of endothelial cells, the quality of the transplanted cornea is of utmost importance [8]. Furthermore, the tissue becomes ineligible for corneal transplantation by therapies that alter the corneal structure to improve vision, such as LASIK [9]. Scientists are utilizing stem cells and tissue-engineering techniques to generate bioengineered cornea, or even individual corneal layers, to address the shortage of eligible corneas for donation [10][11][12].

Tissue engineering utilizes cells, bioactive macromolecules, and scaffolds, or a blend of the mentioned factors [13][14][15][16][17]. Human corneal cell keratoplasty (HCCK) was recently chosen as an advanced corneal surgery technique. The HCCK technique includes transparent carriers to improve human corneal cell behavior [18][19][20]. These lamellar keratoplasties and tissue-engineered full-thickness are recognized as successful transplantations [5]. Although donor corneas are used in these approaches, they still possess some challenges such as allograft tissue availability and rejection [21]. Results have shown that the proliferative ability of cultured human corneal cells can be preserved; thus, cornea tissue engineering (CTE) is recognized as a suitable approach for reconstructing corneal damage [22]. A recent study revealed that human corneal cells (HCCs) have adequate efficacy for cell

propagation, but they might show low biocompatibility, weak light transmittance, and poor mechanical properties [23][24][25]. There are several methods of producing tissue-engineered scaffolds that completely resemble corneal structures [9][26][27][28][29]. Among them, 3D bioprinting technology is one of the potential approaches for producing artificial target tissue scaffolds. For example, the advantage of choosing this method in scaffold construction is the induction of the natural process during embryogenetic tissue formation and imitation [30][31][32]. Overall, 3D printing is attractive due to its high spatial resolution, and the simultaneous processing of cells and materials [33]. The conventional 3D printer consists of a classic inkjet, nozzles, and printer heads with material loaded into the cartridges as bioinks [34][35][36][37][38][39].

2. Corneal Anatomy and Physiology

The cornea, known as the window of the eye, is optically transparent, including a special structure that is avascular anatomically. This dome-shaped and specialized tissue is located in the anterior part of the eye. Two major roles of the cornea are protecting the eye from harsh environments, and transmitting over 80% of light to inner portions [23]. The cornea is composed of three arranged and transparent layers, and two membranes: The cornea includes the outermost layer of epithelium, stroma, and the innermost layer of endothelium. Additionally, the epithelium and stroma are separated by Bowman's membrane. However, the stroma and endothelium are separated by Descemet's membrane [22]. Furthermore, the cornea acts as the last superficial barrier of the eye, providing safety from external potential dangers, and infections [40]. Moreover, to maintain and protect the integrity of the eye surface, corneal nerves play a vital role [23]. Consequently, corneal regeneration is obtained by nerve density, and corneal sensation factors after transplantation [4].

In addition, the aqueous humor is located at the eye's surface, and the function of the cornea depends on its malleability [41]. Moreover, it should be noted that the tear film is placed in the outermost portion of the eye, and acts as a reservoir for antibacterial and growth factors [9]. Additionally, one of the most critical roles of tear film in maintaining homeostasis, proliferation, and repair is covering the corneal surface. The anatomical importance of the cornea, which includes five transparent and arranged layers, corresponds to a wide-angle lens [13].

2.1. Corneal Epithelium

The epithelium is the outermost layer of the corneal tissue, and acts critically in the refraction of light into the eye [42][43][44]. The epithelium is a highly innervated tissue with nerve endings terminating at corneal epithelial layers [45]. The epithelium is a multilayered tissue and has five cell layers which occupy 10% of the corneal structure, and is about 50 µm thick [22]. The epithelium, a biological barrier, is responsible for the transfer of all soluble constituents and water out or into the stroma to maintain proper corneal light transparency, providing a smooth layer [23]. There are three cell types in the epithelial layer of the cornea. These cell types consist of 3–4 layers of flattened squamous cells, 1–3 layers of wing cells, and a single layer of columnar basal cells. It should be noted that these cells are held together by tight junctions [1]. These cell types are regenerated every 7–10 days continuously by the limbus stem cells (LSCs) [46].

There are some challenges in the regeneration of the epithelial layer by tissue engineering approaches, such as mimicking its arranged complexity, maintaining integrity as a sufficient barrier, and replacing epithelial cells continually [47][48][49]. In general, the epithelial layer, as the outermost layer, can keep the eye safe from mechanical damage, infection, and injuries [4]. In addition, it has a role in protecting the retina from UV damage [4].

2.2. Corneal Stroma

The stroma occupies 90% of the corneal tissue and 5% of corneal keratocyte cells (CKCs), and is an acellular layer but also a dense connective layer derived from neural crest cells [40]. The stroma comprises over 200 noncellular collagenous lamellae that are fully uniform, small, and aligned collagen fibers [7]. When injuries occur, flattened fibroblasts are activated. These lie quiescently, typically to produce collagen, then stabilize collagenous lamellae, and secrete the stromal components [2]. There are two important properties of a healthy stroma layer: optical transparency, and suitable mechanical strength [12][13][14]. Optical transparency is needed for biophysical properties, and suitable mechanical strength can be decreased when this organized structure is disturbed. Light transmittance can be reduced as a result of stromal damage and disruption. The stroma expresses two major challenges for the tissue engineer: equal mechanical stability, and high optical transparency [50].

2.3. Corneal Endothelium

Although the endothelium is the thinnest layer of the corneal tissue, it is important for maintaining function, and the ability to maintain corneal reproduction [1]. It is necessary to maintain dehydration by keeping optimal optical clarity [51]. Originally, the human endothelial cells (HECs) consist of about 5000 cells/mm^2, while the number of HECs shows loss with increasing age. In general, the major challenge for tissue-engineered transplantation is the HECs cell number of out 2500 cells/mm^2 [52]. The endothelium functions as a leaking pump of the corneal structure by leaking from the stroma layer in the presence of excessive stromal hydration (above 80%) [53]. The pumping-leak function process contains Na^+ and K^+-ATPase pumps that occupy the basolateral membrane. The main function of pumping-leak is to maintain stromal relative dehydration through transporting ions and water from the stroma to the tear film and aqueous humor [54][55][56]. The main characterization challenge is the efficiency measurement of the transplanted HECs [57]. There are some selective glucose transporters in this layer, permitting nutrition transformation from the aqueous humor to feed the epithelial and CKCs. Therefore, the main function of the endothelial layer is optical transparency with regulated hydrophilic proteoglycan and collagen interfibrillar spacing. In addition, endothelial distortion might lead to a loss in pump function [58].

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