WS11.9 Bacterial *cis*-2-unsaturated fatty acids found in the cystic fibrosis (CF) airway play a role in bacterial interspecies signalling during polymicrobial infection of the CF lung

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There is an increasing appreciation of the polymicrobial nature of many bacterial infections such as those associated with cystic fibrosis (CF) and of the potentially important role for interspecies interactions in influencing both bacterial virulence and response to therapy. Patients with CF are commonly co-infected with *Pseudomonas aeruginosa* and other pathogens including *Burkholderia cenocepacia* and *Stenotrophomonas maltophilia*. These latter bacteria produce signal molecules of the diffusible signal factor (DSF) family, which are *cis*-2-unsaturated fatty acids. We have previously shown by *in vitro* studies that DSF from *S. maltophilia* leads to altered biofilm formation and increased resistance to antibiotics by *P. aeruginosa*; these responses of *P. aeruginosa* require the sensor kinase PA1396. Here we show that DSF signals are present in sputum taken from patients with CF. Presence of these DSF signals was correlated with patient colonisation by *S. maltophilia* and/or *B. cenocepacia*. In animal experiments using CF transmembrane conductance regulator knockout mice, the presence of DSF promoted *P. aeruginosa* persistence. Furthermore, antibiotic resistance of *P. aeruginosa* biofilms grown on human airway epithelial cells was enhanced in the presence of DSF. Taken together, these data provide substantial evidence that interspecies DSF-mediated bacterial interactions occur in the CF lung and may influence the efficacy of antibiotic treatment, particularly for chronic infections involving persistence of bacteria.

WS11.10 Proteomic analysis of the chronically infected CF airways

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Objectives: Progressive lung disease, driven by inflammation secondary to chronic bacterial infection, constitutes the chief burden of CF. We describe a systems biology investigation of the pathogenesis of *Pseudomonas aeruginosa* infected CF airways aiming to identify biomarkers/pathways as potential targets for improved therapy or for use as prognostic indicators.
Methods: We employed multi-dimensional LC-MS/MS to semi-quantitatively contrast the cellular protein profiles of sputum from CF and control cohorts. Importantly, our approach effectively assesses the activity of CF cells directly in their in vivo environment, so taking into account the interactions between host and the highly complex CF microbiome.
Results: 119 of the 2309 human proteins detected were common to all samples (36 CF + 12 control). Of these, 49 were down-regulated and 29 up-regulated in CF ($p < 0.05$). Additionally, 21 proteins were detected exclusively in all CF samples and 17 proteins exclusively in all controls. Analysis for biological relevance using Ingenuity Pathway Analysis (IPA) software identified molecular and cellular functions belonging to the categories of Cell Death; Cellular Movement; Protein Synthesis, Degradation, Trafficking & Post-Translational Modification; Cell-to-Cell Signalling and Interaction; Free Radical Scavenging; and Cellular Assembly and Organisation as divergent between the study cohorts.
Conclusions: Comparison of the infected CF cellular proteome with IPA disease profiles showed up-regulation of proteins previously identified in Respiratory, Immunological and Inflammatory Diseases, and down-regulation of proteins associated with Cancer and Neurological Disease.