

Evolution of the microbiome and adaptation of *Pseudomonas aeruginosa* after lung transplantation in cystic fibrosis patients

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Objectives

The airways of cystic fibrosis (CF) patients are colonized by various microorganisms. *Pseudomonas aeruginosa* is predominant in adults, causing chronic infections and contributing to lung destruction. Lung transplantation (LT) is a recognized treatment for CF patients with end-stage disease. However, the lung graft is frequently colonized by *P. aeruginosa* residing in the sinuses of the recipient. Presence of *P. aeruginosa* in the new lungs has been associated with graft rejection. The lung graft thus represents an unique opportunity to study *in vivo* colonization and adaptation to a novel environment, a key step of bacterial pathogenesis. Our work aims to decipher how bacteria adapted for years to the CF environment will colonize the non-CF allograft.

Methods

Lower airway samples of CF-patients were collected at regular time intervals before LT and during 2 years after LT. A longitudinal metagenomic study was performed to evaluate the dynamics of bacterial populations during graft colonization. In parallel, *P. aeruginosa* strains were isolated from these airway samples and their genotype was characterized. Phenotypic and genetic changes were screened to identify particular traits involved in the adaptation to the allograft.

Results

Our metagenomic study showed that: i) colonization of the allograft by *P. aeruginosa* occurred in the first days after LT, ii) presence of *P. aeruginosa* in the graft is associated with a drastic decrease of the microbial diversity and richness. *P. aeruginosa* isolates had the same genotype pre- and post-LT, suggesting that the same strain is able to colonize the allograft. After 3 months, *P. aeruginosa* isolates displayed an increase in biofilm formation and swimming motility capacities when compared to pre-LT isolates. These adaptive phenotypes could be essential for efficient colonization of the allograft by *P. aeruginosa*. Deep sequencing analysis allowed us to reconstruct the phylogenetic history of the isolated *P. aeruginosa*, and the dynamics of mutation acquisition after LT in the whole *P. aeruginosa* population. In addition, we identified mutations probably involved in the extinction of several lineages of *P. aeruginosa* colonizing the allograft.

Conclusion

A better understanding of the dynamics of bacterial adaptation and competition within a novel environment might help to design new preventive strategies aiming to minimize graft colonization and rejection.