Challenges and Future Prospects of Biotechnology

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1 Introduction

There has been a tremendous progress in the field of biotechnology over the years, and its application cuts across agriculture, marine biotechnology, bioengineering, bio-manufacturing, biomedical engineering, drug discovery, vaccine development and in environmental microbiology (Daniotti & Re, 2021). Despite its numerous benefits, biotechnology remains low due to several socio-economic, ethical, health, or political concerns (Ivase et al., 2019). Therefore, this chapter reviews the challenges and future prospects of biotechnology.

Biotechnology posed a great promising area based on current and future applications of it, to solve medical, environment, energy, agricultural, and military problems. This promise is from direct application of biotechnology and from the growing area of multidisciplinary research that combines biotechnology with other sciences like materials science, physics, chemistry, and engineering just to name a few. However, there is also growing concern over possible dangers from this area of science based on the potential for mishaps from honest scientists and applications purposefully developed to cause harmful or even devastating effects (Munis et al., 2019). The areas of biotechnology with tremendous future opportunities that can impact all include: (a) Drugs and pharmaceuticals development; (b) Medical device and diagnostics; (c) Noninvasive sensor in agriculture; (d) Rapid testing of

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pathological conditions; (e) Quick testing for food adulteration; (f) Precision agriculture and biofortification; and (g) Machine learning and artificial intelligence in biotechnology.

2 Marine Biotechnology in Sustainable Industrial Development

2.1 Discovery of New Products

It is estimated that over 90% of marine biodiversity is completely unknown as our knowledge of the environment is restricted. This is due to the technical difficulty of accessing deep seas, thus impeding the collection of samples (Daniotti & Re, 2021). Also, majority of organisms isolated from the marine environment are difficult to analyze and therefore taxonomic classification is complex, resulting in potential errors that could compromise the entire process of drug discovery due to the impossibility of reproducing the isolation event and the subsequent identification of the bioactive compound (Kasanah & Triyanto, 2019).

2.2 Sustainable Production

When using marine organisms for the production of high value-added substances and biofuels, the vulnerability of the marine environment must be considered because the quantities supplied directly by marine organisms do not support industrial requirements and the more limited ones of the drug discovery process (Vlachou et al., 2018). The unswerving collection of bioactive compounds of industrial interest is never maintainable, particularly as most of these species are at the verge of extinction and their unwarranted abuse could destroy the intricate balance of the ecosystem (Daniotti & Re, 2021).

2.3 Extremozymes in Biotechnology Applications

There is usually low yield or activity of enzymes when they are cultivated on a large bioreactor scale, usually required for commercial applications, and this has been a significant drawback in utilizing extremozymes in biotechnology (Sarmiento et al., 2015). Active alcohol dehydrogenase (HvADH), laccase (LccA) enzymes and bacterioruberin and halocins proteins produced from *Haloferax volcanii* must be done on a large scale to realize their true biotechnological capacity (Haque et al., 2020), but expression and purification of bulk quantities of highly active proteins in a halophilic environment is however demanding as co-purification of unwanted nonspecific proteins with the target protein is often encountered following affinity tagged protein purification (Sarmiento et al., 2015). When using *Haloferax volcanii* as the host, their intrinsic ability to form biofilms is a deadlock on large-scale protein over expression (Chimileski et al., 2014), since these biofilms can interfere with expensive sensors present in the bioreactor during the fermentation process and may also alter the characteristics of expressed proteins. Furthermore, when culturing *Haloferax volcanii,* there is the need to use reactors made of alternative materials rather than the readily available stainless steel as the molar concentration of salt required to grow this organism can quickly corrode stainless-steel bioreactors (Haque et al., 2020).

3 Agricultural Biotechnology

3.1 Plant Biotechnology

New technologies, especially in transgenes and gene editing, will be required as the demands of human beings such as higher contents of vitamins and micronutrients found in cereals, increased shelf lives of vegetables and fruits and reduced allergens increases perpetually (Nguyen & Ly, 2018). There is still a large gap in successfully creating new crop varieties with desired traits for human consumption, even when gene/genome editing technologies have been successfully tried in many research laboratories (Moshelion & Altman, 2015). Also, having an insight into the roles of genes governing complex traits to actively improve agronomic performance or control adaptations to abiotic stresses is a matter of concern, as genetically modified organisms (GMOs), transgenic crops, and recombinant DNA technology are the future trends in plant biotechnology. The complex traits of interest include a crop's ability to grow efficiently in drought, salinity, acidic, or aluminum-containing soils, competition with weeds, flowering time, heterosis, and durable resistance to diseases (Nguyen & Ly, 2018).

There is a rise in energy prices because of the reduction of fossil fuels and this rise requires new processes for the production of renewable energy sources called biofuels (Nguyen & Ly, 2018). One of the favorable materials for biofuel production through enzymatic fermentation and chemical transformations is lignocelluloses (Den et al., 2018), but a major challenge for biotechnology in the degradation of the stable polymer chain into sugar molecules for further fermentation and conversion is the modification or alteration of the properties of the polysaccharide profile in the cell walls of plant materials (Popa, 2018).

3.2 Animal Biotechnology

Semen sexing technology for selecting the sex of embryos relies on the principle of flow cytometric separation of fluorescence labeled sex chromosomes, but the low number of sexed sperms produced and the occurrence of sperms being damaged during the sorting process that reduces the efficiency of fertilization in later steps are the main drawbacks of this technique (Espinosa-Cervantes & Cordova-Izquierdo, 2013). Cloned animals derived from cloning technology on the other hand, often suffer from severe injuries or are not able to reproduce (Nguyen & Ly, 2018). In animal biotechnology, the issues of animal welfare should also be taken into consideration. Depending on one's personal beliefs, some people oppose the use of animals for any purpose, while others have specific concerns about the impacts that genetic engineering and cloning may bring by producing human therapeutic or industrial proteins (Nabavizadeh et al., 2016).

Another drawback in animal biotechnology is in the field of transplantation of living cells, tissues, or organs, where there is always shortage of organs for clinical implantation in patients who need a replacement organ at the end stage of failure (Nguyen & Ly, 2018). Although, tissues or organs from some animals from the order primates or from pigs could serve as candidates for transplantation in humans, but the lifespans of the donor animals are shorter than humans; therefore, the aging of the grafted tissues at a quicker rate is still a challenge in xenotransplantation technology (Hryhorowicz et al., 2017). Only a few temporarily successful cases of xenotransplantation have thus far been published as animal rights activists have also objected to xenotransplantation on ethical grounds.

3.3 Microbial Biotechnology

Research in microbial biotechnology is focused on three main areas in various application fields; agricultural practices, microbial enzymes for industry, and environment treatments. Stubble, straw, and sawdust which are byproducts in agriculture and forestation production contain stubborn polymers like lignin, cellulose, and hemicellulose, which are a challenge for the development of new technology for biodegradation to convert them into biofuels, feeds, and biofertilizers (Kilbane, 2016). Reactions of some enzymes such as lipozyme, lipase, cellulase, amylase, and xylose isomerase in organisms are efficiently performed under physiological conditions, but industrial conditions are far different with high substrate concentrations, sheering forces, high or low temperatures, and organic solvents. In addition, the requirements of regiospecific, chemospecific, and stereospecific reactions are challenging for industrial and pharmaceutical enzymes (Chapman et al., 2018). Therefore, most enzymes found in soil and water microbes are not able to display their desired activities under industrial conditions (Nguyen & Ly, 2018).

3.4 Health and Medicinal Biotechnology

Functional genomics is still a big challenge in gene identification, analysis of gene interactions, and the relationships between genotypes and phenotypes in complex diseases (Nguyen & Ly, 2018).

3.5 Environmental Biotechnology

Environmental challenges require newer technologies for environmental control, protection, and remediation. The constituents of environmental contaminants are becoming diverse, and as such, require more effective microorganisms for environmental treatment and management (Vujic et al., 2015). Also, genetically modified organisms are seen as biohazard to the environment in some industrial processes (Nguyen & Ly, 2018). In general, the intricate balances between hosts, pests, humans, and the environment should be seen as a challenge for biotechnology in the future.

4 Challenges Faced in Using CCRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)

One of the key challenges in using CRISPR (clustered regularly interspaced short palindromic repeats) is designing the RNA guide. Research has shown that some RNA guides are less efficient than others, some are inactive while others are promiscuous, and in the absence of a good RNA guide, multiple off-target effects can occur. In addition, several potential RNA guides can perform the same editing task, but each has different off-target outcomes. As a result, selecting the right RNA for the task at hand adds to the challenge of achieving proper design. In other words, the specificity and precision of CRISPR is largely conditioned by the type and specificity of the RNA guide (Vogel & Ben-Ouagrham-Gormley, 2018).

5 Future Prospects of Biotechnology in Machine Learning and Artificial Intelligence in Biotechnology

The rapid progress in biotechnology and in information technology has occurred in parallel over the last twenty years. The large data available and the new experimental technologies developed in the recent years make it easier and cheaper to carry out several biotechnology experiments that would have taken years to complete. The large amounts of data mostly derived through omics-technologies that are generated and stored, in the biotechnology research, create an array of new opportunities for researchers, as well as for companies that offer products and services in this area. At this point artificial intelligence (AI) and machine learning (ML) technologies to process, explore, and analyze these large data are new emerging area in biotechnology and therefore, AI and ML are promising areas important in advancing the benefits of biotechnology. Adaptation of AI and ML will allow biotechnology to solve complex societal challenges through its own systematic testing. For example, now electronic health records systems are gradually integrating in health sector so that health-related data can be accessed globally, opening the door to a holistic outlook (Sharma, 2020). Machine learning technology also holds promise for the future of the clinical trial. Biotech companies can quickly analyze data from current trials to predict the effectiveness of treatments down to a molecular level; they can also revisit data from previous trials to see if anything may have been missed, or if there may be new or different uses for an existing drug (Brian, 2020).

6 The Future Prospects of Biotechnology in Medicine, Medical Device, and Diagnostics

Genetic engineering can potentially regulate hereditary diseases. Brain-computer interfaces developed by using new nanomaterials that provide bidirectional neural communication will enable the patients to write words which they are imagine or to control the devices. These noninvasive interfaces may seem utopian, but can be a marvel of genetic engineering in the new era. In addition, studies are being carried out on treatments that may extend life, such as telomere modifications and reversing aging.

In modern medicine, doctors evaluate patients to clinically diagnose, treat, and prevent diseases. Thus, there are also benefits of a treatment regime that is based on the genotype of each individual to include epigenetic factors for the development of individualized medication selection, dose adjustment and individualized therapies to overcome a more traditional trail-and-error approach. For example, in the field of oncology, which plays a role in the prevention, management, and treatment of non-future cancers, there have been enormous strides that can be attributed to the development of immunotherapy, genomic and genetic engineering technology (Munis et al., 2019).

Another new face of modern genetic engineering is CRISPR/Cas9 technology and its therapeutic potential is excellent. As technology develops, the therapeutic potential of CRISPR/Cas9 will continue to increase. Nonetheless, CRISPR/Cas9 has many difficulties in fully developing its potential. Cas9 nickases and mutants that reduce nonspecific DNA binding are designed to alleviate these problems, although this is a problematic solution. The gene cargo distribution system remains the biggest obstacle to the routine use of CRISPR/Cas9, and a multipurpose delivery method has not yet emerged (Lino et al., 2018). Gene therapy is an experimental method to correct a defective gene that is responsible for the emergence of the disease. In addition to advances in delivery and expression technologies, future efforts will focus on new areas of gene therapy practice, such as new resistance genes and chimeric T-cell receptors. The sequence of the human genome is useful in many fields, from molecular medicine to human evolution. With the development of gene therapy technologies, the modelling of genetic diseases also increased (Kulkarni et al., 2018). In recent years, the renowned method of gene therapy has been used to treat a number of diseases on genetic models developed by CRISPR technology. For example, metabolic diseases, cardiovascular diseases, monogenic diseases. Also developed drugs are tested on these genetic models. If the correct gene is determined and the appropriate vectors are selected, then there should not be disease that cannot be treated.

7 Nanotechnology and Medical Biotechnology

Advances in nanotechnology also provide a rich framework for future developments in medical biotechnology. Related to disease prevention is the widespread use of antibiotics and antibacterial coatings to reduce the impact of infection on causing the failure of implanted medical devices. Nonetheless, such approaches have limited effectiveness. Nanotechnology now provides the tools for nano-texturing the surfaces of materials for medical implants, with the aim to mimic the bactericidal properties of some animal, plant and insect species, and their topographical features. For example, the surface nanostructures of cicada, dragonfly and butterfly wings, shark skin, gecko feet, taro and lotus leaves provide self-cleaning and bactericidal properties (Jaggessar et al., 2017). That type of bioinspiration provides great innovations in providing some biological-like characteristics that can be used to guide the surface structuration and synthesis of materials into functional devices and processes.

In biological systems there is a self-assembly y of molecules to create elegant nanostructured systems. A central feature of such biological nanostructured systems is the assembly of phospholipid bilayer membranes that both provide compartments (i.e., biological cells) to rationalize the overall function of complex organisms (e.g., plants, animals) and also to provide an environment in which to stabilize membrane proteins to assist in the sensing and actuating functions of biological cells (Bentley et al., 2018). These components of biological cells provide the basis for transport of ions and molecules between the cell and the surrounding environment inside the body, which supports the ability of cells to participate in physiological control of the body. Extending the concept of bioinspiration to include such elegant nanostructured biological self-assembly then provides an additional dimension to applying nanotechnology to medical biotechnology. That additional dimension is to include nanostructured bio-membranes into hybrid medical devices that can provide the ability for the medical device to communicate ions and molecules with the body. This then leads to the notion that an implanted medical device should integrate and

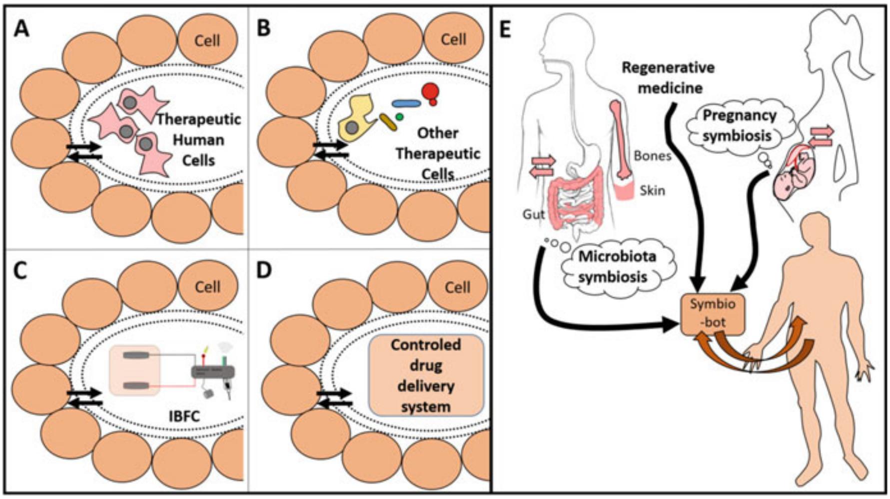

Fig. 1 Examples of symbiotic devices (symbio-bots) (**a**–**d**) that can be created in a bio-inspired way (**e**). Each device is separated with a smart porous packaging that allows a duplex communication. Therapeutic cells (**a**, **b**) need a porous encapsulation y that avoids an immune reaction and allows protection from both sides. They may be human cells, as MSC or specialized cells such as β-cell from Langerhans islets (**a**), or other eukaryotic or prokaryotic cells (**b**). Panel (**c**) shows an IBFC linked to an electronic medical device. Panel (**d**) shows a generic device delivering a therapeutic molecule. Panel (**e**) Existing symbiosis (i.e., microbiota or pregnancy) are a source of bioinspiration to establish a duplex communication between the body and its implants. Regenerative medicine should embrace this concept of bioinspiration for a better design and integration of implants, especially for future symbio-bots (reproduced with permission from Alcaraz et al. (2018))

become symbiotic with the body (Fig. 1). This extends the definition of a biocompatible system to one that requires stable exchange of materials between the implanted device and the body. Having this novel concept in mind will guide research in a new field between medical implant and regenerative medicine to create actual symbiotic devices (Alcaraz et al., 2018).

8 The Use of Digestible Sensors

Additionally, a treatment method in the future of medicine is the digestible sensors placed in pills. Data from these sensors are transmitted to doctors and family. Thanks to the biotechnology industry, more objects can now be printed using 3D printers. In the near future, printing of medical devices in underdeveloped areas and printing of live tissues, cells, or drugs may be imagined. But everyone is able to print medicines containing patented molecules in their homes, so ethical problems can emerge. Also, 3D printing is not the only way used to create body parts and artificial organs, it can be grown in the laboratory environment using biomaterials. The artificial organ is a device or biological material that is implanted in the body to alter a natural organ or function. The other innovation can be the sensors that can be digested to make a quick diagnosis. These sensors can be swallowed directly for gastrointestinal diseases. Further, the sensors embedded in the tooth can detect jaw movements and speech. More complex microchips that can mimic the whole human body are needed, and this final solution could arrive soon. As the amount of information increases, cognitive computers may be used instead of human in medical decision making (Munis et al., 2019)

9 Conclusion

In summary, despite series of challenges, the future of biotechnology research is strong and very promising. We presume that very soon a day will come, when breakthrough drugs will lead to a world without COVID-19, cancer, or AIDS, and many more life-threatening diseases, a world with sustainable research development that will tackle the need for food, environmental safety, low cost medical devices, energy, and many more societal giant challenges without compromising the world's resources.

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