UNIVERSITY OF LIVERPOOL

Enterprise: Licensing & Ventures

Antivirulence treatment of Pseudomonas aeruginosa microbial keratitis (MK)

Introduction

Microbial keratitis (MK) is a severe infection of the cornea that represents a major cause of vision loss worldwide. Its incidence ranges from 2.6-40.3 per 100,000 people in the UK and reaches 113 per 100,000 in India, accounting for approximately 3.2% (0.5-7.2%) of the 36 million cases of global blindness. Despite prompt antimicrobial therapy, clinical outcomes remain poor, often leading to corneal scarring and permanent visual impairment.

Among the causative pathogens, *Pseudomonas aeruginosa* is responsible for roughly 25% of MK cases. The severity of these infections is primarily driven by the secretion of potent cytotoxins, notably ExoU and ExoS. ExoU-producing *P. aeruginosa* strains are predominant in keratitis and are strongly associated with rapid corneal destruction, increased antimicrobial resistance, and poor visual outcomes.

Unmet Need: MK

Current antimicrobial treatments are insufficient to prevent the destructive effects of ExoU-mediated corneal damage. The dual challenge of rapid tissue necrosis and increasing resistance in ExoU-positive strains underscores the urgent need for novel therapeutic strategies that directly target bacterial virulence mechanisms rather than bacterial growth alone.

UoL Solution

To manage the unmet need, the team at UoL have identified and characterised three small-molecule inhibitors of ExoU. The compound formulation has demonstrated potent inhibitory activity in vitro and ex vivo, and in animal models, to significantly reduce disease severity and morbidity. Targeting ExoU offers a promising adjunctive strategy to improve outcomes in P. aeruginosa keratitis and potentially other ExoU-mediated infections.

Intellectual property

Patent covering the formulation and its use was filed in July 2025.

Team

- Professor Stephen Kaye
  - Consultant Ophthalmologist and clinician-scientist specialising in corneal and external eye diseases.
  - Leads translational research on microbial keratitis and vision restoration.
- Professor David Fernig
  - Expert in protein biochemistry and molecular mechanisms of bacterial virulence.
  - Focuses on developing novel strategies to inhibit bacterial toxins such as ExoU.

Together, they lead a multidisciplinary team combining clinical expertise, molecular biology, and drug discovery to develop innovative treatments targeting ExoU-mediated corneal damage in Pseudomonas aeruginosa infections.

Next Steps

Looking for co-development opportunities for formulation design and safety/toxicology studies.

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