Diversity of *Staphylococcus aureus* during chronic airway infection of cystic fibrosis patients

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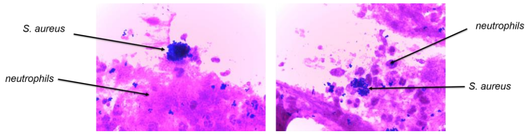
Our study tries to explore to what extend *S. aureus* diversifies in sputa of CF patients being infected for extended periods with *S. aureus*.



Introduction

Cystic fibrosis (CF) is the most frequent genetic disease among caucasians. Due to a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene the chloride channel function of the protein is serverely restricted. This leads to the production of very viscous mucus in exocrine glands, e.g. the lungs, leading to an impaired clearance of the airways. Bacteria such as *Staphylococcus aureus* colonise the lungs very early and cause permanent infections leading to lung insufficency and early death of the patients. *S. aureus* is one of the first pathogens, which can be found in the airways of CF-patients and often stays there for extended periods. The special environment in the CF-airways, the long time of persistence and in many cases frequent antibiotic therapy suggest a high adaptation of the pathogen to its host. As a consequence, *S. aureus* adapts to this environment by changing the phenotype (small colony variants, SCVs, mucoid isolates), acquiring resistance against antibiotics and the presence of different genotypes.

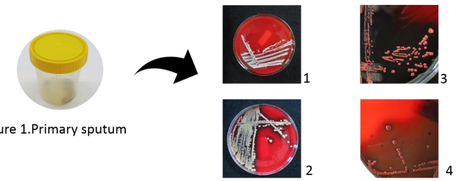
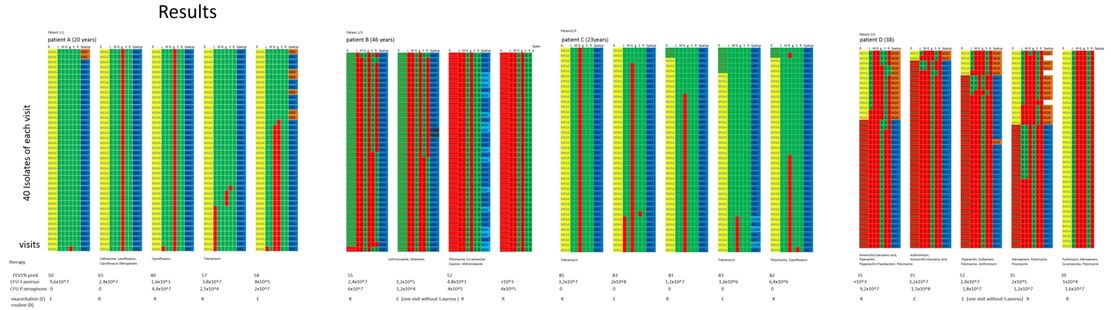


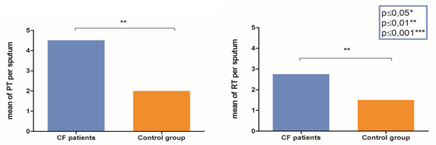
Figure 1.Primary sputum

Results

We followed 14 CF-patients, who were chronically infected by *S. aureus,* for one year: 11 male, 3 female; mean age 28 years. The sputum of the patient was collected on each visit. 40 *S. aureus* colonies were randomly picked and examined concerning their phenotype (PT) (size, mucous characteristic, hemolysis (Fig. 2.1 and 2.2) and ß-toxin-positivity on Columbia blood, Kongored and Schaedler agar plates). The resistotype (RT) was detected by VITEK2 or (in case of SCVs or mucoid strains) by agar diffusion. As a control, 40 *S. aureus* isolates randomly picked from *S. aureus*-positive specimens (lung of non-CF patients (n=7) or from tissue (n=7) were investigated for the same parameters.



The heatmaps illustrate the resistance (red) or susceptibility (green) to ß-lactams, clindamycin, macrolides, gentamicin, levofloxacin, trimethoprim/sulfamethoxazole and rifampicin. Only the data of patients with exacerbations are shown. The antibiotic therapy is listed below the Figure. White space means the data are not jet collected. Molecular typing (*spa*-sequence typing) is shown in the last column of each visit. The main *spa*-type is highlighted in blue, all related types are marked with different shades of blue. All not related types are highlighted in orange.



Different numbers of phenotypes (PT) and resistotypes (RT) were found in each sputum. In sputa of CF-patients up to 20 different PT (mean 4,5; see Fig. on the left) could be characterized, 2,8), wwhereas the control group showed only up to 8 PT (mean 2). Up to 8 different RTs were identified in CF-sputa (mean hile in control specimens up to 3 different (mean 1,5). *Spa*-types varied from one to 7 per sputum of CF-patients (mean 1,9). *Spa*-sequence typing of the control group is in progress.

Conclusions

The high amount of different pheno- and resistotypes, which sometimes change from one visit to the next, reflects the special situation of high selective pressure present in the lungs of CF-patients. Some data indicate a selection of resistotypes by antibiotic therapy leading to higher resistance levels. How far the clinical symptoms of CF are correlated with the number of specific pheno- or resistotypes is subject of further analysis.

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