Micro 201:
Bernhardt Lecture 3 - Envelope Stress Responses
February 5, 2019

Overview:
As you will (re)learn in the coming weeks, sigma factors are key components of bacterial RNA polymerases. Sigmas are responsible for promoter recognition and come in different flavors. Some are of the "housekeeping" variety and others are produced in response to specific signals or stress. Work in both gram-negative and gram-positive model systems over the last 15 years indicates that envelope stress responses are primarily governed by alternative sigma factors or signaling systems called two-component regulatory systems. In the case of the alternative sigma factors, they belong to a distinct subset of transcriptional initiators called extracytoplasmic function (ECF) sigma factors. These ECF sigma factors are typically regulated by a membrane anchored anti-sigma factor that is, in turn, controlled by regulated proteolysis. We will focus a significant portion of our discussion on the σ^E stress response in *E. coli* and how it is regulated by the proteolysis of its inhibitor RseA. As you will learn, the regulatory logic of this system is analogous to that used by eukaryotes to regulate responses to sterol deprivation and protein misfolding in the ER. The first paper for discussion will focus on one of the σ^E activation steps.

The second paper for discussion revolves around the Rcs system of *E. coli*. This histidine kinase-based system has also been implicated in the response to cell envelope stress. However, the mechanism by which the system senses envelope defects has remained mysterious for some time. The paper from the Collet and Typas groups presents data indicating that the sensing mechanism likely involves a lipoprotein called RcsF and whether or not it can be sequestered at the cell surface. The report thus provides functional significance for the surface exposure of lipoproteins and identifies the machine responsible for transporting the protein across the outer membrane.

Papers for discussion:

Benjamin M Alba, Jennifer A Leeds, Christina Onufryk, Chi Zen Lu, Carol A Gross. **DegS and YaeL participate sequentially in the cleavage of RseA to activate the sigma(E)-dependent extracytoplasmic stress response. (2002) Genes Dev 16: 2156-2168**

Seung-Hyun Cho, Joanna Szewczyk, Christina Pesavento, Matylda Zietek, Manuel Banzhaf, Paula Roszczenko, Abir Asmar, Geraldine Laloux, Ann-Kristin Hov, Pauline Leverrier, Charles Van der Henst, Didier Vertommen, Athanasios Typas, and Jean-Francois Collet. **Detecting envelope stress by monitoring beta-barrel assembly. (2014)** *Cell* **159:1652-1664**

General Reviews:

Grabowicz and Silhavy. **Envelope Stress Responses: An interconnected safety net. Trends Biochem Sci (2017) 42: 232-242**