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Opinion Article

The Antimicrobial Resistance and New Routes for Antibiotic Discovery

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Abstract

The excessive use of antibiotics for infections therapy and the lack of research for new antibiotic discovery has lead to antimicrobial resistance (AMR). Many efforts are needed by governments, societies, and industries to slow down the AMR and accelerates the discovery of new antibiotics. Herein a spotlight on the current limitations of AMR understating and the new routes to battle AMR are presented.

Introduction

Antimicrobial resistance (AMR) is the biggest challenge in the current century where humanity is exposed to return to the prebiotic era. Pathogens were able to develop resistance to antibiotics due to the unresponsible use for infections treatments, in food, animal, and agriculture productions [1]. According to the world health organization (WHO) several public health systems are suffering in various parts of the world from the rising infection rates in hospitals. Worldwide the estimated number of deaths in 2050, may reach 10 million in the absence of drastic solutions. Few years after discovering penicillin in 1928, Alexander Fleming warned that excessive use of antibiotics can lead to antibiotic deficiency. Several antibiotics were discovered by the pharmaceutical companies encouraged by the high profit. Thus, antibiotics started to be used for uncontrolled medical treatments. These decrease the death caused by infections and increase the quality of life and average age of populations. Over years, pathogens were able to develop resistance. The survived bacteria from the last antibiotic treatment were able to regrow and heritage the resistance mechanism to the new generations. Consequently, pathogens become more resistible and antibiotics less effective. Meanwhile, the research for new antibiotics lose the interest of the pharmaceutical industry. Since 1987, no new class of antibiotics has been discovered for pathogenic bacteria infection treatments. Nowadays increasing the research fund in public institutes and pharmaceutical laboratories, are resulting in gaining biological knowledge and technological advances that will help to tackle AMR [2].

Two main forms of AMR were reported in pathogenic bacteria so far. Genetic AMR known to be stable and heritable. In this case AMR result from gene mutation which will be transferred to the new generation. The new mutation becomes more resistant to antibiotics with a higher capability to grow even at higher concentrations of antibiotics. Even though the genetic AMR is more detectable, the clinical treatments are more difficult with the need to use aggressive antibiotics with a harder side effect. While the second type is phenotypic AMR is reversible without gene modifications and result from changes in the bacterium cells to decrease their susceptibility against the invasive antibiotics. Most of the current research is focusing on understanding phenotypic AMR rather than the genetic.

New Routes for Antibiotics Discovery

The urgent need to discover new families of antibiotics attract the attention to looking for new targets site in bacterium cells. In most cases, the used route for a new antibiotic discovery by

pharmaceutical research was looking for new inhibitors for the same old targets. Recently, new routes were started to look for targets that are essential to the pathogen replications in an infected host (*in vivo*) and not just in standard laboratory conditions (*in vitro*). Which is currently used for testing the efficiency of antibiotics. This will result in identifying targets (enzymes, channels, replication pathways, and other potential targets) whose inhibition is most likely to be lethal for the pathogen. Apart from target inhibition, new routes for activating certain targets result in bactericidal are were reported. For instance, activation of the HssRS heme sensor system was found to killed pathogenic bacteria *S. aureus*. Also, in vitro and in vivo studies reported that ClpP protease activation results in *S. aureus* bactericidal in biofilms [3].

Another route is related to study the antibiotic structure variation effect on toxicity and how bacteria metabolize the drug inside cells. Opposite to the old way in pharmaceutical industries where hundreds of synthetic structure variations of possible antibiotics are used for bactericidal efficiency to obtain one successful structure. Herein, several studies in deeps for the metabolism of the failed structures using techniques such as Liquid chromatography–mass spectrometry (LC-MS). This help in calculating the quantities of the drug in cells and the conversions happen to each of these structure inside the bacterium cells. Afterwards, using these data can guide to structural modifications that block these metabolic centers for more effective antibiotics [4,5].

More recently, there is growing interest in studying the efficiency of using several antibiotics to treat AMR pathogens in combination. This includes the use of several antibiotics for the same pathogen with help from computational tools and artificial intelligence to predict drug-drug interactions. As well, to find critical points in the growth pathway by multiple analyses of RNA sequencing [6].

Conclusion

The resistance of pathogens to antibiotic toxicity resulted from the overuse use of antibiotics. As well as the lack of research to understand how pathogenic develop AMR. New research are needed to understand the phenotypic AMR, this will lead to further discoveries of new targets and effective design for new antibiotics using new routes.

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Conflict of Interest

No conflict of interest.

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