**Bacterial Stress Responses**

Current research is looking to better their understanding in the processes by which bacteria sense and respond to stress. This area of research is particularly important in pathogenic bacteria. For example, bacteria associated with foodborne illnesses must survive in very diverse environments both inside and outside the host. These bacteria must survive transit in food or water and human bodily defenses within the gastrointestinal tract. In order to survive these extremely diverse conditions, bacteria must sense the changes and respond appropriately with protein activity to elicit a stress response (Boor, 2006).

I had the chance to sit down with an expert in “bacterial decision making,” Matthew Cabeen, Ph.D. Dr. Cabeen is an assistant professor at Oklahoma State University that looks at how bacteria respond to different stressors and the various responses they elicit. His recent study looks at *Bacilla subtilus*, a model organism for gram positive bacteria. To detect stress, *B. subtilus* uses large protein structures known as stressosomes. Each stressosome contains about forty proteins of four different varieties; these proteins are known as RsbR proteins, which act as bacterial stress sensors. As evolution has shown, there has to be a reason four different varieties of stress sensors have stuck around all these years. This brings the question, for what reason has *B. Subtilus* kept four variations of stress sensor proteins throughout evolution? Thus far, no one has been able to determine any distinctions among the four RsbR proteins. Previous methods employed in this area of research have been rather limiting. Bulk-culture experiments, those performed in flasks or agarose pads, have a short observational window. These experiments also lack uniform conditions because the bacteria are constantly altering their own environment.

Dr. Cabeen and his team brought a new approach to the table. Using a microfluidics approach, cells can be observed over a much longer observational window under uniform conditions. Cells are grown under a microscope with a continuous flow of fresh medium working to keep the cells from altering their environment. This method allows any type of stressor to be introduced into the medium flow while being able to look at the specific responses in single cells under uniform conditions. They set out to examine cells exhibiting specific RsbR proteins and monitor the exact stress response elicited from each of the four variations. He found that wild type bacteria, bacteria containing each of the four RsbR proteins, elicited a transient and quick response. The bacteria with RsbRA proteins very closely resembled the wild type. However, RsbRC is slow to turn on and sustained. In fact, the individual cells are pulsating to provide the sustained response. These data suggest that each RsbR protein does in fact elicit a different response to stress. Another contribution from Cabeen’s team found that energy stress does share some of the same responses as environmental stress pathways, but not all. In previous research, it was believed that the bacterial response to energy stress was frequency modulated. When more stress was added, a pulsatile response would increase in frequency with the degree of stress added. However, Dr. Cabeen’s research did not see any frequency modulated responses. As a result, they believe the previous result may have been a direct result of being grown on agarose pads under non uniform conditions.

Now that it has been shown separate RsbR proteins do in fact produce different stress responses, the work is far from over. As you could imagine, this contribution adds to many different aspects in understanding bacterial stress responses, especially in our understanding of pathogenic virulence. Dr. Cabeen shared a few of his upcoming projects with me. In using molecular dissection, fusion proteins can be built in which he can join pieces of different RsbR variants. Ideally, this would determine what regions of the protein are responsible for the responses seen. He also plans to repeat his previous analysis using different stressors to determine if the sensors have any specificity to different types of stress. One could also look at the advantages or disadvantages of a transient and sustained responses to a varying amounts of a particular stress and how these responses affect cell survival. All in all, Dr. Cabeen’s goal is to have a lab full of students excited to produce results in hopes to contribute to our overall understanding of bacterial decision making.

References

Boor, K. J. (2006). Bacterial Stress Responses: What Doesn’t Kill Them Can Make Them Stronger. PLoS Biology, 4(1), e23. http://doi.org/10.1371/journal.pbio.0040023

Cabeen MT, Russell JR, Paulsson J, Losick R (2017) Use of a microfluidic platform to uncover basic features of energy and environmental stress responses in individual cells of Bacillus subtilis. PLOS Genetics 13(7): e1006901. https://doi.org/10.1371/journal.pgen.1006901