FNR/DNR/ANR-REGULON IN GAMMA-PROTEOBACTERIA

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Resume

Motivation: Comparative approach to computer analysis of regulatory signals allows one to predict new signals in bacterial genomes with high accuracy. A prediction is reliable whenever candidate signals are consistently observed in several related genomes.

Results: We describe the FNR-regulon of the E. coli, Haemophilus influenzae, Vibrio cholerae, Salmonella typhi, Klebsiella pneumoniae, Yersinia pestis, Pasteurella multocida, and Actinobacillus actinomycetemcomitans genomes and ANR/DNR regulon in the Pseudomonas aeruginosa, Pseudomonas fluorescens, Pseudomonas putida, Pseudomonas syringae, Pseudomonas stutzer, and Shewanella putrefaciens genomes.

Introduction

FNR is a cytoplasmic O2-responsive regulator consisting of two domains, sensor and DNA-binding regulator. It activates expression of genes that are required for anaerobic respiration and related pathways in gamma-proteobacteria. FNR activates expression of several anaerobic enzymes, in particular, nitrate and nitrite reductases (anaerobic respiration) and pyruvate formate-lyase (anaerobic fermentation). Besides, FNR represses several genes encoding aerobic enzymes, such as cytochrome d ubiquinol oxidase and NADH dehydrogenase.

In Escherichia coli, expression of more than 120 genes that are included in the FNR modulon depends on alternation of the aerobic and anaerobic growth [1, 2].

The ortholog of FNR in Pseudomonas aeruginosa is ANR. This regulatory protein is required for the anaerobic growth of Pseudomonas aeruginosa. The sequences similar to the consensus FNR-binding motif (TTGAT….ATCAA) were found in the promoter regions of several genes for anaerobic metabolism of Pseudomonas aeruginosa, such as arginine deiminase pathway enzymes (arcDABC), nitrite reductase (nirS), nitric oxide reductase (norCB), and azurin (azu).

ANR was experimentally shown to be necessary for denitrification, arginine deiminase activity and cyanide production of P. aeruginosa [3]. Another CRP/FNR-related regulator, DNR is essential for denitrification, ANR and DNR have similar binding signals, and it is impossible to determine what regulator would bind a candidate site by purely computational methods.

Besides, we assume that in some cases both regulators can bind to the same site.

Methods and Algorithms

Application of the comparative approach to the analysis of regulatory signals allows one to reliably predict new sites in bacterial genomes. Observation of candidate sites upstream of orthologous genes in several related genomes makes a prediction more significant. Here we use the comparative approach for the analysis of the FNR/ANR/DNR regulons of gamma-proteobacteria. Bacterial genomes were analyzed using the software package Genome Explorer [4].

Results and Discussion

We describe the FNR-regulon of the E. coli, Haemophilus influenzae, Vibrio cholerae, Salmonella typhi, Klebsiella pneumoniae, Yersinia pestis, Pasteurella multocida, and Actinobacillus actinomycetemcomitans genomes. The core of the regulon seems to be well conserved. Several new members were found in the FNR-regulon of Escherichia coli [5].

The candidate FNR binding sites were found upstream of twelve genes of E.coli that were known to be regulated by FNR. Fifteen new operons were predicted to be potential members of the FNR-regulon of E. coli, FNR-regulons in the other genomes were described for the first time.

In particular, the comparative analysis of Pasteurellaceae (H. influenzae, P. multocida, A. Actinomycetemcomitans) lead to identification of 26 candidate FNR-regulon genes in P. multocida.

We also described the members of ANR/DNR regulon in the Pseudomonas aeruginosa, Pseudomonas fluorescens, Pseudomonas putida, Pseudomonas syringae, Pseudomonas stutzer, and Shewanella putrefaciens genomes. In Pseudomonas aeruginosa, the regulon contains about 30 candidate members.
Generally, the FNR regulons in Enterobacteriaceae, Vibrionaceae, and Pasteurellaceae are similar, and differ from the ANR/DNR regulon of Pseudomonads. However, there still exist genes that are members of these regulons in all studied genomes.

The FNR regulons of enterics/vibrio have a lot of common members and differ from the ANR regulons in pseudomonads. However, some genes belong to the FNR/ANR regulons in all genomes.

This study is the first attempt to describe global regulons in a large and diverse taxonomic group. Its results provide data to analysis of evolution of regulatory interactions in bacterial genomes. Additionally, new regulatory sites were predicted and regulons of several less studied genomes were described.

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References