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Introduction

Corneal Sensitivity in Diabetes

Table 1: Neurotrophic factors in the cornea.

Growth factor	Healthy cornea	Injured cornea	Topical application
Nerve growth factor (NGF)	(i) Found in corneal epithelium and stromal keratocytes	Upregulated during reinnervation after nerve surgical transection, and in dry eye syndrome, in infamed conjunctiva of patients with vernal keratoconjunctivitis	(i) Augments corneal wound healing and provides recovery of corneal sensitivity and photophobia
	(ii) Critical for corneal nerve survival and maintenance, axonal branching, elongation, neuronal sprouting, and regeneration following nerve damage		(ii) Has potent antiviral properties (restrict herpes simplex virus-1)
Brain-derived neurotrophic factor (BDNF)	(i) Found in corneal epithelium and stromal keratocytes, originate from corneal sensory neurons	Expressed after experimental fap surgery in putative corneal stromal and/or infammatory cells in a positive association with neurite extension	
	(ii) Exact role related to corneal nerves is unclear		
Glial cell-derived neurotrophic factor (GDNF)	Expressed in human corneal stromal keratocytes and may operate similarly to or synergistically with NGF by triggering gene transcription governing epithelial cell migration and wound healing	Possibly plays an important role in corneal regeneration and wound healing	Produces complete epithelial healing in a patient with a progressive neurotrophic ulcer
Neurotrophins 3, 4/5 (NT-3, NT-4/5)	(i) NT-3 transcribed in epithelial cells and stromal keratocytes	Minimal changes in NT-3 gene expression following surgical transection of corneal nerves	
	(ii) NT-4 is present in corneal epithelium and is a neurotrophic factor that may be involved in the regulation of stromal keratocytes by epithelial cells		
Ciliary neurotrophic factor (CNTF)	Promotes corneal epithelial wound healing by activating corneal epithelial stem/progenitor cells	(i) Upregulated in corneal epithelium after injury in mice	
		(ii) Down regulated in corneal epithelium of diabetic mice	
Vascular endothelial growth factor (VEGF)	Minimally present	(i) Upregulated in the injured cornea	VEGF supplementation promotes trigeminal nerve repair, and abrogation of VEGF signaling reduces corneal nerve growth
		(ii) Required for e f cient corneal nerve regeneration	
Hepatocyte growth factor (HGF)	Expressed in stromal keratocytes, stimulates corneal epithelial proliferation	Upregulated after corneal epithelial wounding and probably contributes to the epithelial wound healing process	
Keratocyte growth factor (KGF)	(i) Expressed in stromal keratocytes, fbroblasts	Upregulated in corneal epithelial wounding	
	(ii) Stimulates corneal epithelial proliferation, acts specifcally on cells of epithelial origin as a paracrine mediator		
Transforming growth factor-α (TGF-α), interleukin-1β (IL-1β), and platelet-derived growth factor-B (PDGF-B)	(i) Exclusively expressed in the corneal stroma		
	(ii) TGF-α and IL-1β can upregulate the transcription of neurotrophins, such as NGF in 3T3 mouse fbroblasts		

5. Muller LJ, Marfurt CF, Kruse F, Tervo TMT (2003) corneal nerves: structure, contents and function. Exp Eye Res. 76: 521–542.

6. Zander E, Weddell G (1951) Observations on the innervation of the cornea. J Anat. 85:68–99.

7. Vonderahe AR (2001) Corneal and scleral anesthesia of the lower hale of the eye in a case of trauma of the superior maxillary nerve. J Neurol Neurosurg Psychiatry 20: 836–837.

8. Ruskell GL (1999) Ocular fbres of the maxillary nerve in monkeys. J Anat 118: 195–203.

9. Marfurt CF, Murphy CJ, Florczak JL (2001) Morphology and neurochemistry of canine corneal innervation. Invest Ophthalmol Vis Sci 42: 2242–2251.

10. Muller LJ, Pels L, Vrensen GFJM (1996) Ultra structural organization of human corneal nerves. Invest Ophthalmol Vis Sci 37: 476–488.

11. Jones M, Marfurt CF (1998) Peptidergic innervation of the rat cornea. Exp Eye Res 66: 421– 435.

12. Marfurt CF, Cox J, Deek S, Dvorscak L (2010) Anatomy of the human corneal innervation. Exp Eye Res 90: 478–492.

13. Beckers H, Klooster J, Vrensen G, Lamers W (1994) Sympathetic innervation of the rat's eye and peripheral ganglia: an electron microscopic autoradiographic tracing study. Graefe's Arch Clin Exp Ophthalmol 232: 57–65.

14. Patel DV, McGhee CNJ (2005) Mapping of the normal human corneal sub-basal nerve plexus by in vivo laser scanning confocal microscopy. Invest Ophthalmol Vis Sci 46: 4485–4488.