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Chronic *Pseudomonas aeruginosa* infections evade antibiotic therapy and are associated with mortality in cystic fibrosis (CF) patients. We find that *in vitro* resistance evolution of *P. aeruginosa* toward clinically relevant antibiotics leads to phenotypic convergence toward distinct states. These states are associated with collateral sensitivity toward several antibiotic classes and encoded by mutations in antibiotic resistance genes, including transcriptional regulator nfxB. Longitudinal analysis of isolates from CF patients reveals similar and defined phenotypic states, which are associated with extinction of specific sub-lineages in patients. In-depth investigation of chronic *P. aeruginosa* populations in a CF patient during antibiotic therapy revealed dramatic genotypic and phenotypic convergence. Notably, fluoroquinolone-resistant subpopulations harboring nfxB mutations were eradicated by antibiotic therapy as predicted by our *in vitro* data. This study supports the hypothesis that antibiotic treatment of chronic infections can be optimized by targeting phenotypic states associated with specific mutations to improve treatment success in chronic infections.

General information

State: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Research Groups, Bacterial Synthetic Biology, Department of Systems Biology, Department of Biotechnology and Biomedicine, Office for Study Programmes and Student Affairs, CHO Core, iLoop, Infection Microbiology, Copenhagen University Hospital
Pages: 121-134
Publication date: 2018
Peer-reviewed: Yes

Publication information

Journal: Cell
Volume: 172
Issue number: 1-2
ISSN (Print): 0092-8674
Ratings:
BFI (2018): BFI-level 3
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 21.99 SJR 25.137 SNIP 5.008
Web of Science (2017): Impact factor 31.398
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 22.79 SJR 27.691 SNIP 4.946
Web of Science (2016): Impact factor 30.41
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 23.62 SJR 27.712 SNIP 5.294
Web of Science (2015): Impact factor 28.71
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 24.91 SJR 28.505 SNIP 5.66
Web of Science (2014): Impact factor 32.242
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 24.88 SJR 28.254 SNIP 5.889
Web of Science (2013): Impact factor 33.116
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 23.99 SJR 25.117 SNIP 6.315
Web of Science (2012): Impact factor 31.957
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes