Poster Prize of the Day of BioMedical Research 2024
Alumni MedBern Research Award

Interspecies peptide hijacks *S. pneumoniae* transporter to inhibit growth and colonization

Janine Lux[1,2], Hannah Portmann[1], Lucía Sánchez García[1], Maria Erhardt[1], Lalaina Holivololona[1], Laura Laloli[1], Manon F. Licheri[1], Clement Gallay[3], Robert Hoepner[4], Nicholas J. Croucher5, Daniel Straume[6], Jan-Willem Veening[3], Ronald Dijkman[1], Manfred Heller[7], Denis Grandgirard[1], Stephen L. Leib[1], Lucy J. Hathaway[1]*

[1] Institute for Infectious Diseases, Faculty of Medicine, University of Bern, Bern, Switzerland;
[2] Graduate School for Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland;
[3] Department of Fundamental Microbiology, University of Lausanne, Lausanne, Switzerland;
[4] Department of Neurology, Bern University Hospital and University of Bern, Switzerland;
[5] MRC Centre for Global Infectious Disease Analysis, Sir Michael Uren Hub, White City Campus, Imperial College London, London, UK;
[6] Faculty of Chemistry, Biotechnology and Food Science, Norwegian University of Life Sciences, 1430 Ås, Norway;
[7] Proteomics and Mass Spectrometry Core Facility, Department for BioMedical Research (DBMR), University of Bern, Bern, Switzerland

Aim: To identify a previously unknown interspecies communication peptide from *Klebsiella pneumoniae* and analyze its effect on *Streptococcus pneumoniae* (pneumococcus) *in vitro* and *in vivo* with a view to investigating its potential as a therapeutic for pneumococcal diseases.

Methods: The peptide was identified from the *K. pneumoniae* secretome by mass spectrometry and the effects on *S. pneumoniae* analyzed by optical density measurement, time-kill assays, transformation assays and microscopy. The effects on the transcriptome were determined by RNA-Seq and on colonization using primary human airway epithelial cells and an infant rat model. Peptide toxicity was assessed using primary human airway epithelial cells and zebrafish larvae.

Results: The *K. pneumoniae* secretome contained a peptide that suppressed growth of genetically diverse clinical pneumococcal isolates, including antibiotic-resistant strains, in defined medium and human cerebrospinal fluid. Bacteriostatic growth inhibition was dependent on uptake via a functional Ami permease and caused downregulation of genes involved in amino acid and protein metabolism. Furthermore, the peptide caused irregular bacterial shapes, decreased chain length and decreased genetic transformation. Pneumococcal adherence to primary human airway epithelial cells and colonization of rat nasopharynx were also decreased. We did not detect toxicity of the peptide *in vitro* or *in vivo*.

Conclusion: We identified a *K. pneumoniae* peptide which targets the pneumococcal Ami permease to inhibit pneumococcal growth and colonization. The peptide has potential as a therapeutic for pneumococcal diseases, including treatment of antibiotic resistant strains, while avoiding bacterial lysis and dysbiosis.