**Bacteriophage-drug conjugates**

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**Background and aims.** Antimicrobial resistance remains a critical global health challenge with limited effective treatment options. This has renewed interest in bacteriophages (phages), obligate viral predators of bacteria, as alternative or adjunct antimicrobial agents. In this study, we developed phage conjugates for targeted delivery of therapeutics to combat bacterial infections, including those caused by AMR pathogens.

**Methods.** In this study, *Pseudomonas*-specific phages were conjugated with therapeutic payloads via cleavable linkers, enabling pH-responsive drug release in acidic environments typical of infection sites. These engineered phage nanobots function both as antimicrobial agents and targeted drug delivery systems, ensuring high local drug concentrations at infection sites while minimising systemic toxicity.

**Results.** We confirmed successful conjugation of therapeutic agents to phages and demonstrated controlled drug release under mildly acidic conditions. The combination of phages, antibiotics, and a antibiofilm agent significantly reduced *Pseudomonas aeruginosa* biofilm viability by over 5 log units.

**Conclusion/Discussion.** This work presents a novel, multifunctional phage-based delivery system capable of co-delivering phages and therapeutics in a single treatment. The synergistic action of the phage, antibiotic, and antibiofilm agent enhances biofilm disruption and bacterial eradication, offering a promising approach for treating persistent and resistant infections.

**References:**

1. Duong, H.T.T, Iredell, J., and Huang, H. “Phage-drug conjugates”, PCT/AU2022/0514269.