Technology offer:
New lead compounds for dry eye disease and validated dry eye disease rat model

The University of Antwerp has developed a new lead compound and a validated rat model for dry eye disease (DED). Pharmaceutical companies looking for a preclinical candidate for further development in DED related disease can benefit from this established expertise.

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Medicinal Chemistry
University of Antwerp

LMPH
Laboratory of Microbiology, Parasitology and Hygiene
University of Antwerp

Situation before

Dry eye disease (DED) is a chronic, multifactorial disease of the ocular surface and has become a major and increasing healthcare problem due to its high prevalence and economic burden, especially for women who are 3 times more prone to DED. Attempts to re-establish a normal ocular surface have produced a myriad of possible but mostly unsatisfactory remedies. Cyclosporine A (Ikervis™) is the only marketed DED product for DED in Europe but has only demonstrated effectivity in severe keratitis DED patients. The US FDA has approved Xiidra™ for the treatment of DED, but experts in the field of DED have indicated that new and complementary therapies are needed with les side effects.

Technology

The laboratory of Medicinal Chemistry (UAMC) has recently obtained an *in vivo* proof of concept with a multi-target **serine protease inhibitor**, identified from a diverse library of around 300 serine protease inhibitors. Topical application of this compound in the eye of a tear-deficient dry eye rat gave a significant reduction of tissue damage and a significant reduction of the inflammatory parameters, TNF-α and IL-1α, outperforming Restasis™. The laboratory of Microbiology, Parasitology and Hygiene (LMPH) developed a **validated tear-deficient dry eye rat model** for evaluation of new lead compounds (collaboration with UAMC). This model has the advantage that it allows the time-dependent analysis of relevant immunological parameters not present in mice models. LMPH will also develop a new evaporative dry eye rat model (induced by cauterization of the Meibomian gland orifices) which is clinically more relevant since evaporative dry eye comprises the majority of the whole dry eye population.

About the researchers - research group

The **University of Antwerp Medicinal Chemistry** (Prof. K. Augustyns) has all the necessary expertise to run chemical optimization programs and drive projects towards the 'quality lead' stage: the team has state-of-the-art facilities for *in silico* molecular design, synthesis and analysis (400 MHz NMR, 2 UPLC-MS), biophysics/ enzymology (SPR, microtiterplate readers, protein analysis,) and ADME/PK experiments. In addition an infrastructure for automated purification is present (prep LC-MS and SFC).

The **Laboratory of Microbiology, Parasitology and Hygiene** (Prof. P. Cos) has an extended panel of *in vitro* and *in vivo* laboratory models, including an Ocular Surface Disease rat model. The available facilities include a microbiology and a molecular biology lab. Fluorescent microscopes with image analysis and a flow cytometer are available. *In vivo* studies are performed in the Animal Facilities, including an animal surgery with specialized equipment for temperature control and isoflurane anesthesia.

Both laboratories belong to the Antwerp drug Discovery Network (www.addn.be) and to the research Consortium of Excellence Infla-Med (www.uantwerpen.be/infla-med).

A **H2020 MSCA-European Training network was recently granted and will be initiated in January 2018 on the drug development for dry eye disease** (acronym IT-DED^3). Prof. Augustyns is the coordinator of this proposal and Prof. Cos is involved as a beneficiary. All academic key opinion leaders in the field of DED and several SMEs are involved in the project.

More information

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