

Bacteriophage-mediated reduction of uropathogenic *E. coli* from the urogenital epithelium

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Urinary tract infections (UTIs), primarily caused by uropathogenic *Escherichia coli* (UPEC), affect millions annually. UPEC gains exposure to the urinary tract from mucosal reservoirs such as vaginal tract. With rising antibiotic resistance and recurrence, alternative strategies like phage therapy are gaining attention. UPEC-targeting (bacterio)phage/and or phage cocktails may serve as a non-antibiotic method to control UPEC. We explored the potential of lytic phage alone or as a cocktail in preventing UPEC colonization using in vitro and in vivo models. Phages significantly inhibited UPEC growth in both LB medium and simulated vaginal fluid. Pretreatment of human vaginal epithelial cells (VK2/E6E7) and bladder carcinoma cell (HTB9) with lytic phage reduced adhesion and intracellular survival of UPEC compared with controls. Notably, phage pretreatment did not impact phage resistant UPEC strains, indicating that phage lysis was the primary driver of differences. Live confocal microscopy confirmed interaction of SYBR gold-stained phages particles with RFP-expressing UPEC strains in two distinct cell lines. In vivo, daily intravaginal phage administration in humanized microbiota mice (HMBmice) significantly reduced vaginal UPEC burden after 96 hours. Although phage cocktails also reduced bacterial load at 72 hours, the reduction was not statistically significant ($p = 0.083$). UPEC dissemination was observed to uterine and kidney tissues by day 7 post-infection, but burdens were not different between phage and mock-treated groups. In conclusion, we demonstrate that phage and/or phage cocktails can modestly reduce UPEC vaginal colonization, highlighting the potential of phage therapy as a viable treatment option for UTI prevention.

Dr Bishnu Joshi is a research scholar dedicated to understanding the molecular mechanisms of antimicrobial resistance (AMR) and to developing novel non-antibiotic strategies to combat it. He earned his Master's degree in Tropical Animal Health from the Institute of Tropical Medicine, Belgium, as a DGD Fellow, and completed his PhD in Molecular Microbiology at UiT – The Arctic University of Norway, under the supervision of Dr Mona Johannessen.

He is currently a postdoctoral researcher on a collaborative U19 project (Combating Antibiotic-Resistant Bacteria Interdisciplinary Research Units, CARBIRU), working under the mentorship of Dr Katy Patras and Dr Rob Britton. His research focuses on non-antibiotic approaches to preventing mucosal colonisation by AMR pathogens, particularly uropathogenic *Escherichia coli* (UPEC). Specifically, he is exploring bacteriophage-based interventions to inhibit UPEC vaginal colonisation, using both in vitro and in vivo models.

Dr Joshi has published [nine peer-reviewed articles](#) and one book chapter, with more than 1,300 citations and an h-index of 13 on [Google Scholar](#). Beyond his own research, he contributes actively to the scientific community as a peer reviewer for journals including Acta Tropica and Diagnostic Microbiology and Infectious Disease, and as a Guest Editor for Frontiers in Cellular and Infection Microbiology.

