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ANTIBIOTICS RESISTANCE

Concept article.

Antibiotic Resistance and the Ribosome: A key Target in the Battle against Pathogens.

RACHEDI Abdelkrim

Laboratory of Biotoxicology, Pharmacognosy and biological valorisation of plants, Faculty of Natural and Life Sciences, Department of Biology, University of Saida - Dr Moulay Tahar, 20100 Saida, Algeria.

Correspondence: RACHEDI Abdelkrim – Email: abdelkrim.rachedi@univ-saida.dz, bioinformatics@univ-saida.dz
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Abstract

Antibiotic resistance poses a significant global threat to public health, necessitating innovative strategies to combat multidrug-resistant pathogens. In here we focuses on the ribosome as a key target in the fight against antibiotic resistance.

Ribosomes, can be referred to as the "ultimate molecular 3D printers", of the flesh and blood, are ancient molecular machines responsible for protein synthesis. Pathogenic bacteria heavily rely on ribosomes for survival and proliferation.

By disrupting ribosomal function, researchers aim to hinder bacterial protein synthesis, effectively impeding bacterial growth and reducing the spread of antibiotic-resistant strains. Targeting the ribosome offers a promising avenue for the development of novel antibiotics that can overcome resistance mechanisms employed by bacteria.

Ongoing research endeavors seek to understand the intricacies of ribosomal structure and function, identifying vulnerabilities that can be exploited for the design of more effective and specific drugs. We explore, in this article, the significance of ribosomes in biological processes and highlights the ongoing efforts to leverage ribosomal targeting in combating superbugs. Scientists aim to mitigate antibiotic resistance and safeguard public health through gaining insights into ribosomal mechanisms and advancing intervention strategies.

Key words: Antibiotic resistance, Ribosome, Protein synthesis, Multidrug-resistant pathogens, Superbugs, Drug development.

Introduction

Antibiotic resistance is an increasingly urgent global concern, undermining the effectiveness of existing antimicrobial therapies and posing a substantial threat to public health (Wilson, 2014). The emergence of multidrug-resistant pathogens has necessitated the development of innovative approaches to combat this critical problem. One promising avenue of research lies in targeting the ribosome, an ancient and essential molecular machine responsible for protein synthesis. Ribosomes are present in all living organisms and are often described as the "ultimate molecular 3D printers", of the flesh and blood, due to their ability to convert genetic information into specific three-dimensionally structured proteins that execute vital specialized biological functions.

Pathogenic bacteria, which cause a range of infectious diseases, rely heavily on ribosomes for their survival and proliferation. Disrupting the protein synthesis machinery within bacterial ribosomes can have a profound impact on bacterial growth, making ribosomes an attractive target for the development of new antibiotics (Jinzhong et al., 2018). Through interfering with ribosomal function, researchers aim to inhibit bacterial protein synthesis, thereby halting bacterial growth and reducing the spread of antibiotic-resistant strains.

Targeting the ribosome represents a promising avenue for combating antibiotic resistance due to its fundamental role in biological processes. Ribosomes are conserved across diverse bacterial species, making them an ideal target for the design of antibiotics that can circumvent resistance mechanisms employed by bacteria (Wilson, 2014). Scientists and researchers are actively studying the structure and function of ribosomes, Figures 1 and 3, to gain a comprehensive understanding of their mechanisms. Unravelling the intricacies of ribosomal biology can lead to the identification of vulnerabilities that can be exploited in the development of drugs with greater specificity and efficacy.

Of particular concern are superbugs, highly resistant bacterial strains that pose significant challenges in healthcare settings. Ribosomes have been found to play a key role in combating superbugs, and ongoing research efforts are focused on harnessing the potential of ribosomal targeting to overcome antibiotic resistance (Science Museum blog). Researchers aim at gaining deeper insights into ribosomal mechanisms and advancing intervention strategies, to mitigate the

spread of multidrug-resistant pathogens and protect public health.

This article delves into the significance of ribosomes in biological processes, highlighting their role as a focal point in the fight against antibiotic resistance. It explores ongoing research and advancements in ribosomal targeting, aiming to shed light on the potential of ribosome-based interventions in combating superbugs and overcoming antibiotic resistance. Scientists strive to develop effective strategies to safeguard public health and preserve the efficacy of antibiotic therapies by focusing on this critical area of study.

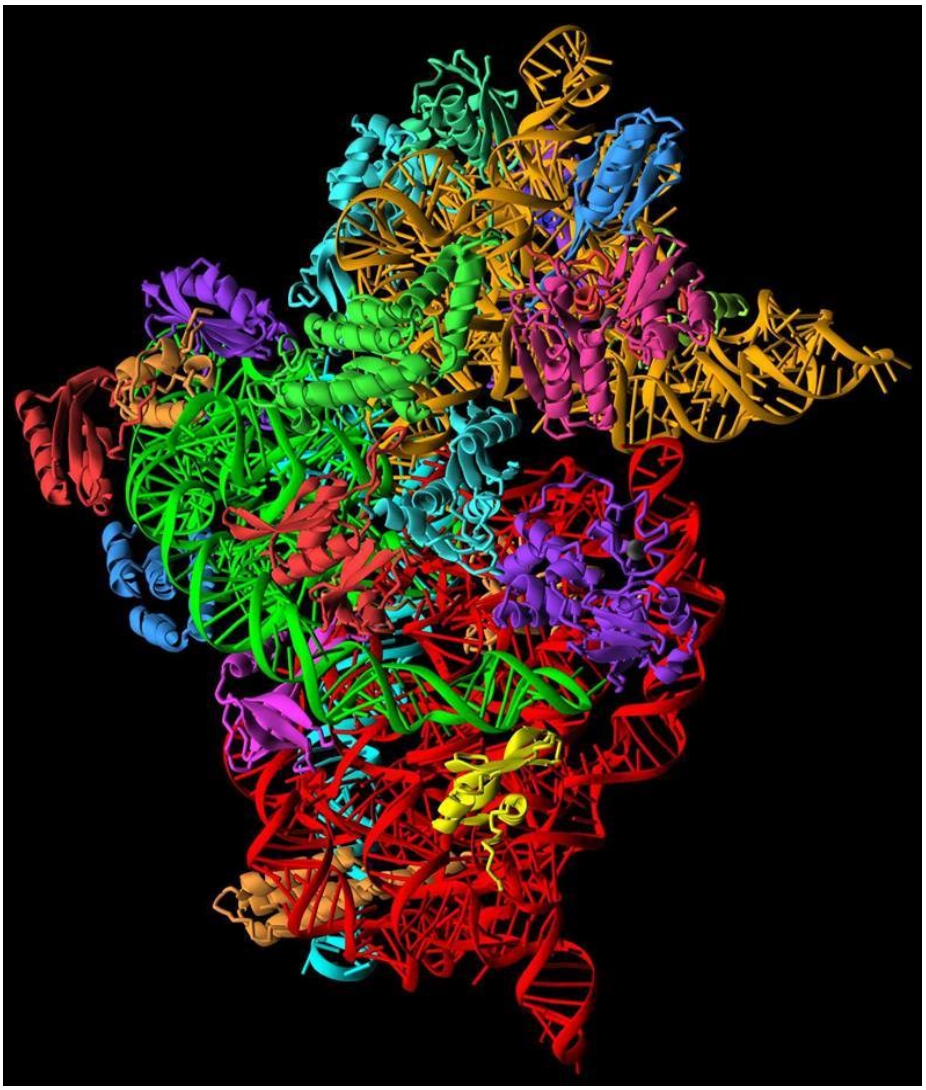

Figure 1. The 30S component, or 'brain' of the ribosome. Credit: Ramakrishnan Lab. https://blog.sciencemuseum.org.uk/ultimate-molecular-machine-plays-key-role-in-superbug-fight

The Ribosome; an Ultimate Molecular 3D Printer

The ribosome, often referred to as the "ultimate molecular 3D printer of flesh and blood" is a complex cellular structure found in all living organisms. It acts as a translation machine, converting genetic information encoded in RNA molecules into functional proteins with specific structures necessary for the correct biology to happen. Ribosomes accomplish this through linking together amino acids in the precise order dictated by the genetic code, Figure 2.

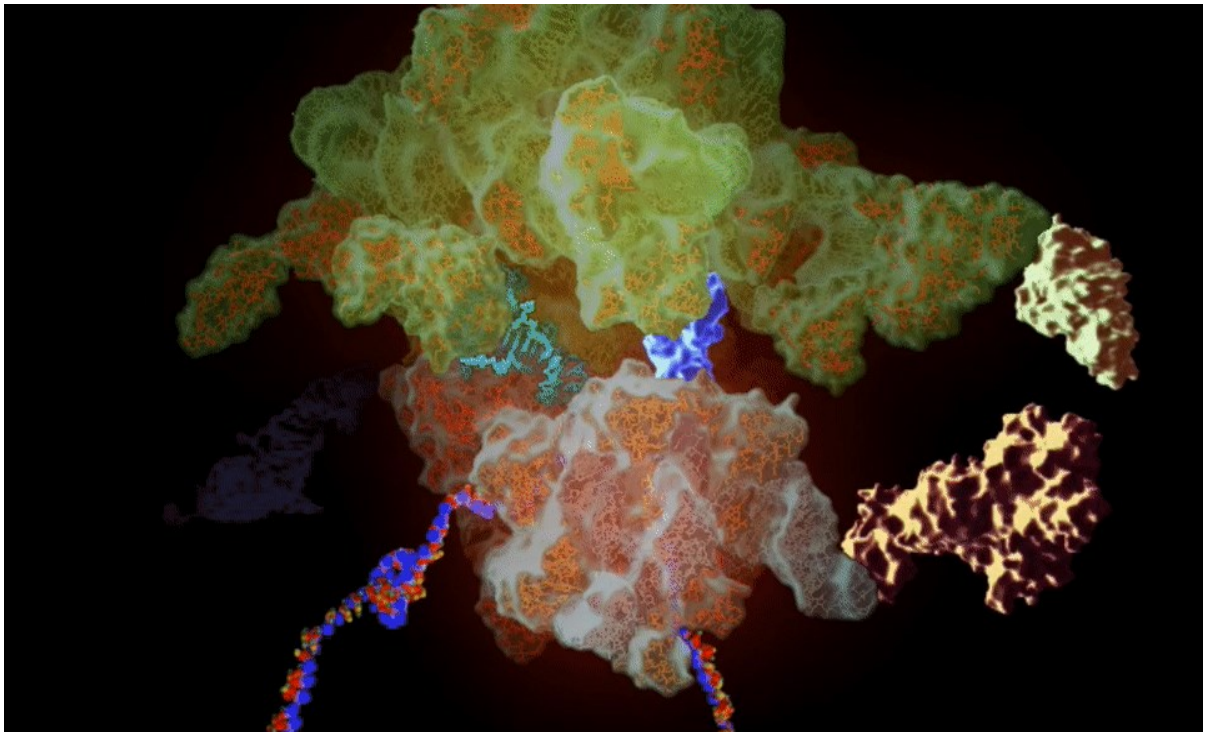

Figure 2. Animated model of protein synthesis by a Ribosome found in bacteria
Credit: Ramakrishnan Lab. https://blog.sciencemuseum.org.uk/wp-content/uploads/2016/05/ezgif.com-video-to-gif.gif

Ribosomes and Pathogenic Bacteria

Ribosomes play a critical role in the life cycle of pathogenic bacteria, which are responsible for causing various infectious diseases. These bacteria heavily rely on ribosomes for their survival and proliferation, making them an attractive target for therapeutic interventions. Disrupting the ribosomal machinery can impede the ability of pathogenic bacteria to synthesize proteins, leading to a significant impact on their growth and proliferation (Jinzhong et al., 2018).

One approach to targeting ribosomes is the development of ribosome-targeted antibiotics. These antibiotics specifically inhibit the activity of bacterial ribosomes, selectively disrupting protein synthesis in pathogenic bacteria while sparing the ribosomes of host cells. These antibiotics would selectively target the bacterial ribosomes and can effectively inhibit bacterial growth and prevent the spread of infections caused by resistant bacteria.

The advantage of targeting ribosomes lies in their conserved structure and function across different bacterial species. Ribosomes are ancient molecular machines that share fundamental characteristics, allowing researchers to develop broad-spectrum antibiotics that can combat a wide range of pathogenic bacteria. This broad-spectrum activity is particularly valuable in the face of antibiotic resistance, as it provides a versatile approach to combating resistant strains.

In recent years, research efforts have focused on gaining a deeper understanding of ribosomal structure, function, and the mechanisms by which ribosome-targeted antibiotics work. The identification of specific vulnerabilities that can be exploited for the design of more effective drugs is potentially within reach through understanding the intricate details of ribosomal biology. This knowledge has paved the way for the development of novel ribosome-targeted antibiotics with enhanced potency, reduced side effects, and improved resistance profiles.

The fight against Antibiotic Resistance

As bacteria evolve and develop resistance mechanisms against conventional antibiotics, finding alternative strategies to combat them becomes crucial. Targeting the ribosome presents a promising avenue, as it represents a fundamental and conserved biological process across diverse bacterial species. Research projects working on interfering with ribosomal function would potentially result in inhibiting bacterial protein synthesis and ultimately halting bacterial growth and reduce the spread of antibiotic-resistant strains (Wilson, 2014).

Ribosome-targeted antibiotics work by binding to specific sites within the ribosome, inhibiting its function and disrupting the accurate synthesis of proteins. This interference with protein synthesis compromises the survival and replication of bacteria, effectively reducing their ability to cause infections (Wilson, 2014).

Moreover, targeting the ribosome has the potential to overcome certain resistance mechanisms employed by bacteria. While bacteria can develop resistance to antibiotics through various mechanisms, such as modifying drug targets or enhancing efflux pumps, the ribosome represents a fundamental process that is difficult for bacteria to evade without severely impairing their own survival. Targeting the ribosome allowed researchers to circumvent some of the common resistance mechanisms employed by bacteria, making ribosome-targeted antibiotics a promising strategy in combating antibiotic-resistant strains.

Research and Advancements

Advancements in technology and techniques, such as cryo-electron microscopy and X-ray crystallography, have revolutionized the field of ribosomal research. These techniques enable researchers to visualize the three-dimensional structure of ribosomes at high resolution, providing insights into their molecular architecture and functional mechanisms, see the Figures 3 & 4. Scientific research in analysing these structures, would pinpoint specific sites within the ribosome that are critical for protein synthesis and can potentially be targeted by antibiotics.

Figure 3. Cryo-Electron Microscopy Structure of the 70s ribosome of *Enterococcus Faecalis*.
Source: the Protein Databank (PDB) entry code 6WUB; can be explored using the SSFS tool https://bioinformaticstools.org/ssfs/ssfs.php?qry=6WUB

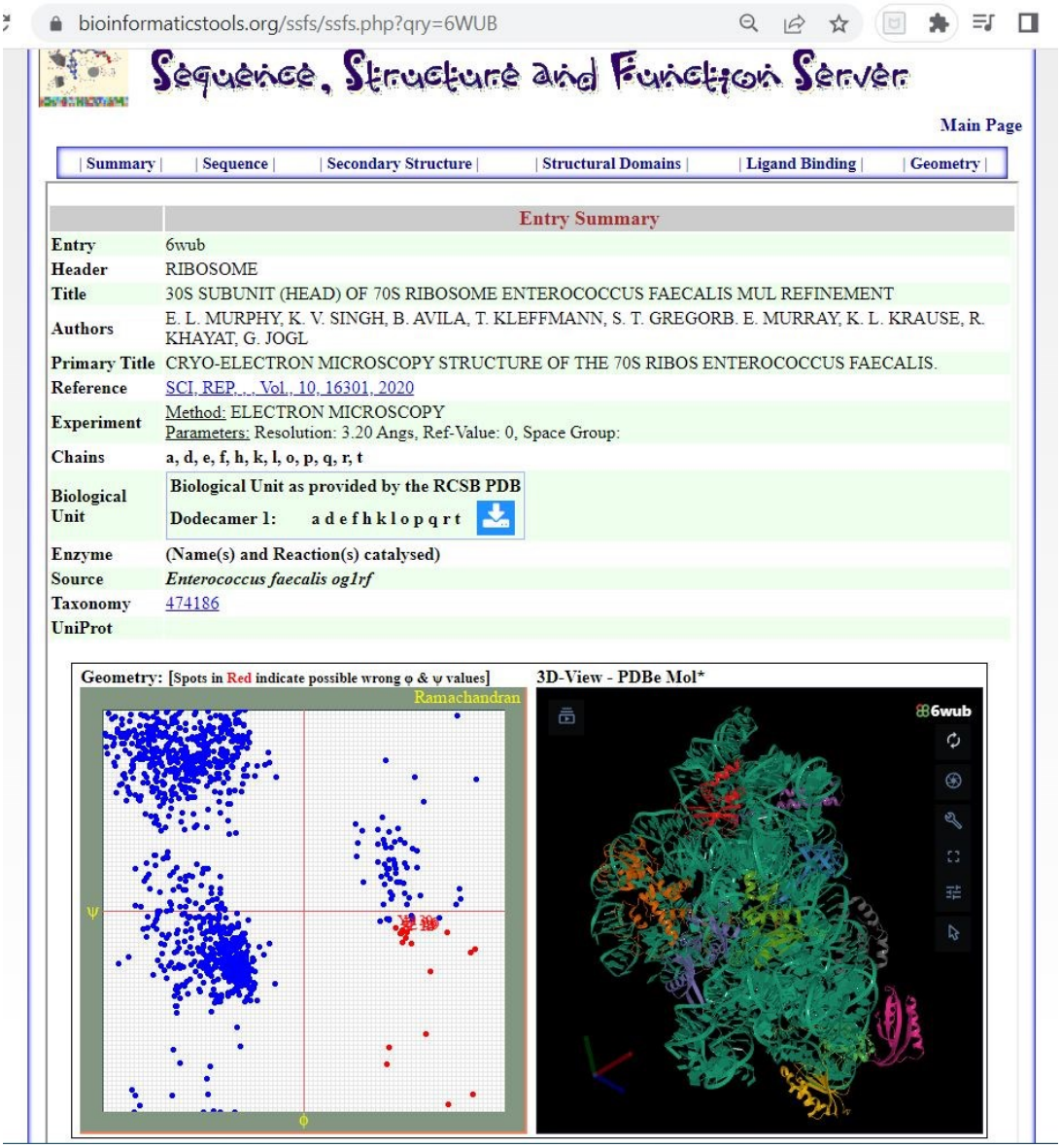

Figure 4. The SSFS✳ tool showing important details of the PDB entry 6WUB related to the 30S Ribosome structure. https://bioinformaticstools.org/ssfs/ssfs.php?qry=6WUB.

✳ SSFS: **Sequence, Structure and Function Server** by the Structural Biology & Bioinformatics Groups, Biology Dept, Faculty of Science, University of Saida, Algeria
نظام **التركيب الأولي، التركيب الفراغي والوظيفة البيولوجية**، فريق البيولوجيا ثلاثية الأبعاد و المعلوماتية الحيوية، قسم البيولوجيا، كلية العلوم، جامعة سعيدة، الجزائر
☛ https://bioinformatics.univ-saida.dz/bit2/?arg=SB3

Moreover, studying the ribosome allows researchers to understand the mechanisms by which ribosome-targeted antibiotics interact with the ribosome and inhibit protein synthesis. This knowledge aids in the design and optimization of antibiotics that can effectively bind to the ribosome and disrupt its function, thereby halting bacterial growth.

One area of focus in ribosomal research is the development of antibiotics that exhibit high specificity for bacterial ribosomes while sparing eukaryotic ribosomes found in human cells. This selectivity is crucial to minimize potential side effects and toxicity to the host organism. Understanding the subtle differences between bacterial and human ribosomes, can help in the design endeavours of novel antibiotics that selectively target bacterial ribosomes, enhancing their efficacy and safety profile.

A number of research projects are investigating novel mechanisms of action for ribosome-targeted antibiotics. Exploration of the different modes of interference with ribosomal function, such as inhibition of specific steps in the protein synthesis process or disruption of ribosome assembly, scientists aim also to expand the repertoire of antibiotics and overcome existing resistance mechanisms.

Furthermore, advancements in computational modelling and virtual screening techniques have facilitated the identification and optimization of potential ribosome-targeted antibiotics. Computational biology and computer simulations in addition to large-scale virtual screening of compound libraries, would result in vast number of molecules and predict their binding affinity and potential efficacy against the ribosome. This computational approach accelerates the discovery and development of novel antibiotics, potentially shortening the timeline for bringing new drugs to the market.

The link between Ribosomes and Superbugs

Superbugs, referring to highly resistant bacterial strains, pose a significant challenge in healthcare settings. Ribosomes have been found to play a key role in combating superbugs, and ongoing research efforts are focused on harnessing the potential of ribosomal targeting to overcome antibiotic resistance (Science Museum blog). For further information on this topic, the article "The Ultimate

Molecular Machine Plays Key Role in Superbug Fight" (source: Science Museum blog) offers a comprehensive overview.

Conclusion

The fight against antibiotic resistance requires innovative approaches that target the fundamental processes essential for bacterial survival. The ribosome, as the ancient molecular machine responsible for protein synthesis, has emerged as a crucial focal point in this battle. Understanding the intricate workings of ribosomes and developing targeted interventions, researchers aim to overcome antibiotic resistance and safeguard public health. Continued research and advancements in this field hold great promise for the development of effective strategies to combat multidrug-resistant pathogens.

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