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Implementation of *in vivo* models to identify potential candidates for DED treatment

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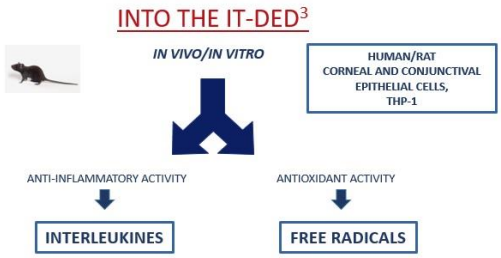
Summary

Meibomian gland dysfunction (MGD) is the most common cause of evaporative dry eye disease (DED) and it is defined as "a chronic, diffuse abnormality of the Meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion."
DED will be induced in rats through cauterization of Meibomian glands. What we expect from this animal model is an increase in tear film osmolarity, tear film evaporation rate, inflammatory cells within the bulbar conjunctiva and corneal cells, stasis of the meibum and glands morphology alteration. Active compounds should ameliorate inflammation and severity of evaporative DED.

State-of-the-art

Gilbard *et al.* occluded the glands openings by cauterization so that Meibomian gland lipids could not be released. Since the lipids could not attach to the eyeball surface to form the tear film lipid layer, it produced dry eyes because the tear film was easily ruptured.
Rats are chosen for basic study of inflammation and therapeutic research, since these animals can reproduce the human clinical MGD with related symptoms.
Other proposed MGD animal models present many disadvantages in terms of time needed for validation and the low success rate. Moreover, gene-deficient mice present other defects that could affect results (e.g. skin and hair defects).
Animal models are necessary to further unravel DED pathophysiology and to evaluate novel therapies, that is why there is still the need to validate more reliable animal models for drug testing.



In vivo and *in vitro* summary of the PhD project.

Techniques

- Cauterization of Meibomian glands
- Removal of exorbital lacrimal gland
- Cell culture
- Multiplex immunoassay
- Flow cytometry
- Electron Paramagnetic Resonance (EPR)
- Immunostaining

Task description

The compounds received from the beneficiaries of the consortium will be tested. To evaluate their anti-inflammatory and antioxidant activities, the compounds will be evaluated in the evaporative dry eye animal model (that needs to be validated and optimized) and the aqueous tear deficient animal model.

For validation, aqueous tear collection, ocular surface staining, and tear fluid analysis will be carried out.