Can bone marrow cells give rise to cornea epithelial cells?

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Received 3 March 2008; accepted 6 March 2008

Summary The corneal epithelium plays a critical role in maintaining the cornea’s transparency and its avascularity. Severe damage to the limbal region results in serious problems with the corneal surface such as persistent epithelial defects, conjunctivalisation with vascularisation, keratinisation, scarring, etc. with associated profound visual loss. In order to rescue such damaged ocular surfaces, corneal epithelial stem cells were used to reconstruct artificial corneas by employing tissue engineering method. This procedure, however, requires a large limbal graft from the healthy eye and it is not possible in patients who have bilateral lesions. Therefore we should find other autologous cells as a source of cells for the reconstruction of the corneal surface. c-kit+ enriched bone marrow stem cells can give rise to different epithelial cells. So we hypothesize that this might apply to the cornea as well. Cultured cell sheets composed of autologous c-kit+ enriched bone marrow stem cells may be used to reconstruct corneal surfaces and can restore vision in patients with bilateral severe disorders of the ocular surface.

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Background

The corneal epithelium plays a critical role in maintaining the cornea’s transparency and its avascularity. On the basis of numerous investigations, it is believed that the corneal epithelial stem cells exist in the basal cell layer of the limbal region. Severe damage to the limbal region results in serious problems with the corneal surface such as persistent epithelial defects, conjunctivalisation with vascularisation, keratinisation, scarring, etc. with associated profound visual loss.

In order to rescue the damaged ocular surfaces, novel surgical modalities have been developed over the past 20 years, aimed at reconstructing the diseased ocular surface epithelium. The concept of ocular surface reconstruction was first introduced via an autologous conjunctival transplantation for unilateral chemical injury reported in 1977 [1]. Thereafter, keratoepithelioplasty and autografts or allografts of limbal transplantations were developed to improve the outcome of ocular surface reconstruction [2,3]. These surgical procedures are...
a kind of in vivo expansion of corneal epithelial cells, thus being considered 'cellular surgery', one form of primitive regenerative medicine. Furthermore, through animal experimentation, the transplantation of a corneal or oral epithelial sheet, free of sub-epithelial tissue, was challenged [4].

In the field of dermatology, the procedure of creating an epithelial sheet of cultured human keratinocytes from the epidermis was established by Green in the 1970’s [5], and it has been used in patients with thermal injury since then. Thus, attention has been focused on the ex vivo expansion of corneal epithelial cells, i.e. a cultivated corneal epithelial sheet. Pellegrini et al. first reported the successful ocular surface reconstruction using autologous cultivated corneal epithelial stem cells in patients with severely affected unilateral ocular surface disease (OSD) [6]. Since then, several researchers have reported that autologous cultivated corneal limbal epithelial cells from uninvolved eyes could be used for effective ocular surface reconstruction in patients with unilateral OSD [7]. But this method is not possible in many cases in which bilateral disease produces total corneal stem cell deficiency in both eyes. Is it possible to use other autologous cells as a source of cells for the reconstruction of the corneal surface?

Hypothesis

Adult stem cells are an attractive source for cell based therapies, in which autologous cells can be used to circumvent immunological problems. Adult stem cells can be isolated from various tissues. Recent studies have revealed that adult stem cells have a broader potential or plasticity than was previously considered. For example, neural stem cells have the ability to differentiate into cells belonging to all three germ layers, when transplanted in early embryos [8]. Similarly, cells isolated from bone marrow have been observed to give rise to neural cells [9], skeletal muscle cells [10], and hepatocytes [11]. Collectively, these findings suggest that various adult tissues can be used in autologous cell-replacement therapies.

Basically, bone marrow contains two stem cell populations: hematopoietic and mesenchymal [12]. The ability of hematopoietic stem cells to give rise to epithelial cells has already been illustrated for the skin, lung, liver, gastrointestinal tract and tooth [13–17]. So we hypothesize that this might apply to the cornea as well.

Bone marrow contains two stem cell populations: hematopoietic and mesenchymal. So the bone marrow cells can be fractionated by the use of c-kit, a cytokine tyrosine kinase receptor expressed by hematopoietic progenitor cells. Isolate bone marrow cells from human iliac bone. Cells were separated into c-kit+ and c-kit- populations by magnetic cell sorting. Hematopoietic progenitor cells (c-kit+ populations) are cultured to create a c-kit+ cell sheet. This cell sheet can then be applied to rescue the damaged ocular surfaces and reconstruct the diseased ocular surface epithelium.

Conclusion

Compared to other forms, an autologous cultivated corneal epithelial sheet is the safest and most reliable form for ocular surface reconstruction. However, bilaterally affected ocular surface disorders cannot be treated by this measure. Thus, at present, one must choose either an allogeneic cultivated corneal epithelial sheet or an autologous cultivated oral mucosal epithelial sheet [18] for the means of ocular surface reconstruction. In doing so, one must consider the fact that with the former, the threat of allogeneic reaction has to be dealt with and in the case of the latter; the sheet is not exactly the same as a corneal epithelium.

c-kit+ enriched bone marrow stem cells can give rise to different epithelial cells. Cultured cell sheets composed of autologous c-kit+ enriched bone marrow stem cells may be used to reconstruct corneal surfaces and can restore vision in patients with bilateral severe disorders of the ocular surface.

Acknowledgement

This study was supported by National Natural Science Foundation of China (Grant No. 30700770).

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