Cellular responses to reactive oxygen species are predicted from molecular mechanisms

Catalysis using iron–sulfur clusters and transition metals can be traced back to the last universal common ancestor. The damage to metalloproteins caused by reactive oxygen species (ROS) can prevent cell growth and survival when unmanaged, thus eliciting an essential stress response that is universal and fundamental in biology. Here we develop a computable multiscale description of the ROS stress response in Escherichia coli, called OxidizeME. We use OxidizeME to explain four key responses to oxidative stress: 1) ROS-induced auxotrophy for branched-chain, aromatic, and sulfurous amino acids; 2) nutrient-dependent sensitivity of growth rate to ROS; 3) ROS-specific differential gene expression separate from global growth-associated differential expression; and 4) coordinated expression of iron–sulfur cluster (ISC) and sulfur assimilation (SUF) systems for iron–sulfur cluster biosynthesis. These results show that we can now develop fundamental and quantitative genotype–phenotype relationships for stress responses on a genome-wide basis.

General information
Publication status: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, Network Reconstruction in Silico Biology, ALE Technology & Software Development, Big Data 2 Knowledge, University of California at San Diego
Pages: 14368-14373
Publication date: 2019
Peer-reviewed: Yes

Publication information
Journal: Proceedings of the National Academy of Sciences of the United States of America
Volume: 116
Issue number: 28
ISSN (Print): 0027-8424
Ratings:
BFI (2019): BFI-level 2
Web of Science (2019): Indexed yes
Original language: English
Keywords: Reactive oxygen species, Oxidative stress, Metabolism, Protein expression, Genome-scale model
DOIs: 10.1073/pnas.1905039116
Source: FindIt
Source-ID: 2450523257
Research output: Contribution to journal › Journal article – Annual report year: 2019 › Research › peer-review