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Presenting Author: Balazs Meresz

E-mail address: mereszbalazs@gmail.com

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Potential new treatment target in bacterial keratitis

Balazs Meresz¹, Inez Bosnyak¹, Dorottya Molitor¹, Bela Kocsis², Kornelia Farkas³, Dora Reglodi¹, Tamas Atlasz^{1,4}, Alexandra Vaczy¹

¹ MTA-PTE PACAP Res. Group, Dept. of Anatomy, University of Pecs Medical School, Pecs, H-7624, Hungary

² Dept. of Medical Microbiology and Immunology, University of Pecs Medical School, Pecs, H-7624, Hungary

³ Institute of Bioanalysis, University of Pecs Medical School, Pecs, H-7624, Hungary

⁴ Faculty of Sciences, Dept. of Sportbiology, University of Pecs, Pecs H-7624, Hungary

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Abstract:

Introduction: Bacterial keratitis is an infection of the corneal tissue caused by various bacterial species. Keratitis is still responsible for the most sight-threatening lesion. Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide, known for its neuroprotective and anti-inflammatory effects, which are mainly mediated through PAC1 receptor (PAC1R). The aim of our research is to investigate the protective role of the PAC1R in endotoxin-induced keratitis model in mice.

Methods: In our study, we induced bacterial keratitis in a CD1-IGS mouse strain by intraperitoneal injection of lipopolysaccharide (LPS). To investigate the role of PAC1R, half of the animals were treated intravitreally with a PAC1R antagonist, maxadilan. 24 hours after injection, optical coherence tomography (OCT) and routine histology were performed. Cytokine arrays were executed to map inflammatory pathways. Five weeks after the LPS administration, a four-step scoring system was used to determine the degree of keratitis.

Results: Based on OCT and histology results, maxadilan attenuated the increase of central corneal thickness and inhibited the activation of inflammatory cytokines. Five weeks later the group receiving LPS and treated with maxadilan showed less severe keratitis.

Conclusion: Our results suggest that targeting the PAC1R could be a promising therapeutic approach for the treatment of bacterial keratitis.

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