

## Phage Therapy against *Pseudomonas aeruginosa* Infections in cystic fibrosis patients

Forti F<sup>1</sup>, Briani F<sup>1</sup>, Horner D<sup>1</sup>, Ghisotti D<sup>1</sup>

<sup>1</sup>Dep. of Biosciences – University of Milan – Italy (Grant No. FFC#17/2015) [[doi.org/bwkh](https://doi.org/bwkh)]

**Keywords:** Phage therapy, *Pseudomonas aeruginosa*, biofilm

**Background and rationale.** *Pseudomonas aeruginosa* is the most common pathogen found in the lung of cystic fibrosis patients (CF). The quality of life of CF patients largely depends on the success or failure of antibiotic treatment. Now, the alarming diffusion of isolates of *P. aeruginosa* multi-resistant to the antibiotics currently in use makes urgently need to develop new antibacterial therapies.

**Hypothesis and objectives.** Phage therapy, the use of the natural enemies of bacteria, is garnering renewed interest as bacterial resistance to antibiotics becomes widespread. This therapy, used for decades in Eastern Europe, can be considered as a therapeutic alternative or a complementary treatment to antibiotics in curing lung infections in CF patients.

**Essential methods.** Advantages on antibiotic therapy are that bacteriophages: 1) multiply at the infection site, increasing their number, whereas antibiotics are metabolized and eliminated from the body; 2) target only specific bacteria, with no effect on commensal flora; 3) contrary to antibiotics that are defined chemical molecules, phages can mutate and overcome bacterial resistance; 4) have the capacity to reach bacteria trapped inside biofilms, the matrix that acts as a shield for pathogenic bacteria in the CF patients lungs.

**Preliminary results.** During this one-year project we isolated and characterized some tens of

phages, selecting 6 of them that presented a different host range on *P. aeruginosa* clinical strains. These 6 phages were mixed in a cocktail and found to be able to efficiently kill a number of different *P. aeruginosa* clinical strains in vitro. We also determined the ability of the phage cocktail to destroy a preformed *P. aeruginosa* biofilm. Electron microscopy indicated that 3 are Podoviridae, 2 Myoviridae and 1 Syphoviridae. The genome sequences of 3 of them have been completed, the other are in progress. Genome analysis of the sequences indicated the absence of any undesirable gene, suggesting that the phages could be used without problems for human therapy. In the future, we intend to validate the efficacy of our phage cocktail in vivo, using two different model systems: the traditional mice model, and a new model that uses the *Galleria mellonella* larvae. The latter is less expensive and ethically acceptable, and can be extended to a high number of different *P. aeruginosa* clinical strains, including multi-resistant strains.

**Expected results and their significance.** We expect that our phage cocktail has the potential for development as a therapeutic to control *P. aeruginosa* infections in CF patients.

**Acknowledgment.** FFC#17/2015: funded by FFC, supported by Delegazione FFC di Taranto e Gruppi di Sostegno FFC di Massafra e Alberobello