Tolerance vs. Resistance: How Researchers at OSU are Taking Steps Toward Combating a Global Health Issue

As the global issue of antibiotic-resistant bacteria continues to progress, researchers are working to better understand the issue and how to combat it. Some disease-causing microbes have become resistant to every available antibiotic. What many people don’t know is that bacteria do not have to be resistant to defeat antibiotics. Through tolerance or persistence, bacteria can be unaffected by antibiotics that work to target them. Cells known as “persisters” are bacterial cells that shut down all metabolic processes, reside in a dormant state, and do not multiply. Since antibiotics work by killing bacteria that are growing and multiplying, they are not successful in targeting persisters. Once persisters leave their dormant state, they are able to multiply, giving rise to a new infection. Persisters play a role in chronic infections occurring in patients with diseases like cystic fibrosis and tuberculosis. Persister cells are particularly difficult to study, but our knowledge of how they work is crucial in our global mission to combat the issue of antibiotic resistance.

Right here on Oklahoma State’s campus, researchers like Dr. Kevin Wilson and his lab members are taking big steps toward understanding these unique cells. Dr. Wilson is an Associate Professor in the Department of Biochemistry and Molecular Biology, and he is no stranger to the world of biochemistry. Dr. Wilson received his undergraduate degree in Biochemistry from the University of Arizona, his Ph.D in Chemistry from the University of Oregon, and completed postdoctoral studies at the University of California, Santa Cruz. His current research focuses on the translation machinery in bacterial cells, with a particular focus of the bacterial ribosome. “Persister cells have always been there, but they are definitely more complicated than originally thought,” Dr. Wilson explains. He also says that many people, even microbiologists, sometimes confuse the terms “tolerance” and “resistance.” Whereas persisters (tolerant cells) are metabolically dormant cells, resistant cells are cells that have acquired a mutation that make them resistant and can give rise to populations of resistant cells. Persister cells are genotypically the same as their surrounding antibiotic-sensitive cells, and once out of their dormant state, their progeny are normal and antibiotic-sensitive. Dr. Wilson points out that the main problem of persistence is that once the persister cells stick around long enough, they will eventually acquire a mutation that makes them resistant to the drug, turning the problem back to antibiotic-resistant cells. He and his lab members work with *E. coli* cells and ampicillin to study persister cells. After growing the bacteria in a petri dish, the bacteria in his lab are treated with an antibiotic. He explains, “If you look in a microscope, amongst the lysed (dead) cells, there are persister cells; they are rare – just one in a million – but they are there and surviving.” When asked why his research takes specific interest to the bacterial ribosome, Dr. Wilson explains, “The ribosome has a lot of targets, and the simple explanation is that the ribosome is major target of the widest range of antibiotics.”

At the molecular level, the goals of Dr. Wilson’s lab are to study the translational machinery in bacterial cells, and how antibiotics disrupt the ribosome and translation. The implications of this type of research are incredibly far-reaching. As for the ultimate goals for his research, Dr. Wilson starts with the question, “How do we ultimately use what we learn to intervene on the growing problem of antibiotic resistance?” He says that we must focus of how to stop persister cells. We must, “target either survival or regrowth” of persisters. Dr. Wilson finishes with an expressives statement explaining the mission of this kind of research: “ultimately, we are interested in figuring out a cocktail of antibiotic and anti-persister cell medicine.” It is research like this being conducted by Dr. Wilson and others at Oklahoma State that puts us closer to our global pursuit of combatting antibiotic resistance.

References

Cho, Junho, et al. “Escherichia Coli Persister Cells Suppress Translation by Selectively Disassembling and Degrading Their Ribosomes.” *Molecular Microbiology*, U.S. National Library of Medicine, Jan. 2015, www.ncbi.nlm.nih.gov/pubmed/25425348.