

The nociceptive pathway in dry eye disease and ocular surface pain models

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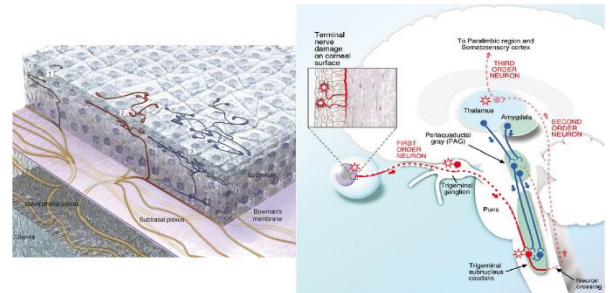
Summary

This project is focused in the study of pain and nociception in the context of Dry Eye Disease. Sensitive terminals in the cornea, whose neuronal cell bodies are placed in the trigeminal ganglion, are responsible of this sensation. From there, the information is sent to the brainstem trigeminal complex and finally is processed by central structures in the brain. The expression pattern of different ligands and receptors implicated in pain will be elucidated in the nociceptive corneal pathway in both wild-type and preclinical models of dry eye pain. These molecules are candidates to be biomarkers of the progression of the disease and emerge as new therapeutic targets.



State-of-the-art

Ocular pain, in particular corneal pain, is considered a core symptom of inflammatory or traumatic disorders affecting the anterior segment of the eye. Its increasing prevalence, morbidity, and the resulting social burden has caused chronic ocular pain to be recognized as a serious public health issue. To date, the management of chronic corneal pain still represents a therapeutic challenge in ophthalmology. A better understanding of the molecular and cellular mechanisms involved are crucial issues for developing effective management and therapeutic strategy to alleviate this debilitating condition. However nowadays, the neuronal circuits involved in corneal nociception and in chronic corneal pain are not fully decrypted. Animal modelling of dry eye pain is crucial to provide new information about this ocular pathology. Thus, a better understanding of the sequence and nature of the events that drive these molecular mechanisms will offer significant promise for the discovery of new mechanisms and targets for the management of chronic ocular pain.



Corneal nociceptive pathway.

From Rosenthal & Borsook, 2012 and Belmonte *et al.*, 2017



Techniques

- Behavioural methods: von Frey filaments, wiping test
- Tearing rate and analysis of the tears
- Clinical evaluation of the ocular surface: slit lamp, *in vivo* confocal microscopy
- Anatomical studies on trigeminal ganglia and brain: immunofluorescence, *in situ* hybridization, microscopy
- Molecular techniques: RNA extraction, qPCR, Western blot, ELISA, MULTIPLEX



Task description

- Characterization of the corneal nociceptive pathway in different preclinical models of dry eye disease and ocular pain.
- Study of the cellular changes at the central neural structures caused by corneal pain.
- Search of new biomarkers of dry eye and eye pain
- Search and evaluation of new therapeutic targets to treat pain in dry eye disease
- Ocular surface clinical evaluation of patients during the secondment at CIC of Quinze-Vingts hospital.
- Training in obtention of marketing authorizations during the secondment in Horus Pharma.