Evolution and diversification of Pseudomonas aeruginosa in the paranasal sinuses of cystic fibrosis children have implications for chronic lung infection

The opportunistic pathogen Pseudomonas aeruginosa is a frequent colonizer of the airways of patients suffering from cystic fibrosis (CF). Depending on early treatment regimens, the colonization will, with high probability, develop into chronic infections sooner or later, and it is important to establish under which conditions the switch to chronic infection takes place. In association with a recently established sinus surgery treatment program for CF patients at the Copenhagen CF Center, colonization of the paranasal sinuses with P. aeruginosa has been investigated, paralleled by sampling of sputum from the same patients. On the basis of genotyping and phenotypic characterization including transcription profiling, the diversity of the P. aeruginosa populations in the sinuses and the lower airways was investigated and compared. The observations made from several children show that the paranasal sinuses constitute an important niche for the colonizing bacteria in many patients. The paranasal sinuses often harbor distinct bacterial subpopulations, and in the early colonization phases there seems to be a migration from the sinuses to the lower airways, suggesting that independent adaptation and evolution take place in the sinuses. Importantly, before the onset of chronic lung infection, lineages with mutations conferring a large fitness benefit in CF airways such as mucA and lasR as well as small colony variants and antibiotic-resistant clones are part of the sinus populations. Thus, the paranasal sinuses potentially constitute a protected niche of adapted clones of P. aeruginosa, which can intermittently seed the lungs and pave the way for subsequent chronic lung infections.