P03.18A *In vivo* validation of phage therapy against Pseudomonas aeruginosa infections using zebrafish as a new model for cystic fibrosis

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To investigate the pathophysiology of cystic fibrosis (CF) several animal models have been developed including mouse, pig, and ferret; however, none of them perfectly recapitulates all human patient symptoms. On the contrary, zebrafish (*Danio rerio*) recently emerged as a powerful genetic model system to better understand CF onset and to develop new pharmacological treatments. Indeed, zebrafish embryos present only innate immune system and the zebrafish cftr gene is highly conserved with the human orthologue. cftr-loss-of-function zebrafish embryos mimic CF human defects in response to infection of *P. aeruginosa*, presenting a dampened respiratory burst response, a reduced neutrophil migration and defects in endocrine organs function.

In our previous work, we demonstrated that P. aeruginosa infection in mice and *Galleria mellonella* larvae could be cured by administration of phages, the natural enemies of bacteria. Phage therapy, used for decades in Eastern Europe, is gathering interest as a therapeutic alternative or a complementary treatment to antibiotics. The goal of this project is to in vivo validate the efficacy of phage therapy against *P. aeruginosa* infections using the CF-zebrafish animal model. Both wild-type and cftr-loss-of-function zebrafish embryos, were infected with *P. aeruginosa* by microinjection, followed by phage administration. The therapeutic effects of phages was evaluated, following embryo mortality, bacterial burden, neutrophil migration and immune response. In addition, we plan to combine the phage treatment with antibiotics to verify if combination of the two treatments has a positive outcome against *P. aeruginosa* infections.

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