00460 Novel Strategies for Treating Pathogenic Corneal Bacterial Biofilms

Aung Thet[1], *Joey Yam*[2], *Michael Givskov*[2], *Liang Yang*[1], *Roger Beuerman*[1]
[1]Singapore Eye Research Institute, [2]Nanyang Technological University

Aims: Microbial infections of the cornea are potentially devastating and can result in permanent visual loss, requiring surgery. Biofilm infections can impose serious problems such as tolerance to antibiotics and immune defense, resistance formation against antibiotics and progress to chronic infection. Although there are lots of evidences showing the critical role of biofilm cascades in other body systems, there is a research gap investigating the biofilm's role on corneal surface and its control strategies.

Methodology: We investigated that corneal bacterial infection is a biofilm mode of infection, which induced cyclic-di-GMP signaling (an essential messenger that regulates biofilm formation) or expressed the abundance of extra-cellular DNA (a major constituent of biofilm matrix) on mouse and rabbit corneas.

Result: Large biofilm-like phagocyte-tolerant aggregations were observed in the rabbit and mouse corneas infected by atypical mycobacteria, PAO1 wild type. In contrast, the PAO1/p_{lac}-yhjH strain (P. aeruginosa c-di-GMP depleted strain) was unable to form phagocyte tolerant microcolonies. Application of the c-di-GMP reducing agent (Sodium Nitroprusside) is able to repress the development of Colistin-tolerant subpopulations of in vitro P. aeruginosa biofilms and further enhance the killing efficiency of Colistin in vivo P.aeruginosa corneal biofilms. Combination of DNase (destruction of extracellular DNA, biofilm matrix barrier) and antibiotics showed the better treatment efficacy than antibiotics alone in in vitro and in vivo mycobacterial corneal biofilm model.

Conclusion: In conclusion, we have shown for the first time that biofilm plays a critical role in corneal bacterial infections leading to the drug and immune tolerance microcolonies and drugs targeting the destruction of biofilm matrix or inhibiting the biofilm signaling pathway is suggested to use in drug tolerance corneal infection cases in real clinical scenarios.