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# Editorial: Cell therapy to tissue engineering: Cutting edge research in ocular surface regeneration

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## Editorial on the Research Topic

### Cell therapy to tissue engineering: Cutting edge research in ocular surface regeneration

The ocular surface is a unique sensory ecosystem consisting of the cornea, conjunctiva, and adnexal elements, which are coated by a thin layer of the pre-ocular tear film (1). There is a delicate physiological balance between the diverse epithelial sub-types that blend into each other at the muco-cutaneous junction and at the limbus (1, 2). A dynamic equilibrium is also maintained by the different types of glands, their secretions, the movement of the eyelids, and the lacrimal drainage apparatus. Any immunological or traumatic insult can disturb this fragile microenvironment and set into motion a domino effect of inflammation that ultimately leads to corneal damage and vision impairment. Unfortunately, corneal damage in ocular surface disease is usually not amenable to corneal transplantation. This peculiar limitation has spawned research into regenerative approaches including stem cells and bioengineering.

This special issue on the Research Topic of ocular surface regeneration includes some of the cutting edge developments in cell therapy and tissue engineering (Singh et al.; Ramos et al.; Chen et al.; Li et al.). Recent developments in regenerative medicine have opened the door to the use of novel therapeutics with encouraging outcomes. This includes ocular surface regeneration using limbal tissues, cultured cells, and biomaterials. The approach of stem cell-based therapy has been spectacularly successful in the management of blinding chronic sequelae of chemical injuries [Li et al.; (3)]. Once considered incurable, ocular surface disease due to limbal stem cell deficiency is perhaps one of the best examples of both successful bench to bedside translational research and surgical innovation in ophthalmology (4). Besides limbal epithelial stem cell transplantation, epithelial transdifferentiation approaches have also been used for treating ocular surface epitheliopathy using oral mucosal stem cells (5).

Now the horizon for application of cell therapy is being expanded to corneal opacification due to scarring using mesenchymal stem cells (6). This is the leading cause of corneal blindness in developing countries where the burden of corneal blindness is the greatest. Unlike in the West, most causes of blinding corneal opacification in these populations carry an extremely poor prognosis for corneal transplantation (7). Attempts

are ongoing to develop hydrogels and 3-D printed corneas for the treatment of corneal stromal pathologies like trauma, infections, and keratoconus (8, 9). Proof-of-concept and early clinical application of endothelial cell therapy for corneal edema and endothelial dysfunction has already shown promise (10). It is very likely that in the near future the cornea will become the first tissue to have regenerative therapy for each individual element in the form of epithelial, stromal, and endothelial therapy.

There is also great interest in regenerative approaches for the lacrimal and meibomian glands, that are important adnexal elements and critical to the health of the ocular surface [Chen et al.; (11)]. Damage to the lacrimal gland is the main cause of aqueous tear deficiency, and currently only palliative medical therapy is available for the treatment of this chronic condition (12). Three major approaches are being adopted, in the form of repair, regeneration, or replacement of the lacrimal gland (11). These goals are quite audacious but if successful will bring relief to people suffering from dry eye disease. The regenerative approaches for the treatment of dry eye disease also include development of biomaterials, nanomedicine, hydrogels, and drug-eluting contact lenses [Singh et al.; (13)].

The ocular surface is exceptional in terms of the range of research that is being done for developing regenerative approaches for each individual element be it the cornea, the conjunctiva, or the lacrimal glands. These developments are exciting and could pave the way for disruptive new therapies in the future. Once of the challenges would be to achieve the right balance between efficacy, safety, and affordability. As researchers we must not lose sight of

those who are most desperately in need of these new therapies. Therefore, an equal emphasis must be placed on developing low-cost products that are easy to deliver (14). Despite the technological sophistication, if the solution is not affordable or accessible, it will not be widely adapted or used.

## Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

## Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## References

- Lee V, Rompolas P. Corneal regeneration: insights in epithelial stem cell heterogeneity and dynamics. *Curr Opin Genet Dev.* (2022) 77:101981. doi: 10.1016/j.gde.2022.101981
- Di Girolamo N, Park M. Cell identity changes in ocular surface Epithelia. *Prog Retin Eye Res.* (2022) 20:101148. doi: 10.1016/j.preteyeres.2022.101148
- Shanbhag SS, Nikpoor N, Rao Donthinani P, Singh V, Chodosh J, Basu S. Autologous limbal stem cell transplantation: a systematic review of clinical outcomes with different surgical techniques. *Br J Ophthalmol.* (2020) 104:247–53. doi: 10.1136/bjophthalmol-2019-314081
- Kate A, Basu S. A Review of the diagnosis and treatment of limbal stem cell deficiency. *Front Med (Lausanne).* (2022) 9:836009. doi: 10.3389/fmed.2022.836009
- Komai S, Inatomi T, Nakamura T, Ueta M, Horiguchi G, Teramukai S, et al. Long-term outcome of cultivated oral mucosal epithelial transplantation for fornix reconstruction in chronic cicatrizing diseases. *Br J Ophthalmol.* (2022) 106:1355–62. doi: 10.1136/bjophthalmol-2020-318547
- Shukla S, Shanbhag SS, Tavakkoli F, Varma S, Singh V, Basu S. Limbal epithelial and mesenchymal stem cell therapy for corneal regeneration. *Curr Eye Res.* (2020) 45:265–77. doi: 10.1080/02713683.2019.1639765
- Das AV, Basu S. Indications and prognosis for keratoplasty in eyes with severe visual impairment and blindness due to corneal disease in India. *Br J Ophthalmol.* (2021) 105:17–21. doi: 10.1136/bjophthalmol-2019-315361
- Chameettachal S, Prasad D, Parekh Y, Basu S, Singh V, Bokara KK, et al. Prevention of corneal myofibroblastic differentiation *in vitro* using a biomimetic ecm hydrogel for corneal tissue regeneration. *ACS Appl Bio Mater.* (2021) 4:533–44. doi: 10.1021/acsabm.0c01112
- Ghosh A, Singh VK, Singh V, Basu S, Pati F. Recent Advancements in Molecular Therapeutics for Corneal Scar Treatment. *Cells.* (2022) 11:3310. doi: 10.3390/cells11203310
- Kitazawa K, Sotozono C, Kinoshita S. Current advancements in corneal cell-based therapy. *Asia Pac J Ophthalmol (Phila).* (2022) 11:335–45. doi: 10.1097/APO.0000000000000530
- Veernala I, Jaffet J, Fried J, Mertsch S, Schrader S, Basu S, et al. Lacrimal gland regeneration: the unmet challenges and promise for dry eye therapy. *Ocul Surf.* (2022) 25:129–41. doi: 10.1016/j.jtos.2022.06.005
- Singh S, Basu S. The human lacrimal gland: historical perspectives, current understanding, and recent advances. *Curr Eye Res.* (2020) 45:1188–98. doi: 10.1080/02713683.2020.1774065
- Thacker M, Singh V, Basu S, Singh S. Biomaterials for dry eye disease treatment: current overview and future perspectives. *Exp Eye Res.* (2023) 226:109339. doi: 10.1016/j.exer.2022.109339
- Thokala P, Singh A, Singh VK, Rathi VM, Basu S, Singh V, et al. Economic, clinical and social impact of simple limbal epithelial transplantation for limbal stem cell deficiency. *Br J Ophthalmol.* (2022) 106:923–8. doi: 10.1136/bjophthalmol-2020-318642