Tabari Biomedical Student Research Journal

OPEN ACCESS

# VIEWPOINT: Combating Antimicrobial Resistance Crisis, the Role of Biotechnology

**Morteza Ghandadi**

Pharmaceutical Sciences Research Center, Hemoglobinopathy Institute and Department of Pharmacognosy and Pharmaceutical Biotechnology, Mazandaran University of Medical Sciences, Sari, Iran.
**Email:** Ghandadi@yahoo.com
**ORCID:** 0000-0002-7623-8846

**10.18502/tbsrj.v2i1.2576** **Published: 31 Mar 2020**

Biotechnology is a multidisciplinary filed defined as every technology in which a product is produced or modified using living systems. It usually overlaps with genetics, molecular biology, bioengineering, microbiology, and immunology. Besides agriculture and domestication of animals, which are clearly in accordance with the broad definition of biotechnology, baking breed and fermentation of beer, are examples of ancient forms of biotechnology. In the fermentation of beer, specific yeasts convert sugars of grains to alcohols like ethanol. Although the basic mechanism of fermentation has not been recognized until Louis Pasteur works, it is assumed as the first use of biotechnology. In the early twentieth century, with the help of expanding knowledge of microbiology, Chaim Weizmann developed a process using Clostridium acetobutylicum to produce acetone from corn starch. The next important step in modern biotechnology was discovery and production of antibiotics. Following works of Alexander Fleming, Howard Florey, Ernst Boris Chain, and Norman Heatley, penicillin was discovered and purified from a mold called Penicillium. Afterward golden era of antibiotics has been begun and various classes of antibiotics as microbial secondary metabolites were introduced which led to fabulous control of infectious disease. Excessive demands of these antibiotics along with other fermentation-based products led to the development of large-scale fermentation and industrial biotechnology process. Another revolution in biotechnology have happened in the 1970s when technical problems of transporting a gene from one species to another have been solved and human insulin as first recombinant proteins were produced. Today recombinant proteins and microbial secondary metabolites have captured a large share of the pharmaceutical market and pharmaceutical biotechnology is one of the main branches of biotechnology.

As much as antibiotics have discovered and extensively utilized to combat infectious disease, pathogenic microbes have developed more and more resistance and today antimicrobial resistance is a serious public health challenge all over the world. Unfortunately, from early 1960s introduction of new class of antibiotics has been reduced and most of the pharmaceutical industries ceased their antibiotic discovery projects. Rediscovery of already known antibiotic producing microbes and failure of combinatorial chemistry in the antibiotic development led to enhancement of costs of antibiotic discovery projects and in consequence, pharmaceutical industries have abandoned their antibiotic development projects. This problem intensifies antimicrobial resistance crisis because old class of antibiotics becomes ineffective and no new class is introducing to fight resistant microbes.

Biotechnology can help to circumvent the antimicrobial resistance challenge by various strategies. Microbial secondary metabolites have always been an important source of antibiotics but using conventional methods in culture and isolation of microbes from



[ DOI: 10.18502/tbsrj.v2i1.2576 ]

natural samples have mostly led to rediscovery of already known bacterial and fungal strains. On the other hand, it has been estimated that more than 99% of microbial species in our plant are inaccessible and cannot be cultured or recognized using basic microbiological methods. There are two strategies to circumvent this problem. It has been demonstrated that various ecologic environments are host of different microbial species. Therefore, first strategy is sampling from unstudied and extreme environments especially aquatic environment. This has led to isolation and identification of various new bacterial and fungal species in which new secondary metabolites have also reported. Sampling from aquatic environment has demonstrated promising results, for example, actinomycete genera Salinispora have been isolated from oceanic samples. It is an obligate marine actinomycete genera rich in the new secondary metabolites including a potent proteasome inhibitor Salinosporamide which is in phase III clinical trial for the glioblastoma treatment (1). The second strategy is in situ cultivation using diffusion chambers and iChip technology. In 2015, a manuscript has been published in Nature reported discovery of an antibiotic without detectable resistance using iChip. Actually, an uncultivable bacterium called Eleftheria terrae was isolated and cultivated by iChip. Further analysis of E. terrae extracts has led to isolation and characterization of an antibiotic termed teixobactin. No mutant strain of Staphylococcus aureus or Mycobacterium tuberculosis has found in the experiment, which can develop resistance against teixobactin (2).

Genomics approaches may also help discovery of new antibiotics. Complete sequencing of some known antibiotic-producing microbial strains and bioinformatics analysis of their genome has revealed various silent/cryptic secondary metabolite gene clusters. Cloning of these gene clusters in a new host or genetic manipulation of them using various gene-editing tools in their original strain can lead to expression and subsequently production of new secondary metabolites. Metagenomics also proposed as an approach to find new antibiotics, but it is a technically challenging, time consuming and expensive technique so it may not be as practical as other strategies.

Phage therapy is another strategy to circumvent antibacterial resistance. In this approach, certain bacteriophages with the ability to kill resistant bacteria are utilized to eradicate bacterial infections. This strategy is rapidly evolving in various experimental as well as clinical trials and have demonstrated promising antimicrobial results, but the development of regulatory policies is still very challenging in this field.

In conclusion, the main problem in antimicrobial resistance is lack of new class of antibiotics. The disinclination of pharmaceutical industries to antibiotic discovery projects due to the low economic efficiency also exacerbates the situation. Therefore, it is responsibility of universities, research centers and non-profitable health care organizations to focus on the antibiotic discovery. Furthermore, investigating unstudied and extreme environment for new antibiotic-producing microbes, in situ cultivation methods including iChip to isolate and investigate uncultivable microbial strains and phage therapy seem promising approaches to combat antimicrobial resistance crisis.

## References

1. Jensen PR, Moore BS, Fenical W. The marine actinomycete genus Salinispora: a model organism for secondary metabolite discovery. Natural product reports. 2015;32(5):738-51.

2. Ling LL, Schneider T, Peoples AJ, Spoering AL, Engels I, Conlon BP, et al. A new antibiotic kills pathogen without detectable resistance. Nature. 2015;517(7535):455-9.



[ DOI: 10.18502/tbsrj.v2i1.2576 ]