Biochemical mechanisms determine the functional compatibility of heterologous genes - DTU Orbit (28/04/2019)

Biochemical mechanisms determine the functional compatibility of heterologous genes
Elucidating the factors governing the functional compatibility of horizontally transferred genes is important to understand bacterial evolution, including the emergence and spread of antibiotic resistance, and to successfully engineer biological systems. In silico efforts and work using single-gene libraries have suggested that sequence composition is a strong barrier for the successful integration of heterologous genes. Here we sample 200 diverse genes, representing >80% of sequenced antibiotic resistance genes, to interrogate the factors governing genetic compatibility in new hosts. In contrast to previous work, we find that GC content, codon usage, and mRNA-folding energy are of minor importance for the compatibility of mechanistically diverse gene products at moderate expression. Instead, we identify the phylogenetic origin, and the dependence of a resistance mechanism on host physiology, as major factors governing the functionality and fitness of antibiotic resistance genes. These findings emphasize the importance of biochemical mechanism for heterologous gene compatibility, and suggest physiological constraints as a pivotal feature orienting the evolution of antibiotic resistance.

General information
Published status: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Bacterial Synthetic Biology, Research Groups, Department of Biotechnology and Biomedicine, Technical University of Denmark
Contributors: Porse, A., Schou, T. S., Munck, C., Ellabaan, M. M. H., Sommer, M. O. A.
Number of pages: 11
Publication date: 2018
Peer-reviewed: Yes

Publication information
Journal: Nature Communications
Volume: 9
Article number: 522
ISSN (Print): 2041-1723
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
Original language: English
Electronic versions:
PorseEtAlFinalPublishedVersion.pdf
DOIs:
10.1038/s41467-018-02944-3
Research output: Contribution to journal › Journal article – Annual report year: 2018 › Research › peer-review