Adaptive Laboratory Evolution of Antibiotic Resistance Using Different Selection Regimes Lead to Similar Phenotypes and Genotypes - DTU Orbit (26/02/2019)

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Antibiotic resistance is a global threat to human health, wherefore it is crucial to study the mechanisms of antibiotic resistance as well as its emergence and dissemination. One way to analyze the acquisition of de novo mutations conferring antibiotic resistance is adaptive laboratory evolution. However, various evolution methods exist that utilize different population sizes, selection strengths, and bottlenecks. While evolution in increasing drug gradients guarantees high-level antibiotic resistance promising to identify the most potent resistance conferring mutations, other selection regimes are simpler to implement and therefore allow higher throughput. The specific regimen of adaptive evolution may have a profound impact on the adapted cell state. Indeed, substantial effects of the selection regime on the resulting geno- and phenotypes have been reported in the literature. In this study we compare the geno- and phenotypes of Escherichia coli after evolution to Amikacin, Piperacillin, and Tetracycline under four different selection regimes. Interestingly, key mutations that confer antibiotic resistance as well as phenotypic changes like collateral sensitivity and cross-resistance emerge independently of the selection regime. Yet, lineages that underwent evolution under mild selection displayed a growth advantage independently of the acquired level of antibiotic resistance compared to lineages adapted under maximal selection in a drug gradient. Our data suggests that even though different selection regimes result in subtle genotypic and phenotypic differences key adaptations appear independently of the selection regime.

General information
State: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Bacterial Synthetic Biology, Department of Applied Mathematics and Computer Science, Research Groups
Contributors: Jahn, L. J., Munck, C., Ellabaan, M. M. H., Sommer, M. O. A.
Number of pages: 14
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Microbiology
Volume: 8
Article number: 816
ISSN (Print): 1664-302X
Ratings:
BFI (2019): BFI-level 1
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.19 SJR 1.699 SNIP 1.174
Web of Science (2017): Impact factor 4.019
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.16 SJR 1.759 SNIP 1.161
Web of Science (2016): Impact factor 4.076
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.15 SJR 1.869 SNIP 1.193
Web of Science (2015): Impact factor 4.165
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 3.76 SJR 1.879 SNIP 1.148
Web of Science (2014): Impact factor 3.989
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 3.56 SJR 1.776 SNIP 0.949
Web of Science (2013): Impact factor 3.941
ISI indexed (2013): ISI indexed no
Web of Science (2013): Indexed yes