Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

transmembrane conductance regulator (CFTR) modulators improve sweat chloride, lung function, and nutritional status [2], but despite these improvements, approximately 80% of PwCF are infected with *P. aeruginosa* [2]. Lytic bacteriophages (phages) offer an alternative or adjunctive approach for treatment of chronic MDR *P. aeruginosa* lung infections. Phages are natural, species-specific viruses that infect bacteria and amplify locally and can penetrate biofilm using specific depolymerizing enzymes [3]. Our goal is to develop a nebulized phage therapy for the treatment of chronic *P. aeruginosa* pulmonary infections in PwCF.

Methods: A panel of more than 100 clinical *P. aeruginosa* bacterial strains isolated from U.S. and European CF patient sputum samples were used for phage isolation and characterization. Isolated natural phages were sequenced and analyzed. Phage host range was established by plaque assay, and activity within biofilms was determined by BacTiter-Glo and crystal violet staining. A breathing simulator was used to determine the delivered dose by nebulization of a phage cocktail. Droplet size distribution was tested by laser diffraction. Phage distribution within the aerosols was analyzed by quantitative polymerase chain reaction and New Generation Impactor (Copoley Scientific). Phage safety was demonstrated in ex vivo and in vivo models.

Results: Lytic phages with wide host range coverage against clinical *P. aeruginosa* strains were selected and evaluated for additional characterization. Genomic analysis confirmed absence of undesirable genes. The selected combination targeted most of the strains in the panel and significantly reduced *P. aeruginosa* embedded in biofilm. Breathing simulation results revealed phage viability after nebulization, and all tested phages were distributed homogeneously within the aerosol. Safety assessments conducted using human epithelial cells and animal models demonstrated that treatment with BX004 was safe and well tolerated.

Conclusions: BX004 demonstrated a broad host range against CF clinical *P. aeruginosa* isolates; potent in vitro antimicrobial activity, including within biofilm; and high viability after delivery by nebulization. Nebulized phage therapy may offer a novel treatment approach for chronic *P. aeruginosa* pulmonary infections in PwCF with *P. aeruginosa* infection.

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532

Humoral and cell-mediated responses to BNT162b2 mRNA vaccine against SARS-CoV-2 in people with cystic fibrosis

V. Daccò[1], L. Cariani[2], G. Alicandro[1,3], C. Rosazza[1], B. Orena[2], F. Ferraro[4], C. Lanfranchi[4], M. Liporace[4], C. Colombo[1,3]. *[1]Cystic Fibrosis Center, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]Microbiology Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [3]Pathophysiology and Transplantation, University of Milan, Milan, Italy; [4]University of Milan, Milan, Italy*

Background: The BNT162b2 mRNA vaccine (Pfizer-BioNTech) was the first anti-SARS-CoV-2 vaccine approved and has shown 95% efficacy against severe COVID-19. The vaccine elicits a combined humoral and cellular adaptive immune response, albeit with high between-subject variability. The humoral response wanes 4 to 6 months after vaccination and, considered alone, does not appear to be indicative of protective immune memory. The role of cell-mediated immune response, which may be more relevant in the long-term protection against SARS-CoV-2, has not been clarified. Our aim was to evaluate the humoral and cell-mediated immune responses induced by administration of the BNT162b2 vaccine 6 to 8 months after the second dose in people with cystic fibrosis (PwCF) and the possible relationship between the anti-SARS-CoV-2 immunoglobulin (Ig) G-S antibodies (Spike protein) titer and the CD4+/CD8+ cell-mediated response.

Methods: One hundred thirteen PwCF (43 male, median age 21, range 11–64) were enrolled, including 12 patients with virologically confirmed prior SARS-CoV-2 infection. Patients receiving chronic steroid therapy and transplant recipients were excluded. Serum IgG-S was determined by Elecsys anti-SARS-CoV-2 S (Roche) enzyme immunoassay with cut-off for positive response at 0.8 U/mL; cell-mediated immune response was measured using the STANDARDTM F CoviFERON FIA (interferon-gamma) system, a new rapid interferon gamma release assay (IGRA), with cut-off for positive response at 0.30 U/mL on standard F2400 (SD Biosensor, Inc. Korea).

Results: All patients showed a humoral response 6 to 8 months after the second vaccine dose, with a median antibody titer of 1,288 U/mL (interquartile range [IQR] 610–2397). PwCF who were previously infected by SARS-CoV-2 had higher antibody titers than those naïve to the virus (median 6,302, IQR 4272–8349 vs 1,180, IQR 535–1742; $p < 0.001$). Sixty-one patients (54%) developed a cell-mediated immune response against SARS-CoV-2. Antibody titer was higher in patients with a positive cell-mediated response (median 1453, IQR 778–4473) than in those without (median 1054, IQR 510–1498) ($p = 0.01$).

Conclusions: All patients developed an adequate humoral response after two doses of BNT162b2 vaccine; the antibody titer was higher in patients with previous SARS-CoV-2 infection than in naïve patients. We documented a cell-mediated response in 54% of patients, and this was associated with a higher antibody titer. Further studies are needed to understand whether development of cell-mediated immune response is elicited with greater protection against severe COVID-19 in PwCF. If this were the case, this rapid and relatively inexpensive test might be a useful tool to determine the best timing for additional vaccine doses in this clinically vulnerable population.

533

Small-molecule interference of the *Pseudomonas aeruginosa* glyoxylate pathway

N. Evans[1], K. Valladares[2], P. Pukkanasut[3], S. Velu[3], J. Scoffield[1]. *[1]Microbiology, University of Alabama at Birmingham, Birmingham, AL; [2]Division of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL; [3]Chemistry, University of Alabama at Birmingham, Birmingham, AL*

Background: *Pseudomonas aeruginosa* has been shown to use the glyoxylate pathway during chronic cystic fibrosis (CF) airway disease to persist during chronic infection, metabolize nutrients, and upregulate virulence factors. Studies have demonstrated that isocitrate lyase (ICL), the first enzyme in the glyoxylate pathway, is constitutively upregulated in *P. aeruginosa* isolates from the lungs of people with CF but not in isolates from acute infections. These findings illustrate the importance of ICL for chronic infection of *P. aeruginosa* and, combined with the lack of ICL orthologs in humans, make it an attractive target for antimicrobials.

Methods: A small-molecule compound library was screened in silico via a docking model to ICL. The top 40 candidates were selected by their docking score, commercial availability, and feasibility of synthesis. These small molecules were screened for their ability to inhibit *P. aeruginosa* growth (OD_{600}) when grown in minimal media acetate, which requires ICL activity, and not inhibit the bacterium when it was grown in minimal media containing glucose or succinate. Strains PAO1 (acute wound isolate) and FRD1 (chronic CF isolate) were used in this study. Small molecules that inhibited *P. aeruginosa* on acetate, but not glucose and succinate, were further characterized for their ability to disrupt alginate, pyocyanin, pyoverdine formation, and biofilm development, which are virulence factors that require optimal ICL activity. We also tested the ability of candidate compounds to rescue *Drosophila melanogaster* from killing by *P. aeruginosa*.

Results: Five candidate compounds were able to inhibit *P. aeruginosa* growth on acetate, in addition to glucose and succinate, but one small-molecule candidate, designated 37A, reduced growth on acetate but not when *P. aeruginosa* was grown on glucose and succinate, indicating that 37A may selectively inhibit ICL activity, which is required for growth on acetate. Small molecule 37A also decreased production of biofilm,