Understanding the Effects of Ribosome Targeting Antibiotics: an Analysis of the Research Done by Dr. Kevin Wilson

Dr. Kevin Wilson's lab focuses on the stress response of antibiotic resistant bacteria. A stress response is the result that occurs when an organism is exposed to negative stimuli. He primarily studies bactericidal antibiotics that target ribosomes. His lab has found that when antibiotics that target ribosomes are able to bind to said ribosomes, they are capable of doing significant damage. However, ribosome assembly pathways can be inhibited; this produces ribosomes that are not completely assembled, therefore preventing the antibiotics from binding. A bacteria's ability to temporarily circumvent the binding of antibiotics to ribosomes can allow for antibiotic tolerance. Dr. Wilson has found that toxins secreted by bacteria during a stress response are what prevent antibiotic binding.

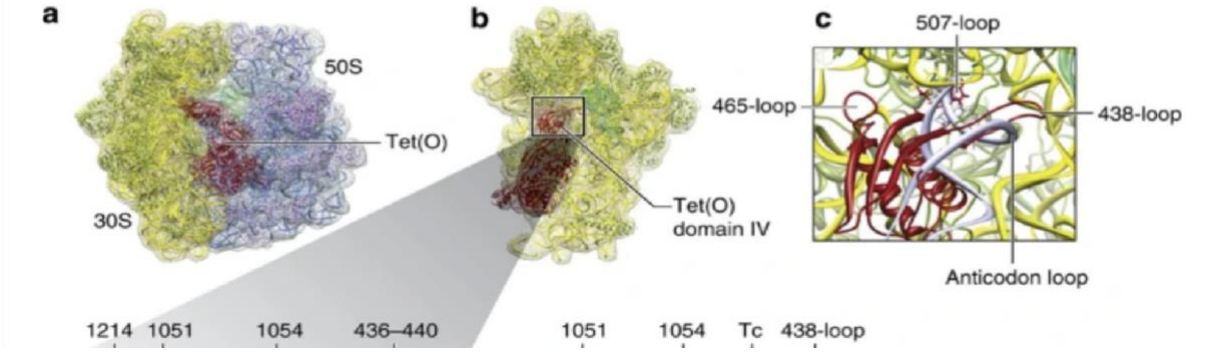
Dr. Wilson's interest in his research stems from the need to find a solution to antibiotic resistance. The future of his research is geared towards the creation of antibiotics that do not produce the stress response that is currently initiated in resistant strains by the antibiotics used today. One particular idea that he wishes to explore is that of directly targeting the ribosome assembly pathway instead of the ribosomes themselves. For now, he is focusing on documenting and exploring the stress response produced by current antibiotics with the hopes to expand upon his research in the future.

Dr. Wilson cited his paper *Mechanism of Tetracycline Resistance by Ribosomal Protection Protein Tet(O)* as an article that encapsulates what his lab is currently focused on. In his paper, his lab investigates the stress responses that renders tetracycline ineffective. Tetracycline is an antibiotic that targets a small subunit of the bacterial ribosome. Due to the location in which tetracycline binds, aminoacyl-tRNA is blocked from approaching the A-site codon during the decoding process. Simplified, this prevents the ribosome from being able to synthesize proteins due to disruption in translation.

The bacteria's goal in order to survive is to mitigate this result; this is what is denoted as a stress response. Mitigation occurs through prevention of tetracycline binding, or in the case that binding has occurred, modification of the system. Prevention is enacted by either protective proteins secreted by the bacteria to block tetracycline or the movement of tetracycline out of the surrounding environment. When tetracycline binds, the modifications that occur can affect tetracycline or the ribosome itself.

Dr. Wilson's paper focuses on a protein called Tet(o). In his paper he details the binding of Tet(o) to the ribosome. Through a series of advanced imaging, he was able to deduce that Tet(o) disrupts the binding of tetracycline due to structure components and lack of space. His team backed this claim by identifying the binding sites of Tet(o) and then altering their structure at points they deemed critical in disrupting tetracycline binding. The end result was bacteria that was less resistant to tetracycline implying that they correctly identified the critical sites and more importantly the possible mechanism that allows Tet(o) to increase antibiotic resistance.

Figure 3: Cryo-EM map-fitted atomic model of the 70S ribosome bound with Tet(O).



Interestingly, Dr. Wilson also cares about the human microbiome. He put emphasis on the fact that due to the nature of ribosomes, the antibiotics that would stem from his research will still target bacteria in mass, but not specific pathogens. It seems as though Dr. Wilson has reconciled the conflict in his research and that of maintaining microbiota diversity with the fact that his research would produce antibiotics that are currently desperately needed. The diversity of microbiota, albeit important, does not supersede the life threatening impact of antibiotic resistance. Dr. Wilson implied that when other options are viable they should be utilized, but until then finding new solutions to the most detrimental issues is the priority.

References

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