Micro 201
Heller Lecture 3/ Class 27- Toxin-Antitoxin Systems
May 2, 2017

Overview:

Toxin-antitoxin (TA) systems are genetic modules encoding for a stable toxin, which typically targets an essential cellular process, and a labile, neutralizing antitoxin; these systems are found ubiquitously on plasmids and prokaryotic chromosomes. On plasmids, TA systems play a role in plasmid maintenance via a mechanism known as "post-segregational killing", whereas chromosomally encoded TA systems are thought to play a role in the bacterial stress response. TA systems are grouped into several different types based on the mechanism by which the antitoxin neutralizes toxin function. As background reading, I have provided a 2011 review by Yamaguchi, Park, and Inouye. Please make sure to read through this before coming to class as we will only have a short lecture period before jumping right into the discussion papers.

The first paper we will discuss comes from Mike Laub's lab at MIT. In this paper they describe the discovery and characterization of the SocAB TA system from *Caulobacter crescentus*. This TA system is unique both in its cellular target and the mechanism by which it regulates toxicity, and I think this paper nicely highlights the incredible diversity amongst TA systems. The second discussion paper (Maisonneuve et al. 2013) pertains to the role of TA systems in the formation of drug-tolerant persister cells. The authors present evidence that the signaling molecule ppGpp triggers the persister phenotype by activating TA systems. If time permits, we will also discuss a short follow-up paper (Germain et al., 2015), which expands upon this model. I know the other two papers are long, so just pay special attention to their model in Figure 1. If you would like to learn more about the mechanisms involved in bacterial persistence, see the review I have included under extra readings.

Discussion papers

1. Aakre CD, Phung TN, Huang D, Laub MT. A Bacterial Toxin Inhibits DNA Replication Elongation through a Direct Interaction with the β Sliding Clamp. *Molecular Cell*. Elsevier Inc; 2013 Dec 12;52(5):617–28.

2. Maisonneuve E, Castro-Camargo M, Gerdes K. (p)ppGpp Controls Bacterial Persistence by Stochastic Induction of Toxin-Antitoxin Activity. *Cell*. 2013 Aug;154(5):1140–50.

3. Germain E, Roghanian M, Gerdes K, Maisonneuve E. Stochastic induction of persister cells by HipA through (p)ppGpp-mediated activation of mRNA endonucleases. *Proceedings of the National Academy of Sciences*. 2015 Apr 21;112(16):5171–6. **(At least Figure 1)**

Background reading

4. Yamaguchi Y, Park J-H, Inouye M. Toxin-Antitoxin Systems in Bacteria and Archaea. *Annu Rev Genet*. 2011 Dec 15;45(1):61–79.

Extra reading

5. Maisonneuve E, Gerdes K. Molecular Mechanisms Underlying Bacterial Persisters. *Cell*. Elsevier Inc; 2014 Apr 24;157(3):539–48.