Autotransduction and Antibiotic Resistance in *Staphylococcus aureus*

Antibiotic resistance is a growing problem in today’s society as abuse and misuse of antibiotics is increasing. When an antibiotic becomes unable to kill or control the growth of bacteria, the bacteria can quickly spread and transfer to more people. The inability to treat the bacteria can cause prolonged suffering to the affected people and can even lead to death. The more understanding we have about resistant strands of bacteria, the more we can do to prevent different strands of bacteria from becoming resistant. John Haaber and his team recently published a study in which they specifically focused on the antibiotic resistance of *Staphylococcus aureus.* This bacteria has subpopulations that are resistant to Methicillin and other subpopulations that are developing resistance to other antibiotics. His team discovered that the bacteria *Staphylococcus aureus* can use prophages to gain antibiotic resistance from other bacterial cells. This is important because we now understand that bacteria can not only use phages as biological weapons against their competitors, but also as a means to collect and incorporate valuable genetic information from these competitors. This is the same method that *S. aureus* uses to become resistant to otherwise lethal antibiotics.

Although *S. aureus* is incredibly dangerous to humans, it is also present asymptomatically on the skin and inside the noses of 30% of humans. This is important because as Methicillin resistant *S. aureus* becomes more prevalent it can pass on this advantage to the bacteria residing on people who don’t even know they are infected. The ability for *S. aureus* to adapt is accredited to the extensive mobility of phages, pathogenicity islands, plasmids and transposons within the bacteria. Phages play a significant part in gene transduction, which is a key element in the study of bacterial resistance. During transduction a phage is released from a bacterial cell and eventually finds a competing bacterial host into which it injects its genetic material. The prophage is then replicated inside the host and becomes so numerous that it causes the host to lyse. When this occurs the host cell’s genetic material is released as well and can be picked up by the replicated phages. If the host cell has DNA that codes for antibiotic resistance, then that DNA can be picked up by the phages as well and brought back to the original bacterial cells that released the phage. In this paper Haaber uses the term ‘autotransduction’ to describe the event in which the phage, which now contains genetic material from the lysed bacteria, injects this new DNA into its original bacterial host so the host can acquire new genetic elements. Because the original lysogenic host is already carrying a prophage, it is immune to phage mediated killing, so it can receive the genetic material without lysing.

There are several important experiments that Haaber’s team conducted to further our knowledge about the acquisition of antibiotic resistance by *S. aureus*. The experiments all explore the relationship between prophages and their host. The first benefit of a prophage/host relationship is the host’s ability to use its prophages as weapons against its non-lysogenic competitors. The team cultured 8325-SR (lysogenic) and USA300 (non-lysogenic) together and found that although the growth rate of the lysogenic strand was slower, the presence of the non-lysogenic target was not detected at the end of the experiment. This showed the complete lysis of all competitor (non-lysogenic) cells. The second benefit of phages to their host cell is the ability of the phages to protect the host cell against infection by related prophages. The third benefit to their relationship is the ability to acquire genes from competitors that encode for advantageous phenotypes. To study this ability, the team co-cultured 8325-S (lysogenic and resistant to streptomycin) with three non-lysogenic strains. One strain was resistant to erythromycin, one was resistant to chloramphenicol and the third was resistant to tetracycline. The lysogenic strain can be set apart from the non-lysogenic strains because it has a non-haemolyic phenotype. When each non-lysogenic strain was cultured with the lysogenic strain, the result was the presence of cells that were not only all non-haemolytic (implying that only the lysogenic strain survived), but the cells all showed double resistance to both streptomycin and the other antibiotic to which each of the three non-lysogenic strains was resistant. This demonstrated that the lysogenic strain not only survived, but it also received the antibiotic resistant genes from the other strains. Another experiment the team conducted demonstrated the ability of *S. aureus* to receive antibiotic resistance even during antibiotic selection. The team co-cultured 8325-SR with 8325-4 chrom (which is resistant to erythromycin) and gradually increased the concentration of erythromycin in the plate. When the team introduced high concentrations of erythromycin, high enough to kill off 8325-SR, the original lysogenic strains of 8325-SR declined. However, new strains of 8325-SR emerged with erythromycin resistant abilities. When the same test was run again in the presence of citrate, which deactivates the phages, the lysogenic 8325-SR did not survive. This showed the necessity of phages in the autotransduction of antibiotic resistant genes.

Because of the demonstrated advantages lysogenic bacteria have when using autotransduction, the team hypothesized that the bacteria would have a fairly easy time establishing its presence in a new environment with existing competitive bacteria. To demonstrate this advantage, the team took lysogenic 8325-SR and plated it on an agar with existing phage-susceptible strain USA300. After one day, the growth of both bacterial colonies stopped and then the presence of both began to decline throughout the next 16 days. 8325-SR experienced a 200-fold decrease while USA300 experienced a 5,000-fold decrease. Another important outcome of this experiment was that there was a number of 8325-SR colonies that showed resistance to tetracycline, which must have been transferred from USA300 even without antibiotic selection.

Through the number of experiments this lab conducted we learned that *S. aureus* uses its phages through a process of autotransduction to receive antibiotic resistance from phage susceptible targets. The team also demonstrated that lysogenic hosts are immune to phage attack when they are carrying similar phages and that the phage can then inject genetic material into the lysogenic host without causing the host to lyse. The *S. aureus* cells can also use phages as biological weapons which they send out to lyse competitor cells. The results from the experiments conducted are not only important to *S. aureus*, as it has been demonstrated by other scientists that similar tests using other bacterial types yield similar results. For example, an experiment conducted by Zinder and Lederberg demonstrated that this same process of transducing particles entering lysogenic cells can occur in Salmonella. This shows that autotransduction is not unique to *S. aureus* and further tests can be conducted on a variety of bacterial types to determine if they too use autotransduction as a form of defense. The more we know about the transfer of resistance the more we can combat its spread in the future. We may also be able to use phages against the cells themselves to treat infections. More research will need to be accomplished to determine the extent of the use of phages in other types of bacteria and in which situations these phages can be used to our advantage in future treatments.

References

Haaber, Jakob, et al. “Bacterial Viruses Enable Their Host to Acquire Antibiotic Resistance Genes from Neighbouring Cells.” *Nature Communications*, vol. 7, 2016, p. 13333.