Antibiotic combination therapy can select for broad-spectrum multidrug resistance in Pseudomonas aeruginosa - DTU Orbit (08/11/2017)

Antibiotic combination therapy can select for broad-spectrum multidrug resistance in *Pseudomonas aeruginosa*
Combination therapy with several antibiotics is one strategy that has been applied in order to limit the spread of antimicrobial resistance. We compared the de novo evolution of resistance during combination therapy with the β-lactam ceftazidime and the fluoroquinolone ciprofloxacin with the resistance evolved after single-drug exposure. Combination therapy selected for mutants that displayed broad-spectrum resistance, and a major resistance mechanism was mutational inactivation of the repressor gene *mexR* that regulates the multidrug efflux operon *mexAB–oprM*. Deregulation of this operon led to a broad-spectrum resistance phenotype that decreased susceptibility to the combination of drugs applied during selection as well as to unrelated antibiotic classes. Mutants isolated after single-drug exposure displayed narrow-spectrum resistance and carried mutations in the MexCD–OprJ efflux pump regulator gene nfxB conferring ciprofloxacin resistance, or in the gene encoding the non-essential penicillin-binding protein DacB conferring ceftazidime resistance. Reconstruction of resistance mutations by allelic replacement and in vitro fitness assays revealed that in contrast to single antibiotic use, combination therapy consistently selected for mutants with enhanced fitness expressing broad-spectrum resistance mechanisms.

General information

State: Published
Organisations: National Veterinary Institute, Section for Bacteriology, Pathology and Parasitology, Department of Systems Biology, Infection Microbiology, Infection Microbiology, University of Copenhagen, Rigshospitalet, Technical University of Denmark
Authors: Vestergaard, M. (Ekstern), Paulander, W. (Ekstern), Marvig, R. L. (Ekstern), Clasen, J. (Intern), Jochumsen, N. (Ekstern), Molin, S. (Intern), Jelsbak, L. (Intern), Ingmer, H. (Ekstern), Folkesson, S. A. (Intern)
Number of pages: 8
Pages: 48-55
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information

Journal: International Journal of Antimicrobial Agents
Volume: 47
ISSN (Print): 0924-8579
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.565 SNIP 1.285 CiteScore 3.38
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.683 SNIP 1.54 CiteScore 3.45
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.475 SNIP 1.641 CiteScore 3.45
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.693 SNIP 1.58 CiteScore 3.63
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.624 SNIP 1.495 CiteScore 3.57
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.38 SNIP 1.315 CiteScore 3.15
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.323 SNIP 1.207
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.019 SNIP 1.013
Web of Science (2009): Indexed yes

BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.186 SNIP 1.064
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.862 SNIP 0.994
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.924 SNIP 1.01
Scopus rating (2005): SJR 0.939 SNIP 1.13
Scopus rating (2004): SJR 0.693 SNIP 1.063
Scopus rating (2003): SJR 0.742 SNIP 1.02
Scopus rating (2002): SJR 0.64 SNIP 0.743
Scopus rating (2001): SJR 0.565 SNIP 0.739
Scopus rating (2000): SJR 0.441 SNIP 0.738
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.342 SNIP 0.561
Original language: English
Antibiotics, Combination therapy, Multidrug resistance, β-Lactams, Fluoroquinolones, Drug efflux
Electronic versions:
Antibiotic_combination_therapy_can_select_for_broad_spectrum_multidrug_resistance_in_Pseudomonas_aeruginosa.pdf
DOIs:
10.1016/j.ijantimicag.2015.09.014
Source: FindIt
Source-ID: 2287637339
Publication: Research - peer-review › Journal article – Annual report year: 2015