

## LONGITUDINAL STUDY OF *PSEUDOMONAS AERUGINOSA* ISOLATES FROM CYSTIC FIBROSIS LUNGS

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**Background:** Chronic infection by *P. aeruginosa* in lungs of cystic fibrosis (CF) patients is an example of long-term persistent infections. In contrast to acute infections, which damage the host by virulence factors, chronic infections involve considerable genetic adaptation of the pathogens during their coexistence with the host.

**Objective:** We aim to determine the most significant adaptive changes during the development of *P. aeruginosa* in cases of CF chronic infection.

**Method:** We have investigated in detail one CF patient who has been chronically infected since 1991 by only one genotype, the 'b' clone, a transmissible colonizer isolated from several patients in the Copenhagen CF centre. Five *P. aeruginosa* isolates from 1991 to 2007 were analysed in this longitudinal study. An intermittent isolate of the same genotype, wt'b', displaying a wildtype phenotype, is regarded as a closely related descendant from a common 'b' clone ancestor. Transcriptomic analysis of global gene expression was employed to characterize and compare the isolates.

**Results:** The expression profiles of all the chronic isolates are very different from those of wt'b', estimated by correlation coefficient factors. The similarities of the different adapted isolates have also decreased over time, indicating that mutations have accumulated. We applied a time factor to the transcriptome data and identified genes which changed consistently over time. The results show that genes related to quorum sensing, virulence factors and motility have decreased during the infection, while genes upregulated in the persistence are mainly involved in antibiotic resistance and metabolic optimization.

**Conclusion:** Our data suggest that a series of adaptive changes occurred in *P. aeruginosa* resulting in a successful CF persistor phenotype. This model may have important consequences for designing new therapies towards CF lung infections and for the understanding of chronic microbial infections in general.