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Searching for New Antibiotics Right Under our Feet

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The golden age of discovery of novel antibiotic classes started in the 1950s and lasted through the 1970s [1]. Since then there has been millions of metric tons of antibiotics produced. The advent of antibiotics has certainly benefited society in enumerable ways over the last several decades. However, Sir Alexander Fleming, who discovered the first antibiotic, was the first who cautioned about the potential resistance to penicillin if used inappropriately [2]. Most consider the over use and irresponsible use of antibiotics to have contributed to the significant increase in resistant strains of bacteria [3]. For example, methicillin was synthesized as the first semisynthetic penicillinase-resistant variant of pencillin in 1961 to fight the pencillinase-producing strains of Staphylococcus aureus. Unfortunately, resistance was soon reported in strains of this bacterium [4]. Most funding for research in recent years has focused on the modification of the existing scaffolding to fight emerging and re-emerging pathogens [1]. Given the fact that new drug discovery has been rare, there is a real concern over the ever-increasing rate of drug resistant bacteria. In fact, most classes of antibiotics on the market were discovered in the socalled golden age of drug discovery [5]. A January 2015 article in Nature, was the most recent to describe a new antibiotic over the last five years. The fact is that there is a limited arsenal of drugs to fight the ever-increasing numbers of multi-drug resistant strains of bacteria [6]. Despite a focus on education with regard to proper use of antibiotics there has been an exponential increase in antibiotic resistance [7]. We actually see a difference in the rate of resistance between the developing world and developed world. A major reason is the fact that most of the antibiotics are now available without a prescription as over-the counter in developed nations [6]. Availability and inappropriate use is most certainly contributing to the global antibiotic resistance crisis.

According to the Centers for Disease Control and Prevention (CDC), at least 2 million people per year become infected with bacteria that are resistant to antibiotics, which results in at least 23,000 deaths as a direct result of these infections. The growing gap between how fast microbes are developing resistance and the development of new antimicrobials is a major public health threat [6]. The evolution of microbial drug resistance necessitates the discovery of new structural classes of antimicrobials.

Natural products based drug discovery played a crucial role in the development of modern medicine [5]. About 70% of all known anti-bacterial agents owe their development to natural products [7]. However, it has been concluded that most of the culturable bacteria from soils has been described and most prior to the 1960s [8,9]. Many studies have demonstrated the existence of bacteria in samples that cannot be cultured in the laboratory [5,9,10]. According to these studies, an estimated 99% of bacterial species fail to grow under normal laboratory condi- tions. Culturing techniques continue to evolve without a notiable increase in so-called described culturable strains [11]. If techniques could be developed to isolate and characterize more microbes it is believed it would provide additional opportunities for new antibiotics to be described and characterized [9].

Dr. Lewis at Northeastern University showed that marine microorganisms that had never been described before could grow in artificial media in colonies with the use of diffusion chambers in their natural habitat with the presence of other microorganisms [10]. Dr. Slava Epstein also at Northeastern University described an improvement to this method to isolate bacterial colonies that has produced newly characterized culturable bacterial strains [5]. This technique seems to work because of its ability to reduce competition among different strains of bacteria. The technique also utilizes the natural environment in which the bacteria originate, whether that is in water or soil.Usually the environment is limited or has unique resources and growth factors not found in normal laboratory settings. The bacteria are isolated by membranes yet allowed to grow in their natural environment by utilizing diffusible grow factors from the natural environment. With reduced competition and more natural resources, the bacteria naturally grow in isolation. After establishing a colony of growth the bacteria are further cultivated on media to increase the growth of the isolated bacteria. Use of this technology provides an opportunity for new antibiotic discovery among other useful benefits to society [5].

A crowdsourcing antibiotic discovery campaign titled, the Small World Initiative (www.smallworldinitiative.org), has been established across not only the United States but across the world. According to the website, there are more than 250 participating undergraduate institutions and high schools across 38 U.S. states, Puerto Rico and 14 countries. This effort provides the starting material for further research and development into new anti- biotics. This initiative seeks to encourage more students to pursue careers in science, while participating in an effort to contribute to the diminishing supply of effective antibiotics. Students in microbiology classes are work- ing to find the next antibiotics through a systematic search for putative antibiotic-producing soil microorganisms. These students work to characterize their own isolated microorganisms and to “challenge” pathogen-relatives to discover putative antibiotic producers. The so-called pathogen-relatives are associated with the identified ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter bau- mannii, Pseudomonas aeruginosa and Enterobacter species).

The combination of crowdsourcing and the aforementioned isolation methods have allowed unique and real-world experiences for undergraduate students to experience both the nature of science and positively contribute to the antibiotic resistance crisis and health threat. A new generation of microbiologist will hopefully help to blunt the diminishing supply of antibiotics and help to somewhat alleviate this serious health threat.

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