Population proteome investigation of *Pseudomonas aeruginosa* clinical isolates collected from cystic fibrosis patient airways

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Overview

- ***P. aeruginosa* populations collected from CF airways were cultured, harvested and proteome analyzed.**
- ***P. aeruginosa* populations exhibited distinct *ex vivo* proteome according to the originated CF lung regions .**
- **Protein-level changes were consistent with functional diversification of *P. aeruginosa* populations in different lung regions.**

Introduction

The majority of cystic fibrosis (CF) patients suffer from chronic airway infections with *Pseudomonas aeruginosa* (*PA*). Unfortunately, *PA* infections cause lung inflammation and injury, resulting in permanent lung function decline. By their mid-thirties, many CF patients undergo lung transplantation, which is often seen as the last resort[1]. The CF diseased lungs (Fig. 1) collected after transplantation present an unusual opportunity to study the *in vivo* bacterial infections and host responses in CF patients.

Recent studies show that single lineages of infecting *P. aeruginosa* diversify into populations with markedly different genotypes and phenotypes[2]. We hypothesize that such *PA* diversification may have functional relationship with the clinical observation that different regions in a CF lung exhibit relatively different degrees of lung damage (Fig. 1). To characterize the functional diversification of *PA* isolates in CF lungs, we examined the population proteomes of 96 *PA* isolates collected from airway secretions of each lung region.

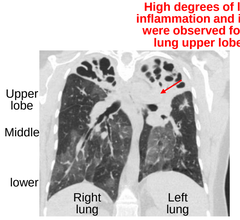
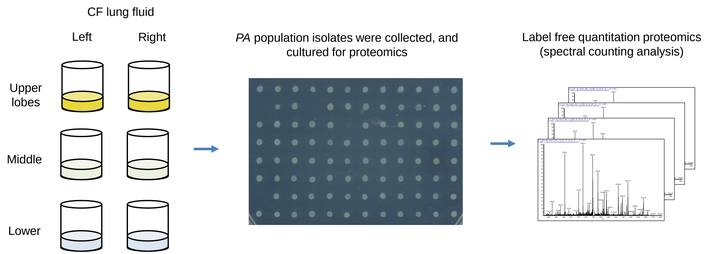
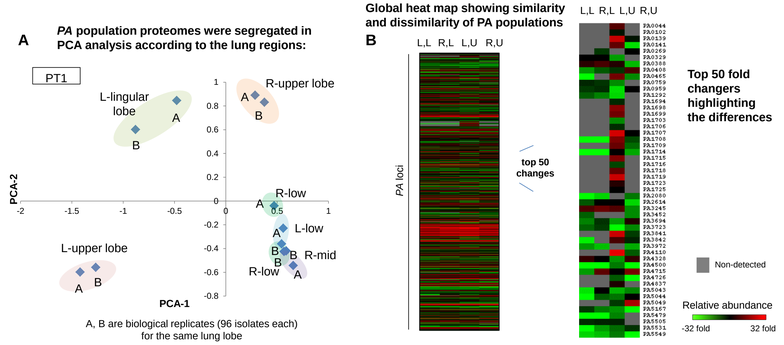


Fig.1 CT scan of CF diseased lung showed heterogeneity of lung damage.

Methods



Results



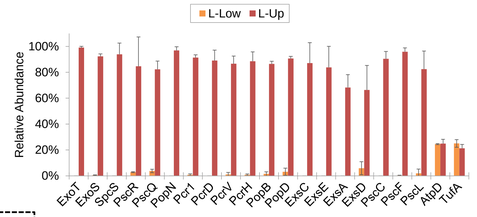
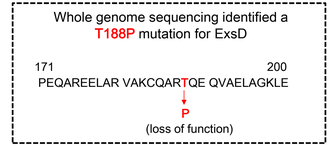
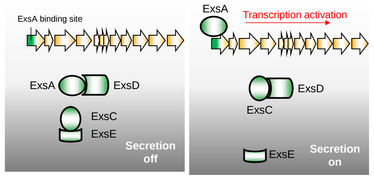
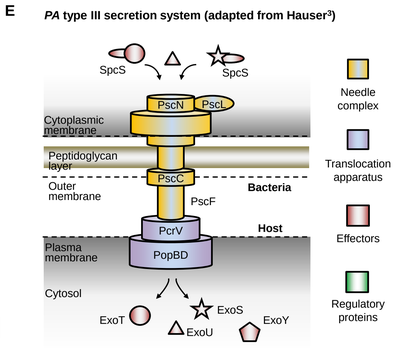


Fig. 2 Distinct *PA* population proteomes were observed for different lung regions. The type III secretion proteins were found dramatically up-regulated in left-upper lobes.

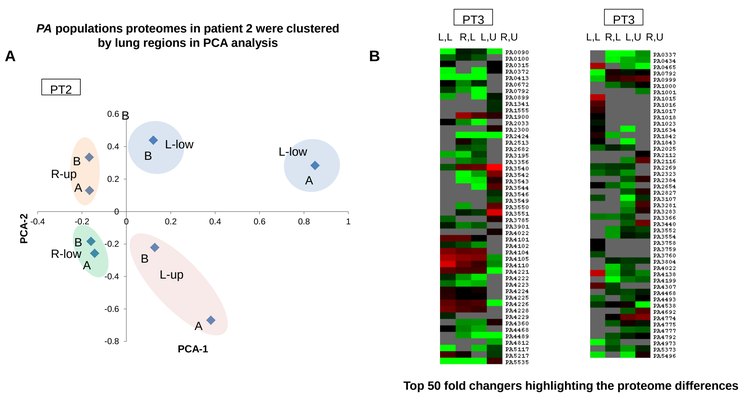


Loss of function of ExsD causes constitutive expression of type III secretion factors.





Results



Top 50 fold changers highlighting the proteome differences

Fig. 3 Lung region-specific *PA* population proteomes were also observed in other CF patients.

Conclusion

- **Heritable changes within the infecting bacterial population can be revealed through population proteome analyses from cultured cells.**
- **Population proteome analysis indicates that lung region-specific evolution results in population diversity within patient lungs.**
- **Results revealed increased expression of virulence factors in regions that suffered increased damage.**
- **Whole genome sequencing confirmed this heritable change and revealed mutations in a negative regulator (ExsD) of type III secretion.**

Acknowledgements

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References

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3. Hauser AR et al, Nat Rev Microbiol. 2009, 7(9):654-65.