

Is The Ribosome Targeted By Adaptive Mutations - DTU Orbit (08/11/2017)

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Introduction: RNA polymerase and ribosomes, composing the macromolecular synthesis machinery (MMSM), carry out the central processes of transcription and translation, but are usually seen as mechanical elements with no regulatory function. Extensive investigations of gene regulation and the high degree of evolutionary conservation of the cellular MMSM tend to support this view. However, under certain selective conditions the machinery itself may be targeted by adaptive mutations, which result in fitness-increasing phenotypic changes. Here we investigate and characterize the role of ribosomal mutations in adaptive evolution. Methods: Several mutations in ribosomal genes have been identified in the genome analysis of nearly 700 *Pseudomonas aeruginosa* isolates from infected cystic fibrosis patients. Among these mutations we have repeatedly identified insertions, deletions and substitutions in specific ribosomal genes. The bacterial phenotypes of the mutated strains will be investigated. Results: Preliminary assays show that mutant strains have reduced growth rate and an altered antibiotic resistance pattern. The selection for mutations in ribosomal protein genes is partly explainable by the antibiotic treatment of the patient. However, other mutations cannot be directly associated with antibiotic resistance. Conclusions: Clarification of the potential pleiotropic consequences of the specific mutations in ribosomal proteins is important for our understanding of biological evolution, and will have impacts on the design of new treatment strategies to combat microbial infections.

General information

State: Published

Organisations: Novo Nordisk Foundation Center for Biosustainability

Authors: Jimenez Fernandez, A. (Intern), Molin, S. (Intern), Johansen, H. K. (Intern)

Pages: 33-33

Publication date: 2015

Host publication information

Title of host publication: The Danish Microbiological Society Annual Congress 2015 : Programme & Abstracts

Place of publication: Copenhagen

Main Research Area: Technical/natural sciences

Conference: The Danish Microbiological Society Annual Congress 2015, Copenhagen, Denmark, 09/11/2015 - 09/11/2015

Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015