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Controlling ETEC colonization on cultures of an intestinal pig cell line with a T4-like phage

Alice Ferreira [1,2], Carina Almeida [3], Daniela Silva [3], Maria Elisa Rodrigues [1,2], Mariana Henriques [1,2], Joana Azeredo [1,2], Ana Oliveira [1,2*]

1. CEB - Centre of Biological Engineering, LIBRO – Lab. de Investigação em Biofilmes Rosário Oliveira, University of Minho, Braga, Portugal
2. LABBELS – Associate Laboratory, Braga, Guimarães, Portugal
3. ALS ControlVet, Zona Industrial de Tondela ZIMII, Lote 6, 3460-605 Tondela, Portugal

Correspondence:
anaoliveira@deb.uminho.pt

Enterotoxigenic *Escherichia coli* (ETEC) colonizes the intestine of young pigs causing severe diarrhoea and consequently bringing high producing costs. The rise of antibiotic selective pressure together with on-going limitation on their use demands news strategies to tackle this pathology. The pertinence of using phages to tackle this problematic is being explored, and in this work, the efficacy of a T4-like phage vB_EcoM_FJ1 (FJ1) in reducing the load of ETEC O9:H9 (Sta, F5/F41) was assessed. FJ1 has a 170,053 bp genome, and of the 270 coding sequences none corresponds to identified undesirable proteins, such as integrases or transposases. Envisaging the oral application to piglets, FJ1 was previously encapsulated on $CaCO_3$/alginate. Assays were performed on 15-day cultures of the intestinal pig cell lineIPEC-1 seeded in transwell inserts. Phage treatment occurred 2 hours after ETEC infection, when, in average, $5x10^5 CFU.cm^{-2}$ were adhered to cultured cells. Encapsulated phage provided reductions of, approximately, 2.3 Log $CFU.cm^{-2}$ and 2.8 Log $CFU.cm^{-2}$ on adhered bacteria, respectively 3 and 6 hours after administration. The repeated exposure of the host to FJ1 led to the emergence of phage-insensitive mutants, phenotype that brought fitness costs to the host strain: they were 90% more vulnerable to the pig complement system and less efficient in adhering to cultured cells (in about 90%). Overall, FJ1 is presented here as promising to fight against ETEC infections through oral administration to piglets.