in the supernatant of a liquid culture were extracted with dichloromethane and with ethyl acetate. Metabolomics studies (UHPLC-DAD-ESI/QTOF, UV and UPLC-Orbitrap, MS) were performed.
Results: Multivariate Analyses of the LC-MS data showed that first colonization ***Pa*** strains could be differentiated from chronic colonization ones. These ***Pa*** strains produced notably more Alkyl- Quinolones (AQ) derivatives, especially five AQs that were discriminant: HQC5, HQNOC7, HQNOC7:1, Db-PQS C9 and HQNOC9:1. However, the production of HHQ was equivalent between strain types. The HHQ/HQNOC9:1 ratio was then observed to be significantly different between chronic and primo-colonizing strains by using both UV (*p* value = 0.003) and HRMS data (*p* value = 1.5E-5).
Conclusions: Some of the AQ derivatives can be used as biomarkers for an improve management of CF patients as well as a better definition of the clinical stages of ***Pa*** infection. Detection of AQs directly in biological fluids as well as development of AQ biosensors could facilitate the implementation of such diagnostic tools.

ePS6.04
2-Alkyl-4-quinolone quorum sensing signal molecules are potential biomarkers in cystic fibrosis pseudomonal infection

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Objectives: *Pseudomonas aeruginosa* (*P.aeruginosa*) is an important respiratory pathogen in cystic fibrosis (CF) and is associated with increased mortality and lung function decline.
P. aeruginosa produces intercellular signalling molecules including 2-alkyl-4-quinolones (AQs), which regulate virulence factor production and biofilm formation in the CF airways. As AQs are detectable in sputum, plasma and urine of adults with CF and chronic pulmonary infection of *P. aeruginosa,* they are potential biomarkers of infection. Using culture-independent methods, we explored the correlation of AQs measured in sputum, plasma and urine with live *P. aeruginosa* load in CF adults.
Methods: Using a live/dead cell separation technique, we analysed 75 sputum samples at clinical stability and 49 paired sputum samples at the beginning and end of antibiotic treatment following pulmonary exacerbation in CF adults. *P. aeruginosa* load obtained from quantitative Polymerase Chain Reaction (qPCR) was compared with the presence and concentration of AQs measured previously in sputum, plasma and urine.
Results: At clinical stability, the AQs which showed correlation consistently in all sample types (sputum, plasma and urine) with live *P. aeruginosa* load were HHQ, NHQ and HQNO. During infective exacerbations, positive correlations were observed with NHQ and HHQ pre-antibiotics in all sample types and a reduction of live *P. aeruginosa* load was associated with changes in plasma and urine NHQ levels (Spearman rank correlation, plasma: r = 0.473, p = 0.005, urine: r = 0.445, p = 0.009).
Conclusion: AQ levels measured in adult CF samples are associated with culture-independent live *P. aeruginosa* load in the lungs and have potential as biomarkers of microbial burden of infection during pulmonary exacerbations.

ePS6.05
Performance of a new diagnostic tool for the selection of optimal antibiotics for patients with cystic fibrosis (clinical efficacy data)

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Objectives: AntibioticSelection is a novel culture-based test system employing new microbiological algorithms and enabling the selection of effective antibiotics (Abx) even for polymicrobial drug-resistant infections in patients with cystic fibrosis (CF). AntibioticSelection is a multi-well plate filled with nutrient medium (NM) enabling rapid simultaneous growth of bacteria in mixed biofilms. Clinical specimen is directly plated to the medium. Each well contains NM supplemented with Abx (1 Abx or 1 Abx mix per well; control wells are Abx free). Antibiotics in the NM are at concentrations clinically achievable at the site of infection. Abx are categorized as effective if they completely prevent the growth of all bacteria present in the biospecimen.
Methods: 6-y longitudinal data for the efficacy of the use of Antibiotic Selection (10 patients) vs. conventional antimicrobial susceptibility testing (AST) for antibiotic selection for CF patents.
Results: When ABXs were selected with conventional AST, the median number of hospitalisations due to pulmonary exacerbations in 3 years was around 6. Inflammation markers were elevated in all patients within 7 days of hospitalisation. After the treatment selected with conventional AST, WBC was normalised in 30% of patients and CRP only in 10%. In turn, once switched to AntibioticSelection, both WBC and CRP were normalised in 100% patients. On year 2 and 3 of AntibioticSelection usage the levels of these pro-inflammatory markers were not elevated. These patients had no signs of acute inflammation (p< 0.001%) and required no hospitalisations with the exception of a prophylactic one. We found that FEV, following the use of AntibioticSelection, had increased by 18% and 27% after the 2nd and 3rd years (p< 0.001%). Body Mass Index increased by 19% as well (p< 0.05%).
Conclusion: AntibioticSelection utilizing a novel principle of antibiotic selection based on lung microbiota population response to the antibiotics enables the selection of significantly more effective antibiotics for CF patients.

ePS6.06
Isolating and characterising phages against *Pseudomonas aeruginosa* and *Staphylococcus aureus* in children with cystic fibrosis

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Introduction and objective: Phage therapy to treat chronic lung infections in patients with Cystic Fibrosis (CF) is attractive due to its safety, specificity, natural occurrence and ability to potentially be utilised as a targeted inhaled aerosol therapy. In vitro studies have also shown the ability of phages to penetrate bacterial biofilms and thus help eradicate them.
This study was designed to evaluate the feasibility of isolating, propagating and purifying phages against bacterial isolates commonly seen in children with CF.
Methods: Nine clinical bacterial isolates of *Staphylococcus aureus* (n = 6), non-mucoid *Pseudomonas aeruginosa* (n = 2) and mucoid *Pseudomonas aeruginosa* (n = 1) were obtained from sputa of patients followed up in The Children's Hospital at Westmead CF clinic. Phages for each strain were isolated from cocktails of environmental water samples. The lysates produced were extracted and subjected to phage propagation and purification using the Phage on Tap (PoT) protocol to produce high-titre homogenous phages.
Results: Fourteen morphologically distinct plaques were observed on the respective bacterial culture plates (*S. aureus* n = 8, *P. aeruginosa* n = 6). Five phages (*S. aureus* n = 3 and *P. aeruginosa* n = 2) were selected and amplified to high titres (10^7 to 10^8 plaque-forming units [pfu]/mL). The 3 *S. aureus*

phages showed highly isolate-specific lytic activity. Both *P. aeruginosa* phages that were isolated exhibited a wider host range against all of the *P. aeruginosa* clinical isolates tested, which included both mucoid and non-mucoid strains. The bactericidal activity was further demonstrated on a time-kill curve.
Conclusion: We were able to successfully isolate and purify phages with lytic activity against both mucoid and non-mucoid *P. aeruginosa* as well as *S. aureus* clinical isolates. This pilot study demonstrates the feasibility of isolating phages that may potentially be useful in the treatment of CF patients with chronic respiratory infections.

ePS6.07
Evaluation of the activity of lytic bacteriophages on a representative collection of *Pseudomonas aeruginosa* clinical isolates collected from adult patients with cystic fibrosis

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Objectives: Multi-resistant and pan-resistant *P. aeruginosa* are increasingly found in cystic fibrosis (CF). Bacteriophages (phages) are viruses specifically killing bacteria without affecting human cells and the commensal flora. From this perspective, phage therapy could bring a significant benefit in the treatment of CF. In this study, we evaluated the susceptibility of *P. aeruginosa* clinical isolates from CF patients to an extensive collection of lytic phages.
Methods: A representative collection of 51 *P. aeruginosa* isolates collected from 51 patients in 2016 at the CHUV was gathered according to their different antibiogram profiles. 104 phages maintained in our laboratory were tested in this study. Phagograms were performed by spotting drops of serial dilutions of each phage stock on top of soft-agar plates containing the isolates. After overnight incubation at 37°C, phagograms were determined by checking for lysis zones.
Results: *P. aeruginosa* phages were able to infect 84,3% of the isolates. Phage 4073_0118 had the broadest host range with 45,1% coverage. 72,5% of the strains were susceptible to at least two phages and 70,6% to three phages or more. Only eight strains (15,7%) were fully resistant to all phages.
Conclusion: This study highlighted that our current phage collection has a high coverage of representative *P. aeruginosa* isolates collected from local patients suffering from CF. As at least two phages are necessary to design a cocktail often avoiding the selection of phage-resistant clones, such cocktails could be produced for ca. 70% of the patients with our current phage collection. Next steps will be to.
i. assemble cocktails and study their *in vitro* antibacterial activities,.
ii. isolate phages for the non-properly covered strains, and.
iii. test the best cocktails in a relevant *in vivo* model.

ePS6.08
Intranasal or oral *Lactobacilli* administration: which one is best for fighting against *Pseudomonas aeruginosa* respiratory tract infections?

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Objectives: In CF patients, *Pseudomonas aeruginosa* (Pa) chronic lung infections combined with acquisition of antibiotics resistance leads to therapeutic deadlock. Among non-antibiotic alternative, the use of *Lactobacilli* is promising since its oral administration (OA) stimulates immune system, decreases nosocomial pneumonia & CF exacerbations incidence. IntranasaI administration (IA) stimulates respiratory immunity & modifies lung architecture. Screened from a collection of 50 CF patients expectorations, 3 *Lactobacillus* (*L. paracasei* Lp, *L. salivarius* Ls & *L. brevis* Lb) respiratory strains were identified for its anti-Pa properties *in vitro*.
Methods: Selected strains IA & OA were tested, alone or cocktail (Lpsb, Lsb) for preventive effect in a murine model of acute Pa pneumonia. *Lactobacillus* GG was used as a control. IA & OA of *Lactobacillus* strains (10^6CFU/mice) 18 h prior to PaO1 infection (10^6CFU/mice) was evaluated in 12 groups of C57BL/6 mice (Lpsb, Lsb, Lp, Ls, Lb, Pa, Lpsb+Pa, Lp+Pa, Ls+Pa, Lb+Pa, Lsb+Pa, LGG+Pa) & 3 groups (Lsb, Lsb+Pa, LGG+Pa) respectively. At 24 h PA post-infection (pi), lung & serum were collected for bacterial counts & cytokines analysis.
Results: The Lpsb cocktail increased the survival rate to 7 days (100% $p < 0.001$) compared to Pa group (11.7%). *Lactobacillus* treatment decreased the Pa lung load 24 h pi compared to Pa group with a higher effect for Lpsb, Lsb, Ls & Lb group (reduction $>1\log_{10}$ $p < 0.05$). Interestingly, our *Lactobacillus* strains had better anti-Pa properties than the LGG strain & its IA led to a better reduction of Pa lung load 24 h pi than OA. Preventive *Lactobacillus* treatment decreased proinflammatory cytokines (preliminary results).
Conclusion: This study demonstrated the better protective efficacy of live *Lactobacillus* IA *vs* OA against murine Pa pneumonia. Mechanistic approaches are under progress. *L. salivarius* & *L. brevis* are promising beneficial strains in the context of lung infection in CF.

ePS6.10
Glatiramer acetate improves the killing ability of tobramycin in *Pseudomonas aeruginosa* cultured from cystic fibrosis clinical samples

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Objectives: Glatiramer acetate (GA), is a drug licensed for treatment of multiple sclerosis, with which we have previously reported modest antimicrobial activity against *Pseudomonas aeruginosa* (*Pa*). Peptide in structure, GA is similar to antimicrobial peptides, some of which have been shown to increase antibiotic efficacy. We investigated GA as an antibiotic resistance breaker of clinical cystic fibrosis *Pa* against the common antibiotic, tobramycin.
Methods: Ten clinical *Pa* from CF patients, with a range of antibiograms, were incubated in Mueller-Hinton broth at varying tobramycin (TOB) concentrations, with/without 50 mg/L GA. After overnight incubation, colonies were counted ($n = 3$ experiments). Inhibition Curves of CFU/mL for TOB and TOB+GA were generated by Nonlinear Fit, as a percentage of untreated bacteria (GraphPad Prism). Minimum inhibitory concentrations of 50% (MIC_{50}) and 90% (MIC_{90}) of *Pa* cells were interpolated from the curves.
Results: Across 10 *Pa* strains tested, values of TOB MIC_{50} and MIC_{90} were significantly reduced by addition of GA ($p = 0.004$ and 0.002, respectively), indicating the same inhibition of growth by lower TOB concentrations. Mean TOB MIC_{50} reduced from 26.4 to 12.0 mg/L and mean MIC_{90} dropped from 67.6 to 44.8 mg/L by co-administration of GA. Presence of GA was effective at lowering MICs in both TOB-sensitive ($n = 5$) and -resistant *Pa*; MIC_{50} dropped from 0.420 to 0.259 mg/L and from 52.4 to 23.8 mg/L, respectively.
Conclusion: Both TOB-sensitive and TOB-resistant *Pa* strains demonstrate increased susceptibility to TOB in the presence of GA, *in vitro*. Co-administration of GA could enhance efficacy of TOB in cystic fibrosis, as an antibiotic resistance breaker. With a good safety profile in a chronic condition, glatiramer acetate is a strong candidate for repurposing as an antibiotic adjunct. Work is ongoing onactivity of GA in the presence of sputum for confirmation of potential clinical utility.
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