**Infectious Bacteria During Times of Stress**

Author: Danielle Roufs  
Major: Microbiology  
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

**Key Words:**

Antibiotic-resistance, multidrug-resistance, dormancy, stressers, persisters

There has been a rise in the frequency in multi-drug resistant bacteria as well as antibiotic-resistant bacteria. The resistance in these bacteria can be the cells partaking in a state of dormancy and in forming persister cells to help combat the bacteria’s threats. Dormancy is induced by stressers, molecules that signal to the cell that a change is occurring. Dormancy allows the cell to reduce activity, allowing their chances of survival against antibiotic treatments. The formation of these persister cells can occur after a threat is indicated by a stress signal. These stress signals, or stressers, signal to the bacteria that there is something hostile in the area. In response, the bacteria may make physiological changes in order to increase its chances for survival. There are many studies that have been done on these cells, however, there are many discrepancies in the results.

**Introduction**

The rise of multidrug-resistant bacteria is a cause of concern. These bacteria are causing a fear that some infections may become untreatable due to the bacteria’s persistence. The rise in the frequency of these types of bacteria brings about a question: Why is this happening? These bacteria have formed persister cells that are able to avoid stresses such as antibiotics by entering a dormant state. These dormant cells are known to be a large cause of recurring and/or prolonged infections (1).

Growing cells can differentiate into these persister cells due to cues the cell receives when there is a threat to the bacteria. The general stress response, the SOS response, as well as (p)ppGpp, control and influence the composition and size of these persister cells (I). The formation of these cells occurs when the conditions surrounding these cells allow for activation of the signaling pathways.

**Recent Progress**

While there is not a lot to be known about how these persister cells form and survive, there is still research that is allowing us to better understand their formations and systems in which they use to resist threats. The results from this research have confirmed the previous idea that a bacterial cell’s persistence is connected with dormancy and slow growth. It has become known that these stressers signal for a cell to enter a state of dormancy. This is known as the SOS response (I).

The SOS response includes the protein TisB, which is known to form pores in a bacteria’s inner membrane. Once this has occurred, TisB affects ATP synthesis, slowing it down (1). When ATP synthesis slows down, the bacteria will enter a state of dormancy. A common occurrence when cells enter a dormant state is the formation of biofilms. Biofilms consist of an accumulation of a bacteria and they adhere to a surface to increase the chance of survival. After the environment has changed to more favorable conditions, the bacterial cells when cells exit their state of dormancy and become active, thus continuing to spread and increase the infection. When TisB has been overexpressed, it can also result in the bacteria developing multidrug tolerance (I). Although these tests to confirm this process was only carried out in E. coli, it can be predict that these processes and changes occur in other bacterial processes as well.

There is still more that we hope to learn from future research. It is still not greatly understood how these cells can survive after exposure to antibiotics. There is also confusion as to how different groups that have researched this phenomenon have obtained differing and inconsistent results.

**Discussion**

Persistent cells in bacteria are becoming recognized as one of the major causes for the relapse of infections and the failure of antibiotic treatments. These cells are specialized to survive antibiotic killing. The cells accomplish this by entering a dormant state where the cell does not continue to grow, but rather slows its activity. After antibiotic treatment has stopped, these cells become active again, thus causing the infection to reoccur. These infections vary in variety and can be seen in urinary tract infections and infections of the open wounds and implanted devices.

A persister cell becomes dormant in order to increase its chances of surviving in a hostile environment, whether that be in the presence of antibiotics or other stress-induced responses like acid stress. However, not all dormant cells are antibiotic-resistant. In fact, most of them aren’t. The dormant persister cells that survive during the dormant state have changed physiologically in order to increase its chances at survival. There is a question to be asked though: How do these persister cells develop in the first place?

There isn’t just one factor that would cause persister cells to form. The formation of these cells is caused by a combination of stressers: stochastic and responsive mechanisms. These two things allow the bacteria to respond when threats are presented to them by a stress signal (although a stress signal is not always necessary). When these threats are presented, the bacteria respond by altering both the quality and number of the rate of phenotypic conversion into persister cells. The presence of these stresses, which includes antibiotics, had been shown to stimulate the formation of these persister cells.

These persister cells are able to repair any damage that has occurred to their DNA by SOS induction. This process allows for the DNA to be repaired during the resuscitation phase – the phase in which a bacterium is becoming active after previously being in a dormant state (1). This process allows for bacteria to make repairs to any damage the bacteria may have encountered during its dormant state, whether it be by bacteria or other threats.

However, there is still a lot to be learned about these stressers and how they affect bacterial cells. Many studies have barely scratched the surface of what there is to know about these bacterial behaviors regarding their response to their environment and the formation of persister cells. This research needs to be continued in order to improve treatment of those bacteria that are becoming antibiotic and multidrug-resistant. As mentioned previously, many of these tests have only used E. coli. This testing needs to occur in a more broad range of bacteria in order to get a better view of how bacteria responds in stressful environments. In order to better understand how to overcome these persistent bacteria, we must first understand their methods for survival and how to bypass them.

**References**

1. Gerdes, K., Harms, A., & Maisonneuve, E. “Mechanisms of bacterial persistence during stress and antibiotic exposure”. Science. Vol. 354 (16 Dec 2016): 1390-1399.