

## 4 Obg and Membrane Depolarization Are Part of a Microbial Bet-Hedging Strategy that Leads to Antibiotic Tolerance.

Verstraeten N, Knapen WJ, Kint CI, Liebens V, Van den Bergh B, Dewachter L, Michiels JE, Fu Q, David CC, Fierro AC, Marchal K, Beirlant J, Versées W, Hofkens J, Jansen M, Fauvar M, Michiels J  
Mol Cell. 2015 Jul 2; 59(1):9-21

Save/Follow | Export | Get Article



RECOMMENDATIONS 2 | ABSTRACT | COMMENTS

[expand all](#)

### Recommendations:

Very Good

07 Aug 2015



**Martin Marinus**

**F1000 Microbiology**

University of Massachusetts Medical School, Worcester, MA, USA.

[INTERESTING HYPOTHESIS](#) | [NEW FINDING](#) | [NOVEL DRUG TARGET](#)

DOI: 10.3410/f.725540524.793508205

In this paper, the hypothesis that a conserved GTPase, Obg, is involved in persistence leading to antibiotic resistance is proposed. The evidence tying Obg to expression of a toxin-antitoxin module and the subsequent membrane depolarization, is strong. The central action of Obg on cell metabolism ensures shutdown of cell division, a hallmark of persistence.

#### Disclosures

None declared

[Add a comment](#)

Very Good

22 Dec 2015



**Wolfgang Peti**

**F1000 Structural Biology**

Brown University, Providence, RI, USA.



**Rebecca Page**

**F1000 Structural Biology**

Brown University, Providence, RI, USA.

[NEW FINDING](#) | [NOVEL DRUG TARGET](#)

DOI: 10.3410/f.725540524.793512547

In this paper, the authors show that a conserved GTPase, Obg, plays a critical role in the development of antibiotic tolerance in both *Escherichia coli* and *Pseudomonas aeruginosa*. The authors show that this function of Obg is not related to its role in GTP metabolism or ribosome association. Rather, its role in persistence is dependent on the bacterial alarmone (p)ppGpp, to which it binds directly, and a single Type 1 toxin/antitoxin system *hokB/sokB*.

The authors show that the ability of Obg to induce persistence is due to the production of the HokB membrane-associated peptide, which binds the membrane and causes a loss of membrane potential. However, what is interesting about this system is that rather than killing the cell (which occurs with strong, robust HokB overexpression) the HokB expression level induced by Obg results only in the induction of persistence. The authors then show that this effect of Obg overexpression can be restored by expressing proteorhodopsin, which generates its own membrane potential and counteracts the effect of HokB.

This work is an advance in the field because it provides a clear role for Type 1 toxins in persistence, a phenomenon that has largely been correlated with the activities of Type II toxins, and because it reveals that the pathways used by both types of toxins to mediate persistence converge, through their requirement of ppGpp.

#### Disclosures

None declared

[Add a comment](#)

### Abstract:

#### ABSTRACT

Within bacterial populations, a small fraction of persister cells is transiently capable of surviving exposure to lethal doses of antibiotics. As a bet-hedging strategy, persistence levels are determined both by stochastic induction and by environmental stimuli called responsive diversification. Little is known about the mechanisms that link the low frequency of persisters to environmental signals. Our results support a central role for the conserved GTPase Obg in determining persistence in *Escherichia coli* in response to nutrient starvation. Obg-mediated persistence requires the stringent response alarmone (p)ppGpp and proceeds through transcriptional control of the *hokB-sokB* type I toxin-antitoxin module. In individual cells, increased Obg levels induce HokB expression, which in turn results in a collapse of the membrane potential, leading to dormancy. Obg also controls persistence in *Pseudomonas aeruginosa* and thus constitutes a conserved regulator of antibiotic tolerance. Combined, our findings signify an important step toward unraveling shared genetic mechanisms underlying persistence.



## Comments:

COMMENTS

[add a comment](#)

**F1000 Faculty Reviews** (incorporating *F1000Prime Reports*) are comprehensive, open access, topical reviews written by members of the prestigious **F1000 Faculty**. These peer reviewed articles provide context on emerging themes in biology and medicine.

[view all](#)

Genomics & Genetics | Molecular Biology | Structural Biology | Cell Biology | Biochemistry

**RecA-independent single-stranded DNA oligonucleotide-mediated mutagenesis**

Kenan C Murphy, Martin G Marinus  
F1000 Biology Reports 2010 2:(56) (22 Jul 2010)

[Full text](#) | [PDF](#) | [Abstract on PubMed](#)

Cell Biology | Microbiology | Chemical Biology | Respiratory Disorders | Genomics & Genetics | Immunology | Molecular Medicine | Physiology | Biotechnology | Pharmacology & Drug Discovery | Infectious Diseases

**Duality of lipid mediators in host response against Mycobacterium tuberculosis: good cop, bad cop**

Jillian Dietzold, Archana Gopalakrishnan, Padmini Salgame  
F1000Prime Reports 2015 7:(29) (03 Mar 2015)

[Full text](#) | [PDF](#) | [Abstract on PubMed](#)

Librarian Resources

Press Office

F1000 Specialists

F1000 Updates

About/Contact

Article Recommendations

F1000Prime Reports

F1000Prime Faculty

Blog

Subscribe

F1000 Mobile

About

FAQs

Contact

Articles

Advisory Panel

Blog

Submit

Author Guidelines

Register

About

Contact

Download the  mobile app today