

# Ocular surface regeneration with autologous biomaterials

## Abstract

**Purpose:** To report a mini review on novel biomaterials applied for ocular surface regeneration.

**Methods:** A systematic review of the literature.

**Results:** Human-derived amniotic membrane is the most preferred biomaterial to regenerate ocular surface because of its ease of access and low immunogenicity. Whereas, biological instability, lack of optimized preparation protocols, and risk of transmission of infection are still major issues that make its use controversial. Human blood-derived biomaterials have gained popularity to reconstruct and regenerate the ocular surface with a really basic principle and even low cost. Platelet-rich plasma (PRP) and platelet-rich-fibrin (PRF) are the two types of platelet enriched biomaterials that have been using in various clinical fields to improve wound healing via their excellent chemotactic and physical properties. Autologous biomaterials obtained from blood can be used in order to regenerate ocular surface.

**Conclusion:** This review explores critical needs in ocular surface problems where conventional therapies are not well suited and the current demand to overcome corneal blindness.

**Keywords:** ocular surface regeneration, human-derived amniotic membrane, autologous biomaterials, human blood-derived biomaterials, platelet-rich fibrin

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## Introduction

The “Ocular Surface System” includes the specialized epithelium of the cornea and conjunctiva, main and accessory lacrimal glands, meibomian glands, and eyelashes which are in an excellent relationship to maintenance of smooth and wet characters of the anterior window of the eye ball. Since the primary function of the system components is to provide and protect the transparency of the cornea, the corneal epithelium may attributable the chief element in the system.<sup>1</sup> Because of the continuity of the epithelial barrier of the ocular surface with no breaks, a physician should consider to regenerate the whole surface of the eye with a unique and broad-spectrum treatment strategy. Various ocular and systemic diseases such as dry eye syndrome, blepharitis associated with meibomian gland dysfunction, ocular allergies, surface scarring from topical treatments, chemical injuries, thermal burns, and immunological disorders (e.g. Stevens Johnson syndrome and mucous membrane pemphigoid) can severely disturb the ocular surface integrity that may result in blurry vision, redness, pain, and even blindness and decrease in the quality of life.<sup>2-4</sup> After definite diagnosis, care and management strategies generally demand highly specialized expertise. Although most of the diseases of the ocular surface can be treated with medical strategies, some advanced grade disorders can only be improved with surgical treatments that required some supportive surgical equipments and graft materials.

## Discussion

Successful ocular surface reconstruction includes to restore neuroanatomic integration of the surface epithelium and stem cell

stromal niche at the limbal region. Therefore, there are two main steps to achieve the best results for ocular surface regeneration. Firstly, urgent surface reconstruction with various biomaterials obtained from different sources, and secondly to proceed the grafted surface integrity with the support of stem cell therapies.<sup>5,6</sup> There are several natural biomaterials applied as a surgical graft material such as human-derived amniotic membrane (HAM),<sup>3</sup> conjunctiva,<sup>7</sup> autologous or allogenic lamellar/full thickness corneal grafts<sup>8</sup> and scleral patches,<sup>9</sup> autologous fascia lata,<sup>10</sup> and cadaveric or animal-derived pericardium<sup>11</sup> or dura mater<sup>12</sup> with varying success rates. However, HAM is the most preferred one because of its ease of access and low immunogenicity. The HAM promotes epithelialization by acting as a basement membrane and releases growth factors such as epidermal growth factor and keratocyte growth factor which are important for the wound healing. Further, it has anti-inflammatory and anti-scarring effects by the inhibition of transforming growth factor beta signalling in the regeneration process. However, the preparation of HAM is complicated and even expensive. In addition, a strong tissue banking expertise is crucial to prevent inadvertent complications. The risk of transmission of some serious pathogens such as hepatitis-B and human immune deficiency virus always exist and cannot be excluded even in the presence of very strict procedures. Furthermore, HAM is a natural but an allogenic matrix, and immunologic response to allografts is the major concern even if it is low.<sup>13</sup>

Recently, human blood-derived biomaterials have gained popularity to reconstruct and regenerate the ocular surface with a really basic principle and even low cost. Platelet-rich plasma (PRP) is a first-generation platelet concentrate which was discovered in

1970s.<sup>14</sup> As a consequence of its high amount of platelet, it releases several growth factors such as vascular endothelial growth factor, transforming growth factor beta, epithelial growth factor, platelet-derived growth factor, and matrix proteins as vitronectin, fibronectin, and thrombospondin-1 which are located in the alpha granules of platelets.<sup>15</sup> The preparation process comprises consecutive two centrifugation steps with individual's own blood sample and chemicals such as anti-coagulant, calcified thrombin and calcium chloride.<sup>16</sup> The anti-coagulant is essential to avoid the self-coagulation process and calcified thrombin and calcium chloride should be used for the activation of platelet degranulation. However, the aforementioned chemicals are generally animal-derived which may have an impact on the safety of the application. The PRP has been applied in oral, maxillofacial, orthopedic, cardiovascular, plastic and reconstructive specialties, as well as eye diseases (E-PRP) such as dry eye, corneal epithelial defects and ulcers, and ocular surface regeneration after corneal perforations.<sup>17,18</sup> More recently, platelet-rich fibrin (PRF) was introduced as a second-generation platelet concentrate with its superior features. In order to prepare the PRF; a ten-mL blood sample is withdrawn from a peripheral vein of the individual in a glass tube without anticoagulant.

The blood sample is then centrifuged at 2.700 rpm (approximately 400g) for 12min. After centrifugation, the final sample consists of 3 distinct layers. A fibrin clot is obtained in the middle of the tube between the acellular plasma layer at the top and red corpuscles at the bottom. This fibrin clot is collected from the tube by using forceps. Because of the three-dimensional fibrin architecture and sustained release of growth factors during fibrin degradation make this innovative material very suitable for tissue engineering applications.<sup>19</sup> Moreover, the one-step preparation protocol does not include animal-derived materials and harmful chemicals such as anti-coagulant or thrombin. The Choukroun's PRF was first used in ocular surface regeneration by Can et al.<sup>13</sup> in an animal study. Can emphasized that autologous PRF membrane has excellent mechanical and chemical features and can be used as a growth factor-enriched endogenous scaffold for ocular surface reconstruction. Another study by Can et al.<sup>20</sup> showed that the temporary PRF membrane grafting may be an alternative intervention to avoid impending corneal perforation in cases with severe descemetocoele.

## Conclusion

This review explores critical needs in ocular surface problems where conventional therapies are not well suited and novel strategies are reasonably required. The PRP, PRF and their modifications can be applied as a safe auto-origin graft material for ocular surface regeneration when the conventional methods are not sufficient.

## Conflicts of interest

None.

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