Review Article

The Role of Systems Biology and Synthetic Biology in Appearing and Managing COVID-19

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Abstract

Studies reveal that viruses play important roles in the origins of cellular life and the evolution of all mammals for example. COVID-19 as a modified brutal virus has affected daily life and is slowing down the global economy. This pandemic has killed thousands of sick or infected people, Therefore, the main purpose of the current study stems from the question that how COVID-19 was created and how it will be solved. To conduct the present research, 26 English articles were chosen from among 57 articles published from 2000 to 2020 based on their relation to viral diseases and the availability of the full text in PubMed, Science Direct, ProQuest, and Google Scholar databases. To study the new coronavirus, its genetic sequence should be accessible for us. As understood, synthetic biology takes advantage of the knowledge obtained from systems biology analysis and the conceptual tools made for such purposes. Computational modeling is an amalgam of systems and synthetic biology. These approaches develop systems toxicology as well as stand out in predicting and evaluating the immunogenicity of vaccines as well as improving vaccine formulations through a definite immunological marker. Due to acrimonious and costly episodes of human life and viral diseases such as SARS, MERS, and COVID-19, human beings need national security that can be provided by restoring health care services and educating more health care professionals is more effective than training the military. Dealing with such an issue demands vast knowledge of biotechnology, cell, and molecular biology expertise, and competent approaches based on bioinformatics technology that contains systems biology and synthetic biology. Therefore, such scientific fields need to be highly developed in developing countries to keep their immunity and national security under warranty encountering any biological invasion, most specifically of viral types.

Keywords: Pandemic viral diseases, COVID-19, Systems Biology, Synthetic Biology, Bioterrorism, Vaccine

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Introduction

Life on the earth includes a multitude of cellular organisms, and cellular life is immersed into an ocean of viruses each of which can enforce cellular organisms to fulfill their particular needs. There are around 100 strains of the cold virus and the toxin they are often treated for. It takes us nearly 50 years to go through all the reformed cold viruses. Therefore, various have been here with us for ages. Studies reveal that viruses play important roles in the origins of cellular life and the evolution of all mammals for example. There is no doubt that we unconsciously discount or even pass over the viruses, due to their simplicity and intimate nature, to find out the evolutionary phenomenon of the living things.

Yet, there are things that we are unknown of simple viruses or their roles in evolutionary processes. Our bodies and species often face ongoing fights with diseases. On the other hand, we have an immune system that can protect against such invasive diseases, but when an invader evolves a mechanism to surround the human immune system, it can infect people anywhere. Evolution to evade human immune defense explains why viruses that make colds spread through human populations readily (1, 2).

The emergence of new virus diseases that often receives worldwide attention from scientists, researchers, and the lay public is one of the most moving prospects of virology. There has been mounting interest in the increasing number of viruses leading to unexpected illness and epidemics among humans, wildlife, and for more than two decades.

The Emerging disease is most frequently used to refer to an unknown kind of infection or any other pathogenically changing infection that was already identified and has recently entered any new ecology or geographical environment. Noteworthy is that these diseases reveal some constantly evolving infections reacting to sudden changes in the relationship between the microbe and the body (3,4).

COVID-19 (Coronavirus disease 2019) as a modified brutal virus has affected daily life and is slowing down the global economy. This pandemic has killed thousands of sick or infected people. Due to the high transferability of the virus among people, it is crucial to diagnose the disease at the early stages to curb its spread. Most countries have reduced their manufacturing of the products (5).

Concerns over coronavirus being a bioweapon flourished due to its pandemic's effect on the world is not a conventional form. It seems to be an extensive and indiscriminate attack on global citizens and the economy, which has directly influenced the lives of billions of people. This spread has shown itself as the most effective pattern for future terrorist activities and a new model for circumventing the properties of modern warfare (6). Therefore, the main purpose of the current study stems from the question that how COVID-19 was created and how it will be solved.

Study Method

To conduct the present research, the articles published between 2000 and 2020 were studied. To access the related scientific documentation, an electronic search was carried out using keywords such as COVID-19 and Coronavirus, separately or in combination with systems biology, synthetic biology, systems medicine, and vaccine in PubMed, Science Direct, ProQuest, and Google Scholar databases. Considering the aforementioned keywords, 57 related articles were found and 26 papers were used to serve the purpose of the current study after the initial research. The articles for review were chosen based on their relation to viral diseases, published between 2000-2020 in English, and the availability of the full text.

However, other pieces of research presented at conferences, written in Persian, available as an abstract, or published on various websites were excluded. Having found the related articles, the researchers checked different parts including the topic, abstract, method, results, discussion, and references.

Background

Bioterrorism affects our lives and economy and that is why Terrorist Organizations try to weaken a target economy by applying a series of undemanding technologies in organized and complicated attacks on infrastructures. These attacks often include shootings, explosives, or even biochemical weapons like mustard gas.

Designing and distributing these deadly biological weapons could be quite complex depending on the biological agent in question, for example,

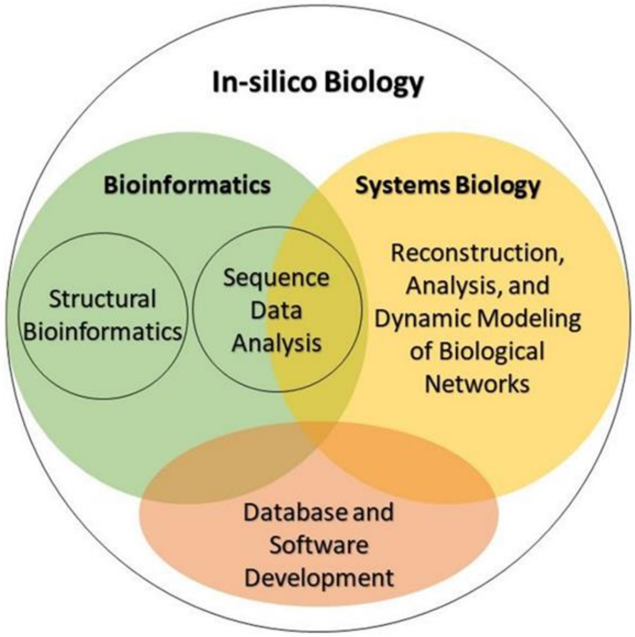

Figure 1. In-silico biology and its sub-branches.

Bacillus anthracis, an outstandingly multi-purpose and deadly pathogenic bacterium that leads to anthrax, usually takes place in any environment and infect almost all the living things.

Anthrax is highly and easily transmittable and its extremely infectious spores get into the body by inhalation of aerosols or ingestion through polluted water supplies. As a result, anthrax is known as a major potential bioweapon. In 2001, five people in the United States died after receiving a mail polluted by anthrax but no one was ever arrested or charged (6-9).

The important point is that a group of cold viruses has developed in a way that exchanges genetic information and constantly creates new viruses. There are approximately 100 types of cold viruses, and any person catches a cold almost twice a year (1).

In contrast, applying synthetic biology to devise new bioweapons from earlier pathogens using CRISPR or DNA synthesis is far more complex in terms of laboratory requirements and expertise. Moreover, operating and managing these agents are more available by biotechnology companies competing aggressively to take the attention of academic, corporate, and government findings**.**

Researchers have also equipped their laboratories with 3D-printed equipment that made complex instruments, once expensive and inaccessible, easily available to anyone interested in biotechnology.

This approves the labor-saving development of weapons to take place anywhere from strict, regulated laboratories to remote facilities and even in one's garage. Therefore, the accessible and easily used technologies enable any investor anywhere to consider and apply an underground bioweapon program. Talent is the only necessity that fills the gap.

Also, terrorist organizations try to own the same infrastructural and scientific capabilities as modern industrial nations qualifying them to potentially generate biochemical supplies.

The infrastructure requirements for biological weapons programs are also made easier since they are cheaper and more versatile in comparison to the nuclear arsenal. This is almost because they can be covered by any improvement in the medical industry, health, and agricultural research (9).

It is worth mentioning that various theories concerning the nature of the recent coronavirus SARS-CoV-2 have occupied the internet during the past few months. They often bring about more engrossing discussions than the ones implied by the authors; for

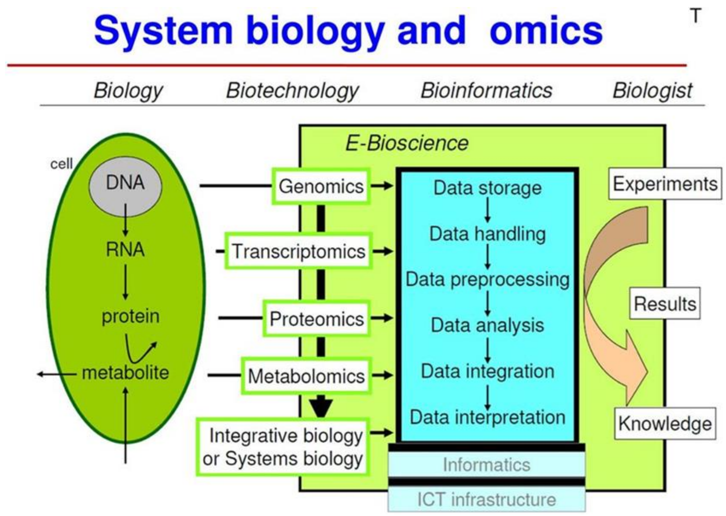

Figure 2. Biotechnology and Systems biology.

instance, the theory behind the new coronavirus, as an intentionally made biological weapon, displays that SARS-CoV-2 is exactly a synthetic organism, which in turn suggests that scientists can formulate man-made viruses.

How far can modern technologies proceed considering the synthetic microorganisms' paradigm?

The recent state of synthetic biology is all we need to understand as a field with all the limitations it has if we ever want to answer these questions. Synthetic biology is highly dependent on prognostic patterns and computer-based formations. Computer programs use the information gathered through years of research about molecular biology, stored in equipped libraries of microorganisms, molecules, and domains, to examine their properties when reformed or combined in silico –done by a computer**.** These plans often form combinations that reasonably are not found in nature, so it is hard to analyze their potential structures for various purposes. Although in-silico models give us useful information and save our time and cost in vitro experimentations, they still seem to be imperfect (10, 11).

Davies, a professor from the University of Edinburgh, published a paper in the open-access journal of Life and analyzed the recent stream of the 'engineering approach' in synthetic biology. While working, he recognized that this approach is interesting for its design-build-test doctrine and that based on the standard existent parts that simplify the general pattern of fabricated structures, it lacks biological understanding.

Any element of a microorganism has a metabolic cost in biology implying that the more constituent you add, the less energy the cell leads to other segments, so the fewer parts for its function, the better. Besides, it is assumed that when new genes are provided, the old genes are removed so that the organism remains usable and it is very important to notice in genetic engineering.

Moreover, the true function of the genes is influenced by the interaction of the parts that existed before. Therefore, as Davies mentions, using a new component, devised for a specific purpose, is much easier than striving to stimulate a similar function with the parts that existed before. Finally, it can be pointed out that evolution does not rely on the combination of constant structures but depends on the continuous modifications of the pre-existing patterns affected by many items. Ultimately, synthetic biology, as a resort for unexplored and unknown phenomena, is not comparable with natural evolution in terms of completeness (12)**.**

It is worthy to mention that series of notions, devices, and approaches that alter or create biological organisms within biotechnology define synthetic biology. Although there is not a single definition for synthetic biology (different studies report specific and general usages), it is mentioned that synthetic biology "aims to improve the process of genetic engineering".

Notably, synthetic biology focuses on the Design-Build-Test (DBT) cycle2, the frequent process of contriving a paradigm, fabricating a physically tangible example, evaluating the potentiality of the functionality of the paradigm, and learning from its imperfection during the progression of genetic engineering while applying the data to creating an upgraded design. Likewise, biological engineers can easily duplicate the DBT cycle to improve the design and the outcome for specific purposes by adopting modern computer technology, equipped laboratories, DNA synthesis, and sequencing technologies cost-effective, and other effective methods for DNA maneuverings.

The age of synthetic biology is initiated in both modern technologies and using the engineering patterns in biological fields. The idea of managing biological systems and adopting the engineering models from other disciplines dates back to the introduction of recombinant DNA technologies during the 1970s. Recently, there has been a cooperative attempt to manipulate both genetic matter and biological organisms.

With this in mind, the potential of some specific technologies that enable biological materials to benefit from engineering paradigms has been escalated. To recognize the possible security opportunities and liability, evaluating novel technologies and policies that lead to inventive or damaging operation of biological matters, structures, and organisms. Several technologies have paved the way, facilitated the experimentations, especially in the DBT cycle, and qualified synthetic biology. What almost explains the recent changes in synthetic biology is the development of the mentioned technologies specifically devised for synthetic biology or general molecular biology and biotechnology manipulated by synthetic biologists. Such technologies are in fact instruments that provide the requirements of biological paradigms and structures. Some noticeable enabling technology fields involve DNA *synthesis and assembly*; *Genome engineering*; Improved *computational modeling*; *Genetic logic*; and *Directed evolution*. Biotechnology, a term used for almost one century, includes the use of biological elements or procedures to serve human goals; however, researchers have used its different forms to refer to millennia (13).

Modern biotechnology projects require gathering, storing, classifying, analyzing, and distributing biological information provided by genomics projects. Likewise, different ways of saving, regaining and analyzing biological data and protein sequence, content, performances, pathways, and networks, in-silico disease simulation using the system biology recently are the focus of bioinformatics. Bioinformatics includes conceptual and practical instruments for spreading, creating, processing, and understanding scientific views and biological input. Thus, synthetic biology tries to facilitate and anticipate the functions of biology engineering (11,14).

It is also important to consider how capable recent scientific methods are regarding virus engineering. Researchers can recreate a virus to make it more remarkable as it starts to expand like the coronavirus. Nevertheless, it is possible to create a new virus that demands another procedure like recreating a new virus from the original one, which is restricted from different perspectives (10,12).

Synthetic biology demands the use of pre-existing constituents meaning that it requires the use of various components of present viruses and their combination to create a new virus (10-13).

Hence, creating a new virus at present is technically hypothetical requiring an unbelievable level of knowledge in any scientific institution. Nonetheless, our recent understanding of molecular science enables us to recognize the potential man-made structures or microorganisms since they are based on existent constituents; an engineered virus probably has identifiable DNA elements of other viruses whose successions are available in libraries. In other words, what we need to understand is making out whether a new virus is synthetic or naturally modified (10).

To study the new coronavirus, its genetic sequence should be accessible for us. This has been notable progress in epidemiology, as pandemics researchers needed to wait for months and years previously to study the microorganism that caused the spread, while the formation of SARS-CoV-2 was recognized in less than a month. Having examined and analyzed the genetic structure, scientists have realized that this virus is a new one (10). We are aware that the backbone was not duplicated from a pre-existing virus but it can be artificially made.

What about modifying a pre-existing virus to mutate? That is to say, we can observe many cases in nature where biotechnologists mutate an existent virus to generate a new one. With this in mind, it was found out that as scientists assessed the SARS-CoV-2 formation and juxtaposed it with other viral formations, approximately, 96 percent similarity was found between SARS-CoV RaTG13 and the new Coronavirus. Having the size of SARS-CoV-2 in mind, this number is significantly high since it is close to 30,000 nucleotides long, around 1,200 nucleotides (10-14).

However, some may resist rejecting certain theories (10). A persuasive argument is that when some known segments of the same viruses are used, purposeful modifications have been probably applied to enable the virus to stick to humans and more specifically infect humans. One of the most astonishing facts about the coronavirus is that the receptor-binding domain – the part that enables SARS-CoV-2 to stick to human cells – was simulated in silico when the sequence of the virus was accessible. Such orders with insufficient capability for the simulations revealed that nature has an unpredictable mechanism.

The epidemiologists and synthetic biologists, who are inspired by the process of molecular interactions, both benefit from studying the evolution of viruses. This can enhance the recent paradigms and pave the way for presenting new frameworks and producing new molecules. Hence, we can claim that studying the evolution of viruses helps synthetic biology to develop and serve as a useful tool (9-13). SARS and MERS got more victims around the world than the COVID-19 pandemic did; however, this worldwide spread has already caused more casualties. What helps us deal with the complicated nature of the mentioned disease in biology is a systems biology approach that makes the virus and mechanisms of disease more tangible (15).

Discussion

What differentiates synthetic biology from systems biology is ‘Engineering’ or ‘Synthesis of innovative functions’. Therefore, systems biology demands a quantitative understanding of present biological systems, while synthetic biology considers the logical engineering of such systems.

As understood, synthetic biology takes advantage of the knowledge obtained from systems biology analysis and the conceptual tools made for such purposes. Taking it to the extreme, synthetic biology is an engineering discipline that demands standard parts that can be improvised using bioinformatics and simulation techniques to create circuits that can be modified (16).

Systems biology is an interdisciplinary field that studies the heterogeneous interplays and the shared functions of a cell or an organism. Technologically, synthetic biology merges engineering and biological science and enables the design and manipulation of a system to be used for certain applications. Synthetic biology and systems both have key roles in the current progress of microbial platforms for energy, matter, and ecological usages.

Noteworthy to mention is that systems biology gives us the required insight to improve the synthetic biology instruments, which leads to easy application and understanding of biological system complications. Therefore, to study microbes and carry out complicated tasks like generating biofuels we need both systems and synthetic biology due to their considerable potential. Both of them focus on science and technology; however, the knowledge of systems biology leads to a better design for synthetic biology tools that provide better insights into systems biology (17).

Systems biology has fostered noticeably as a discipline during the last decade and the new method of systems medicine has emerged as a duplicated expansion of systems biology.

Systems medicine is characterized by the way it is applied to systems biology to understand, adjust, prevent, and improve the growing illnesses and pathologic processes in human health. Although systems biology and systems medicine often overlap, systems biology seeks a basic understanding of biological procedures and a complete paradigm of biologic systems, while systems medicine focuses on the main objective purpose and relevance of translational models that consider the diagnostic, predictive, and therapeutic applications. Given such findings, due to the complexities of biology and medicine, the biological and medical aspects of systems medicine should be evaluated more (18).

Precision medicine, as the primary goal of systems medicine, asserted that these types of medicine demanding to be predictive, preventative, and participatory are not obtained by an increasing evolution rather by the drastic transformation in the application of medicine (19).

Moreover, systems medicine studies Medical cybernetics as a branch of cybernetics that includes a recent working plan for using systems and communication theory, connectionism, and decision theory in biomedical investigation and health-related issues. Medical cybernetics seeks to describe the biological dynamics quantitatively and it studies the intercostal web in human biology, medical decision making, and information processing structures in the living organism (19).

The application of these new methods of systems biology and synthetic biology has assisted biological sciences, clinical medicine, and any related area. In this regard, Toxicology research has recently started to cooperate with a variety of computational and artificial biological approaches for evaluating the toxicological hazard of chemicals. Systems toxicology was first introduced to define the use of systems biology techniques in toxicological studies (20).

Another term is synthetic biology that possibly changes the form of toxicology and reveals how scientific methods like biology, bioengineering, chemical and electrical engineering, and computational modeling are related. Computational modeling merges systems and synthetic biology. Recent improvements in systems and synthetic biology include the engineering of synthetic genetic circuits, gene promoters, proteins, and a variety of synthetic biomolecules (21).

Systems biology in vaccine development

Vaccination prevents and curbs diseases effectively. Various viruses eradicated or effectively curbed by following vaccination curriculum mostly cause fatal epidemics like diphtheria, poliomyelitis, smallpox, and measles. Significantly, systems biology is studied from two main viewpoints; namely, a top-down approach in which the probable transformations, found through trial and error, are predicted deductively and a bottom-up approach that includes inductive clinical research.

The reverse engineering approach, on the other hand, is used in hypothesizing the factors that affect the high-tech tools used to record the global picture related to specific biological instances.

These systems biology approaches stand out in predicting and evaluating the immunogenicity of vaccines as well as improving vaccine formulations through a definite immunological marker (20, 21). Having carried out worldwide research through systems biology, we understand the complicated and interrelated interactions between the invulnerable performance of the host (immunotherapy) and the innately adaptive reactions.

Useful knowledge in immunology and genetics can be provided by an inclusive analysis at the system level of immune reaction to vaccines and immunotherapies (vaccinomics or systems vaccinology). This, in turn, causes great progress in vaccine advancements like the identification of optimal antigens, and antigen formulations (i.e. adjuvant antigens), and influencing the searched cluster of genes and immune tracks that provide the essential adaptive immune reaction.

Besides, it facilitates screening for reactions to vaccines or immunotherapies and perceiving ultimate collapse among individuals took part in clinical trials largely.

In truth, the applicability of such inclusive analysis in epitomizing the treatment to get a better clinical result is remarkable when the recognition of gene records or polymorphic genes associated with immune reactions to immunological approaches are taken into account.

Nonetheless, if vaccinology is going to be used as a worldwide system, systems biology should follow several procedures because this science is still improving. The broadness and complexity of the polymorphous nature of immune reaction genes necessitate several hi-tech and bioinformatics approaches to reasonably operate the extensive genetic data.

Likewise, to categorize natural and immune response-related genetic - gene expression or polymorphism – modifications, it is vital to assess various studies carried out in wider circumstances with the different genetic backgrounds; although, few studies have revealed that genes are balanced facing vaccination causally.

The assessment of the output in definite contexts to merge numerous information types helps us to deal with such issues.

Besides, based on the evaluation of vaccine or immunotherapy, the peripheral blood mononuclear cells do not always reflect the identification of the predictive target cell population.

However, being used in vaccinology and free from cultural, technical, and financial concerns, systems biology shows the path to create new vaccines, renew earlier vaccines, and shift from the "empirical" to "knowledge-based" phase of vaccinology. This, in turn, causes the progress of more prosperous vaccines for human diseases with individual or group-personalized strategies through both preventive and restorative intervention approaches (21).

The synthetic biology approach can be potentially applied to the creation of vaccines to fight pathogenic viruses or bacteria (22).

Nevertheless, making vaccines is implausibly demanding since the antigenic nature of viruses is highly diverse and high metamorphosis velocity does not succeed by applying primary vaccine manufacturing methods and the challenges, included in the processes that bring about serious restrictions. Virus-like particles (VLPs) are reproduced noninfectious viral structures that show the immune defensive quality of the original viruses. Some VLPs, comparable to any natural virus structurally, have been evolved and accredited as vaccines. Recently, a huge research surplus admits that for a safe display of heterologous antigens among several pathogens that are irrelevant to other selected carrier VLPs, it is vital to design VLPs.

Such versatile designs help VLPs to technologically renovate vaccine supply and disease reaction using rational bioengineering. Such opportunities are highly improved by using synthetic biology, recreation, and the creation of innovative biological entities (23).

Bluetongue appears to be one of the highly contagious diseases among ruminants caused by the bluetongue virus (BTV), an arbovirus available in nature in at least 26 different serotypes. In what follows, the improvement of a vaccine platform for BTV will be reported.

Pathogen genomes, later used to manufacture vaccines, can be planned and generated safely and quickly due to the emergence of synthetic biology approaches as well as the progress of converse genetics systems.

BTV vaccines are often described considering "synthetic" viruses that contain outer core proteins of various BTV serotypes integrated into a common tissue-culture adapted backbone. Having the recent industry experience in mind, the synthetic biology approach for vaccine development could save 6 months across the entire vaccine pipeline (24).

Conclusion

The spread of SARS, MERS, and COVID-19 during the past two decades manifest the coincidence of vulnerable viruses and human society that has influenced human lifestyle until now. Due to acrimonious and costly episodes of human life and these viral diseases, human beings have felt the need for better rehabilitation of health care professionals than the military for gaining national security.

Although there may not exist a conspiracy theory or the terrorist-like nature of the COVID-19 virus, the symptoms of the tenacious Covid-1 signify that human societies' greatest concern is not getting equipped with military weapons, particularly nuclear weapons, but is being enabled to encounter deadly viruses that have killed millions of people heartlessly.

Overcoming such a big challenge needs cell and molecular biology expertise, biotechnology, and efficient methods based on bioinformatics technology that includes systems biology and synthetic biology. Such theoretical and practical sciences should aim at the Genetic metamorphosis of fatal viruses to save their risks and benefits.

Developing countries, including Iran, must seriously foster the aforementioned sciences to guarantee their safety against any biological invasion, especially viral type. Moreover, by applying systems biology to medical sciences (i.e. Systems Medicine), and by planning an encyclopedic roadmap in this field, they should make prompt and effective strides to build up their health system (increase the quality of health care and development of medical technologies).

Acknowledgment

None.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. Dodds W. Disease Now and Potential Future Pandemics. The World's Worst Problems. Cham: Springer International Publishing; 2019. p. 31-44.
2. Jalasvuori M. Revolutionary Struggle for Existence: Introduction to Four Intriguing Puzzles in Virus Research. In: Witzany G, editor. Viruses: Essential Agents of Life. Dordrecht: Springer Netherlands; 2012. p. 1-19.
3. Le Duc JW, Nathanson N. Chapter 16 - Emerging Viral Diseases: Why We Need to Worry about Bats, Camels, and Airplanes. In: Katze MG, Korth MJ, Law GL, Nathanson N, editors. Viral Pathogenesis (Third Edition). Boston: Academic Press; 2016. p. 215-31.
4. Howard CR, Fletcher NF. Emerging virus diseases: can we ever expect the unexpected? Emerg Microbes Infect. 2012;1(12):e46.
5. Haleem A, Javaid M, Vaishya R. Effects of COVID-19 pandemic in daily life. Curr Med Res Pract. 2020;10(2):78-9.
6. Moghaddasi H, Arani L, Zarghi A. Features of bioterrorism information system. J Bioterror Biodefense. 2018;9:1-6.
7. Barras V, Greub G. History of biological warfare and bioterrorism. Clin Microbiol Infect. 2014;20(6):497-502.
8. Inglesby TV, Henderson DA, Bartlett JG, Ascher MS, Eitzen E, Friedlander AM, et al. Anthrax as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. JAMA. 1999;281(18):1735-45.
9. D'Souza MH, Patel TR. Biodefense Implications of New-World Hantaviruses. Front Bioeng Biotechnol. 2020;8:925.
10. Pourhossein B, Dabbagh A, Fazeli M. Insights into the SARS-CoV-2 Outbreak; the Great Global Challenge: A Mini Review. J Cell Mol Anesth. 2020;5(1):23-6.
11. Barh D, Yiannakopoulou EC, Salawu EO, Bhattacharjee A, Chowbina S, Nalluri JJ, et al. In silico disease model: from simple networks to complex diseases. Animal Biotechnology. 2020:441-60.
12. Davies JA. Real-World Synthetic Biology: Is It Founded on an Engineering Approach, and Should It Be? Life (Basel). 2019;9(1).
13. National Academies of Sciences E, Medicine, Division on E, Life S, Board on Life S, Board on Chemical S, et al. Biodefense in the Age of Synthetic Biology. Washington (DC): National Academies Press (US). Copyright 2018 by the National Academy of Sciences.
14. Jefferson C, Lentzos F, Marris C. Synthetic biology and biosecurity: challenging the "myths". Front Public Health. 2014;2:115.
15. Nasseri S, Yavarian J, Baghani AN, Azad TM, Nejati A, Nabizadeh R, et al. The presence of SARS-CoV-2 in raw and treated wastewater in 3 cities of Iran: Tehran, Qom and Anzali during coronavirus disease 2019 (COVID-19) outbreak. J Environ Health Sci Eng. 2021:1-12.
16. Serrano L. Synthetic biology: promises and challenges. Mol Syst Biol. 2007;3:158.
17. Liu D, Hoynes-O'Connor A, Zhang F. Bridging the gap between systems biology and synthetic biology. Front Microbiol. 2013;4:211.
18. Clermont G, Auffray C, Moreau Y, Rocke DM, Dalevi D, Dubhashi D, et al. Bridging the gap between systems biology and medicine. Genome Med. 2009;1(9):88.
19. Wolkenhauer O, Auffray C, Jaster R, Steinhoff G, Dammann O. The road from systems biology to systems medicine. Pediatr Res. 2013;73(4 Pt 2):502-7.
20. Behrendorff JB, Gillam EM. Prospects for Applying Synthetic Biology to Toxicology: Future Opportunities and Current Limitations for the Repurposing of Cytochrome P450 Systems. Chem Res Toxicol. 2017;30(1):453-68.
21. Buonaguro L, Wang E, Tornesello ML, Buonaguro FM, Marincola FM. Systems biology applied to vaccine and immunotherapy development. BMC Syst Biol. 2011;5:146.
22. Wang N, Yuan Z, Niu W, Li Q, Guo J. Synthetic biology approach for the development of conditionally replicating HIV-1 vaccine. J Chem Technol Biotechnol. 2017;92(3):455-62.
Charlton Hume HK, Vidigal J, Carrondo MJT, Middelberg APJ, Roldão A, Lua LHL. Synthetic biology for bioengineering virus-like particle vaccines. Biotechnol Bioeng. 2019;116(4):919-35.
24. Nunes SF, Hamers C, Ratinier M, Shaw A, Brunet S, Hudelet P, et al. A synthetic biology approach for a vaccine platform against known and newly emerging serotypes of bluetongue virus. J Virol. 2014;88(21):12222-32.