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Short Communication

Top World Priorities for Mutagenesis Applications

Jimenez RA*
Department of Nanotechnology, Technological University of Zinacantepec, Mexico

***Corresponding author:** Jimenez Rosales A, Department of Nanotechnology, Technological University of Zinacantepec, 106 Av, Libramiento Universidad, San Bartolo el Llano, Zinacantepec, 51361 Mexico

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Humanity will continue to face lots of health, social, political, environmental or technological challenges in the coming decades. Lots of authors have listed some of these problems and pose interesting proposals to the readers, to raise awareness and join efforts at a global level. Similarly, the WHO lists 10 global health threats in 2019 [1] that can be roughly classified in environmental emergencies, global diseases and infections, and quality of life. Though the solutions are not straight forward, mutagenesis may lay the solution to some of these problems.

Mutagenesis as science is wide-ranging and certainly will continue to expand as we gain a better understanding of how cellular genetic tools to alter and repair the coded information work and adapts these into new molecular biology techniques. Science has learned to use these tools for humankind necessities and accelerate the time length for the genomic changes to occur to obtain mutant genes, proteins and microorganisms that have novel functions. Now it is fundamental in genetic engineering for applications in agriculture, medicine, biotechnology, and synthetic biology, to mention a few. The potential application of mutagenesis to improve life quality and prevent disease is enormous.

Greenhouse-gas emissions are a problem in climate change, and reducing these will not be enough. We must find effective methods to retrieve tons of carbon dioxide from the atmosphere and transform them into useful compounds of high added value to society. Fuel sources should be environmentally friendly and energy-efficient. Renewable energies are becoming widely applied and cheaper to install, but as they rely on environmental factors, like sunlight or wind, but as those vary throughout the year, production planning and economic forecasting is hindered. Also, they present negative impacts like land use, habitat loss, wild life treats, and generation of hazardous substances and soil exploitation. Batteries present a practical way to store energy, however, their production cost remains high and generate hazardous waste that requires expensive treatment for its inactivation. On this aspect, microorganism biobatteries pose as an alternative [2] and research continues to understand their potential applications and through mutagenic studies to improve their efficiency.

Microplastics represent a difficult situation, as these are not biodegradable and tons of them are distributed in various ecosystems, including the oceans where are consumed by sea animals and birds. These animals tend to consume the plastic because they confuse it with food, and as they cannot digest it, results in less food for the animal and less energy to carry out vital tasks. Plastic has taken part in the food chain reaching all of its levels, amazingly, microplastics have been found in water and food for human consumption and their consequences remain uncertain. It is a priority to find a solution to biodegrade these materials and clean up the environment. Some microorganisms possess the enzymes required to biodegrade some of the polymeric chains found in plastics [3], and research is moving towards increasing their efficiency and conditions of activity.

Health round the world is a difficult problem to tackle. Considering infectious diseases like influenza, Ebola, SARS, Zika, HIV or coronavirus, can cause a public health emergency as we lack of effective treatments and vaccines [1]. The current outbreak of Wuhan coronavirus in China [4] is evident example that these infections require priority research and development of effective treatments. Other diseases for which exists treatment like tuberculosis, pneumonia, varicella-zoster virus or cytomegalovirus, have now emerged as a public health concern as microbes have developed the ability to fight back the antibiotics. Studies of the genetic changes and mutations that occur to confer or prevent induction of resistance indicate that by controlling the mutation rate and its expression can be one of the therapeutic strategies to combat antibiotic resistance [5].

Noncommunicable diseases like cancer, autoimmune disease or heart attacks, are a leading cause of death and disability, and for which we do not have a cure. These have a multifactorial nature and involve activation of biochemical pathways that have been studied through genetics, proteomics, and metabolomics and current efforts allowed optimizing patient treatment. Nonetheless, there is a long way towards taking a personalized approach in treatments. We must find biomarkers for early and accurate diagnosis, take advantage of informatics and databases, and give treatments with higher efficiency and no side or adverse effects [6]. So far, various studies on mutant variations and polymorphisms have detected genes that promote the onset of some of these diseases and provide relevant insight into metabolic patterns.

According to the UN, world hunger is the complex result of a weak economy, conflicts, and climate change; and it goes in hand with malnutrition, overweight, and obesity. Increase of world population and climate change require the production of efficient and enriched crops and s considerable number of publications in crop mutation breeding and crop genome editing indicate that mutagenesis part of the solution to this problem. Crop mutation breeding allows obtaining of new crop varieties and improvement in quality and productivity. Since genetic variability in plants has intricate processes of heritance, the significant genotypes are hard to be enhanced, so genome-wide association studies, with wild type and mutant genotypes, are required. Given the fact that spontaneous mutations in higher plants

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occur at a lower rate, with the right mutagenic conditions we can diversify genotypes and understand gene function [7].

Mutagenesis has proven to be extremely useful in protein engineering opening new possibilities for novel chemical reactions with high yields, energy-efficient and eco-friendly conditions. Moreover, several genetic tools and molecular biology techniques are available in standardized kits, databases allow information to be constantly updated and available, and the current prices of synthetic genes are decreasing, which allows for more extensive research, high-quality results and in general, a better comprehension of life processes.

Genome editing tools have become very popular controversial. The system CRISPR-cas [9], an enzymatic technology that allows for the edition of a genome *in vivo*, is one of the most debated. It can have tremendous applications to modify genes and has been used in various types of eukaryotic cells like yeast, crop strains, and human fetus; but there is evidence that it is non-specific. Despite the ethical implications, in October 2018 was reported that this technology was used in firstborn gene-edited humans in an effort to confer gene resistance to HIV. The project was stopped by authorities and heavily criticized by several renowned scientists [8,9]. The commotion led the path to the drafting of guidelines that mention that "anyone manipulating the human genome by gene-editing techniques would be held responsible for any related adverse consequences" [10].

These studies shine a light on aspects of the technologies that we, as humans, want to develop with the expansion of current knowledge, and about many other interrogants that we currently have about the mysteries of life. Early this year, just a few days ago, were published results of Hiroyuki Imachi, Ken Takai and their collaborators, who work in the Japan Agency for Marine-Earth Science and Technology in Yokosuka and did a remarkable work that took nearly 12 years. The group was successful in cultivating an Achaea microorganism that lives under very harsh conditions. The organism, named *Prometheoarchaeum syntrophicum*, was isolated from deep-sea mud and grew in a bioreactor fed with methane. In nature *Prometheoarchaeum* is a small coccus that typically grows in association with another microbe, one that produces methane from hydrogen and amino acids that are processed by *Prometheoarchaeum*, thus creating a symbiosis relationship. Their amazing results were that *Prometheoarchaeum syntrophicum* was found empty of organelles and having a complex morphology of branching protrusions. The incredible work has received much praise from the scientific community, as it gives insight of a model of how complex life evolved, as the protrusions are hypothesized to have engulfed the protomitochondria and produced the internal membranes in eukaryotes [11].

So, it appears that our world is moving faster than ever before, but this frenzy transformation can be extraordinary and bring some positive changes. As it is been discussed, there are important problems that require an urgent solution and researchers from different areas and expertise are working hard to make a difference and create solutions that would create a promising future for humankind. In this scenario, mutagenesis represents an important tool at our disposal that if used properly may very well bring efficient solutions to these challenges.

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