

Helicobacter pylori

Prophage

Phage Therapy

Screening and *in silico* characterization of prophages in *Helicobacter pylori* genomes

Rute Ferreira ^{1,2,3*}, Cláudia Sousa ^{1,2}, Eva Presa ^{1,2}, Diana P. Pires ^{1,2}, Mónica Oleastro ⁴, Joana Azaredo ^{1,2}, Céu Figueiredo ^{3,5,6}, Luís D. R. Melo ^{1,2}

1. CEB –Centre of Biological Engineering, University of Minho, Braga, Portugal;
2. LABBELS –Associate Laboratory, Braga, Guimarães, Portugal;
3. i3S - Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal;
4. Department of Infectious Diseases, National Institute of Health Doctor Ricardo Jorge (INSA), Lisbon, Portugal;
5. Ipatimup – Institute of Molecular Pathology and Immunology of the University of Porto;
6. Department of Pathology, Faculty of Medicine, University of Porto, Porto, Portugal

Correspondence:

Dr. Luís Melo: lmelo@deb.uminho.pt

Temperate bacterio(phages) play an important role on the evolution of pathogenic bacteria. Nevertheless, information on their role in *Helicobacter pylori* (an important gastric pathogen bacterium) is scarce.

The present study developed a workflow for the identification of prophages in Portuguese *H. pylori* clinical strains, proposing the use of a new PCR-based screening method. The genome of strains with different PCR profiles were then sequenced.

In the fourteen genomes analysed, nine intact prophages were identified by PHASTER. These prophages were annotated by analogy with other identified phages, where seven contained the integrase gene, corroborating the results obtained in the PCR screening, with only one exception. Still, in PCR screening, the holin gene was identified in 75 % of the strains containing intact phages, but BLASTp homologies only recognized this gene in one of the prophages. Fifty-six percent are podovirus, while in 44 % it was not possible to assign any family, according to the VirFam tool. Using the Resistance Gene Identifier of CARD it was identified the *Acinetobacter* mutant Lpx gene conferring resistance to colistin in two intact prophages. The BLASTp search identified a putative ABC binding cassette transporter in one of the intact prophages. On the bacterial genomes, 71 % have the CRISPR-Cas system classified as evidence level 1 by CRISPRCasFinder, which typically indicate potentially invalid CRISPR arrays.

The use of an initial PCR screening method increased the identification of intact prophage-containing strains from 20 % to 57 %. Furthermore, the few virulence factors identified in prophages, and the possible inactivity of CRISPR-Cas in the bacterial genomes, allow the choice of strains for the isolation of phages for future studies. Overall, our results represent a significant contribution to the knowledge of prophages in *H. pylori*, and provide valuable insights into their potential use in phage therapy.