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Artificial cells: A potentially groundbreaking field of research and therapy

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Abstract
Artificial cells are synthetic constructs that mimic the architecture and functions of biological cells. Artificial cells are designed to replicate the fundamental principles of biological systems while also have the ability to exhibit novel features and functionalities that have not been achieved before. Mainly, Artificial cells are made up of a basic structure like a cell membrane, nucleus, cytoplasm and cellular organelles. Nanotechnology has been used to make substances that possess accurate performance in these structures. There are many roles that artificial cells can play such as drug delivery, bio-sensors, medical applications and energy storage. An additional prominent facet of this technology is interaction with biological systems. The possibility of synthetic cells being compatible with living organisms opens up the potential for interfering with specific biological activities. This element is one of the key areas of research in medicine, aimed at developing novel therapies and comprehending life processes. Nevertheless, artificial cell technology is not exempt from ethical and safety concerns. The interplay between these structures and biological systems may give rise to questions regarding their controllability and safety. Hence, the pursuit of artificial cell research seeks to reconcile ethical and safety concerns with the potential advantages of this technology.

Keywords: Artificial Cells, Synthetic Biology, Therapy, Biotechnology

Introduction
Artificial cells are complex structures which mimic the activities of living cells (1). Basics of these life-like structures are made by blending different materials with biological substances (2).

It is a multidisciplinary field that employs chemistry, biology, physics and engineering to craft cell-like structures able to perform specific functions or behave in certain ways. Thus, constructing artificial cells holds great promise for medicine, biotechnology and environmental remediation among others.

What is the Artifical Cell?
Artificial cells are synthetic biological structures that are made in a laboratory to mimic the basic functions of natural cells or perform similar tasks. These artificial cells are designed and manufactured using the principles of synthetic biology based on the properties and structures of natural cells (Figure 1). Artificial cells typically consist of two main components, a lipid membrane and cellular components within it (3). The lipid membrane functions as a cellular border, enveloping the cell and facilitating its interaction with the external environment. This membrane is an artificially made structure that mimics biological cell membranes. It is meant to regulate external influences and safeguard internal cell structures.

Artificial cells are able to enclose synthetic versions of molecular parts like DNA, enzymes, proteins, RNA and other biomolecules found in natural living systems (4). All these components offer functionality and specificity to the modified cell. Researchers usually construct and study artificial cells for use in biotechnology, medicine, environmental

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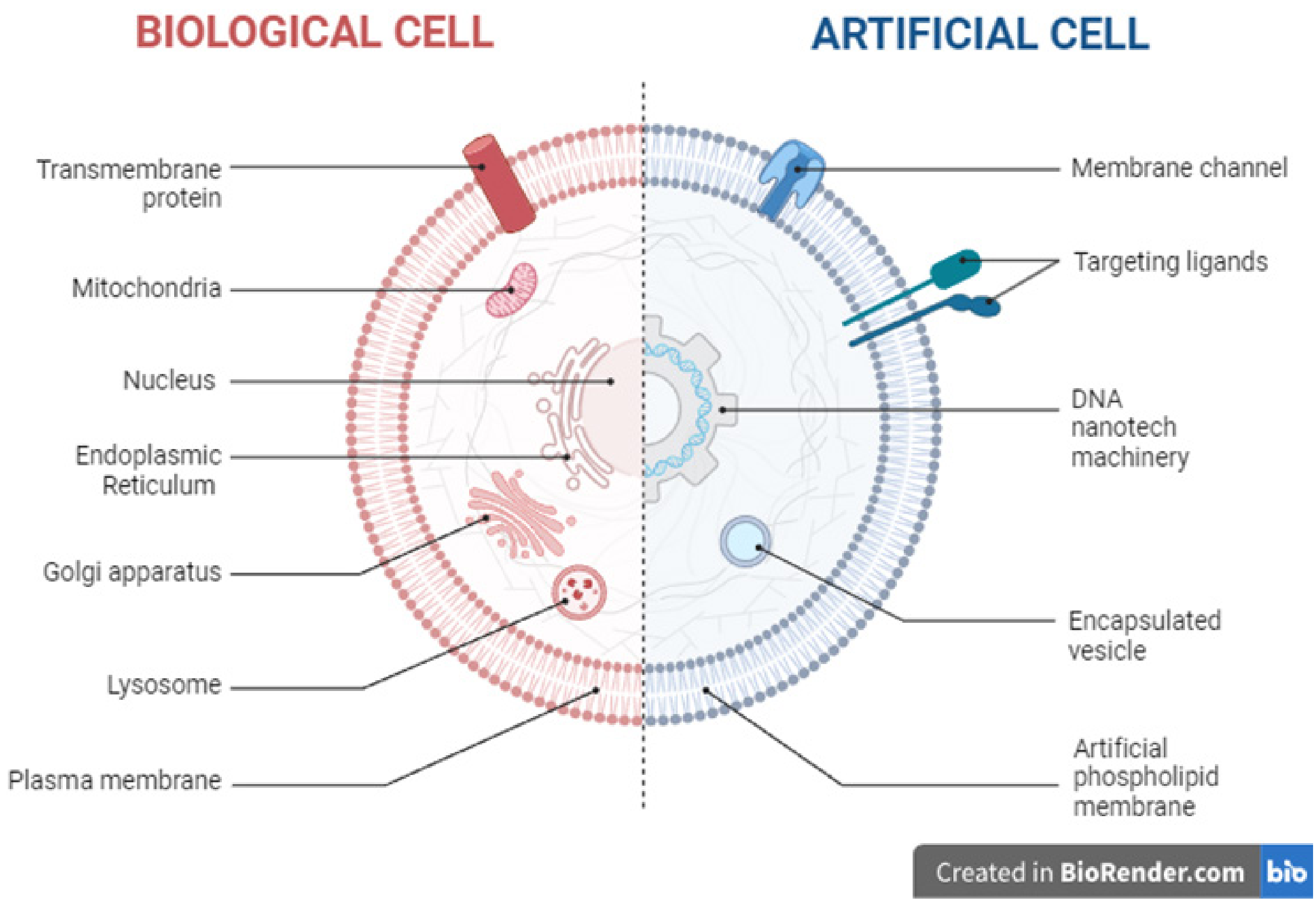

Figure 1. Similarities and Differences Between a Biological Cell and an Artificial Cell.

science and the pharmaceutical industry. Some artificial cells are so complex that they resemble biological systems while others are designed to execute particular functions. For instance, drug delivery artificial cells transport drugs to specific sites for improved targeting during treatment (5-7).

Artificial cell fabrication often involves the incorporation of synthetic biology together with bioengineering (2). The process involves understanding how natural cells work, reproducing biological processes and constructing new parts. Use of artificial cell technology has a lot to offer as it can help explain basic principles of life, provide novel ways of curing diseases and increase its industrial relevance. However, there is a need to monitor and evaluate the ethical, safety, and environmental impacts that would result from this research continuously.

Development of artificial cells throughout history

The endeavor to fabricate artificial cells has been driven by the aspiration to decipher the underlying principles of life and to pioneer advancements in medicine, biotechnology, and materials science.

In the 1950s, the concept of artificial cells began to attract interest through the efforts of biochemists and biophysicists. The concept of "protocell", which emerged in the 1930s, laid the foundation by envisaging basic entities resembling cells (8). In the 1960s, Sydney Fox made a significant advance in the field of artificial cell growth by creating proteinoid microspheres (9). These microspheres are self-assembling entities that exhibit cell-like properties.

Liposomes, discovered by Alec Bangham in the 1970s, emerged as a crucial component in the field of artificial cell research (10). Liposomes, which are vesicles composed of lipid bilayers that imitate cell membranes, have become prominent and are now being used in drug delivery systems. In the late 1980s, Szostak, Oberholzer, and Luisi achieved a significant advancement in the field of artificial cells by encapsulating enzymes within liposomes (11,12). This development brought artificial cells closer to imitating the functional properties of natural cells.

The progress made in polymer chemistry during the 1990s led to the investigation of artificial cells based on polymers. Polymersomes, which are vesicles made from amphiphilic block copolymers, have emerged as alternative architectures that have improved stability and functionality (13). This period represented a transition towards customizing synthetic cells with distinct attributes, exploiting the adaptability of polymers.

The start of the new millennium brought about a significant change in thinking, with a focus on bottom-up methods that emphasized building artificial cells from individual molecular components. The field of synthetic biology was instrumental, as demonstrated by Craig Venter's successful development of a synthetic bacteria in 2010 (14). Simultaneously, DNA nanotechnology has played a significant role in creating and organizing artificial cells with exact architecture.

In recent years, there has been a merging of nanotechnology and the development of biomimetic nanodevices that are inspired by cellular structures. These advancements, including synthetic erythrocytes and artificial thrombocytes, show potential in precise drug administration, diagnostics, and regenerative healthcare (15).

How are artifical Cell designed?

Artificial cells can be generated in two basic ways; top-down and bottom-up (16) (Figure 1). The top-down method entails taking the minimal cell through simplification or modification of the genome of pre-existing live cells. The main objective here is to establish the number of genes that are necessary to support cellular life and create them artificially. This way, a cell can retain its fundamental characteristics such as metabolism, growth, division and evolution while also acquiring new functions or getting rid of unwanted traits. For example, Venter *et al.* made a bacteria called *Mycoplasma genitalium* have 473 genes after they streamlined its genetic material (17). The synthetic cell produced exhibits all the characteristics of a natural one. A recent study conducted by Minoru Kurisu *et al.* has involved the design of a synthetic minimum cell capable of reproducing for multiple generations (18).

The bottom-up approach produces artificial cells from non-biological materials or simple biomolecules that emulate the functions and structures of natural cells. This procedure includes making or mimicking the basic components of a cell, which include cytoplasm, cell membrane, DNA, RNA, ribosome, protein, cytoskeleton as well as metabolism products. It is in this way that cells' intricate features such as motility, perception and response to stimuli can be imitated. For instance, Bausch *et al.* synthesised a model cell membrane composed of a lipid bilayer with microtubules and kinesin (19). The cell membrane incorporates an autonomous cytoskeleton that can move and change shape on its own.

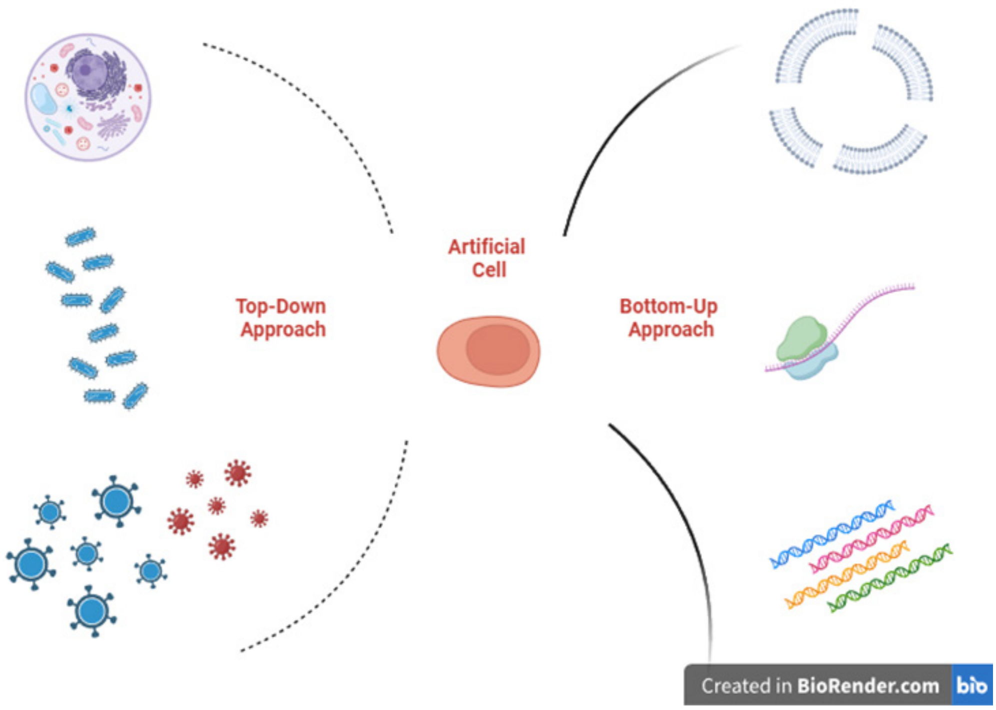

Figure 2. Two basic approaches to artificial cell design. Top Down Approach: Artificial cells are created through top-down approaches that alter natural cells. For example, the organic structures or cytoplasm can be relocated from the membrane of natural cells to that of synthetic cells. By incorporating synthetic or biological substances into the cell membranes of natural cells, artificial cells' properties can be manipulated. The genetic information and expression of these artificial cells can be manipulated by substituting the genomes of their natural counterparts with a synthetic DNA fragment. Bottom-Up Approach: In these methods, artificial cells are obtained by simple molecules coming together to form more complex structures. For example, the self-organisation of lipid or polymer molecules in water forms vesicles, which are small fluid-filled vesicles. These vesicles can form the membrane of artificial cells. By adding biological molecules such as enzymes, catalysts, DNA, RNA into the vesicles or membrane, functions such as metabolism, growth, division and communication of artificial cells can be provided.

The fabrication of a lipid bilayer membrane that mimics the natural cell's membrane is the central focus of artificial cell design (20). Lipids are the building blocks of these membranes hence they self-assemble into double layers due to their amphiphilic nature defined by hydrophobic tails and hydrophilic heads (21). The creation of membranes with such characteristics like stability, flexibility and permeability requires the use of different lipid compositions including phospholipids, fatty acids as well as synthetic lipids (22). A lipid bilayer that serves as a skeleton of synthetic cells can be made through methods such as Electroformation,microfluidics or Lipid film hydration (23-26).

A critical step in this direction is to include biomolecules into the lipid membrane for certain abilities. Artificial cell membranes frequently incorporate proteins, which serve as the primary components of natural cell membranes, in order to replicate them, either with or without certain essential cellular functions. This technique involves reconstitution and genetic engineering as mechanisms of incorporating pure membrane proteins into a lipid bilayer or producing membrane proteins within artificial cells. Proteins have many functions, such as ion transport, signal transmission and molecule recognition among others that enable artificial cells to perform specific tasks (27).

Genetic materials like DNA or RNA can be included into artificial cells accompanied with their protein contents to assist in genetically expressive and regulatory activities. These artificial cells have synthetic DNA sequences coding for particular genes or regulatory elements (28). Such sequences are caged inside the cell to facilitate gene expression, protein synthesis or cellular signaling. Researchers introduce genetic material in these cells; hence, artificial cells can be manipulated to acquire particular functions which may enable them respond to external factors or undertake predetermined actions (28).

It is crucial to design artificial cells which contain bioactive chemicals or payloads. These payloads transported include medicines, enzymes, nanoparticles or genetic elements (29). These cargoes are enclosed within the artificial cell or confined within specialized compartments that resemble the organelles present in natural cells (30). There are several ways to introduce cargos into synthetic cells like microinjection, electroporation and passive diffusion to ensure that they remain stable and functional (31,32).

Nanotechnology-based components in artificial cells frequently utilize nanomaterials. The additional abilities, such as increased sensing, improved drug delivery or more structural stability can be provided by modification of engineered cells using nanoparticles, nanofibres and nanostructures. By means of surface changes, nanomaterials can improve the interaction ability of modified cells with biological systems (33).

The development of modified cells demands progress in microfluidics and microfabrication. Created cells are manipulated and analyzed in a precise manner through the use of microfluidic devices at the scale of micrometers. These systems allow for the production of standardized artificial cells, enable large-scale studies to be conducted and make it possible to simulate complex cellular environments (34).

In the design and optimization of artificial cells, computational modeling and simulation are very important. Computational techniques help in predicting the behaviour of created cells as well as improving their shape, functionality, and interactions within biological systems (35). By replicating biological processes, modeling allows researchers to predict outcomes and guide experimental design prior to implementation.

The use of artificial cells in biotechnology and medicine

The adaptability of artificial cells is what makes them very promising in the field of biotechnology (Figure 4) (Table 1). One area where it is commonly used is drug delivery systems. Specially designed artificial cells for drug encapsulation and transport have resulted in targeted delivery mechanisms that enhance therapeutic efficacy while minimizing side effects (Figure 3). There has been a lot of research on liposomes and they have been employed as carriers of drugs targeted for action within the body (36,37). Instead, artificial cells wrap up drugs so that they do not get destroyed before release at specific points with ultimate effects on drugs' effectiveness. For example, The use of Superparamagnetic artificial cell PLGA-Fe_3O_4 micro/nanocapsules, which exhibit superparamagnetic properties, is highly advantageous for targeted deliveries (38). This is because they possess both target-specific delivery capabilities and magnetic susceptibility.

Moreover, artificial cells are key players in biosensors. They can sense and respond to different biological signals or changes in the environment which enables the development of advanced diagnostic tools (39). In health care, environmental monitoring and other spheres, these cell-based biosensors have their use (40). Such artificial cells that are designed to identify and respond to specific biomarkers or pathogens could be used in early detection of diseases or monitoring environmental pollutants. Jonathan Garamella et al. conducted research that demonstrates the application of synthetic cells as biosensors (41). This study has involved the creation of a synthetic cell that modifies gene expression in reaction to changes in osmotic conditions using a mechanosensitive channel.

Tissue engineering relies on the use of artificial cells that act as a scaffold to promote regeneration and repair of tissues. Presently, ongoing research seeks to understand how these cells can be used to mimic the natural tissue microenvironment, thus facilitating differentiation and maturation of stem cells into organs or tissues (42). A study has demonstrated that cells have been engineered to produce and release a bone morphogenetic protein-2 (BMP-2) in order to prevent or improve bone loss (43). It is worth noting that this approach could potentially solve the donor organ shortage through developing synthetic organs or tissues. In another study, Jorge A. Roacho-Pérez et al. have used artificial cells to create functional heart tissue (44). By manipulating and harmoniously arranging artificial cells to have properties similar to heart cells, it becomes possible to produce tissue patches to repair injured heart tissue following a myocardial infarction.

The application of artificial cells in the treatment of cancer makes a significant difference. These cells are designed to specifically target cancer cells and not harm healthy tissues. For instance, a study demonstrated that when artificial cells were coated with gold nanoparticles, they were able to produce heat upon exposure to laser light, which resulted in the destruction of tumor cells (45). They have the ability to deliver anticancer drugs directly into a tumor site, hence lowering systemic toxicity (46). Modified cells can distinguish between healthy and cancerous cells using different ligands or reactive groups, which increases therapy accuracy (47). An example that shows promise is the advancement of artificial antigen-presenting cells (aAPCs) (48). These artificial cells have the ability to induce and trigger the activation of T cells, which are essential in mounting an immune response against cancer (49). The researchers' objective is to augment the immune system's capacity to identify and combat cancer cells more efficiently by constructing aAPCs with targeted antigens.

Artificial cells can provide deficient or defective enzymes, hormones, or other molecules in the treatment of metabolic diseases such as diabetes (50). For example, in one study, it has been shown that artificial cells which release insulin control blood sugar levels in mice that have diabetes (51).

One of the important areas of use of artificial cells is neurological diseases. The use of artificial cells in this field is of interest to solve various challenges related to the treatment and understanding of conditions affecting the nervous system. Genetically modified T cells have demonstrated efficacy in treating blood cancers and are currently being researched for their potential in treating CNS lymphoma, primary brain tumors, and non-cancerous disorders of the nervous system (52). Conversely, clinical trials are currently evaluating modified T-cell therapeutics for autoimmune illnesses including multiple sclerosis. The objective is to eradicate harmful B-lineage cells or employ antigen-specific regulatory T cells to restrict inflammation and offer neuroprotective substances (53).

The utilization of synthetic cells as alternatives to blood is a highly significant field of study. Hemoglobin-based oxygen carriers (HBOCs) are synthetic red blood cell substitutes designed to facilitate oxygen transportation throughout the body (54). Hemoglobin-based oxygen carriers (HBOCs) are engineered to mimic the oxygen-carrying role of red blood cells, making them especially advantageous in emergency care or regions with scarce availability of donated blood.

The use of microfabrication technology has enabled the de-

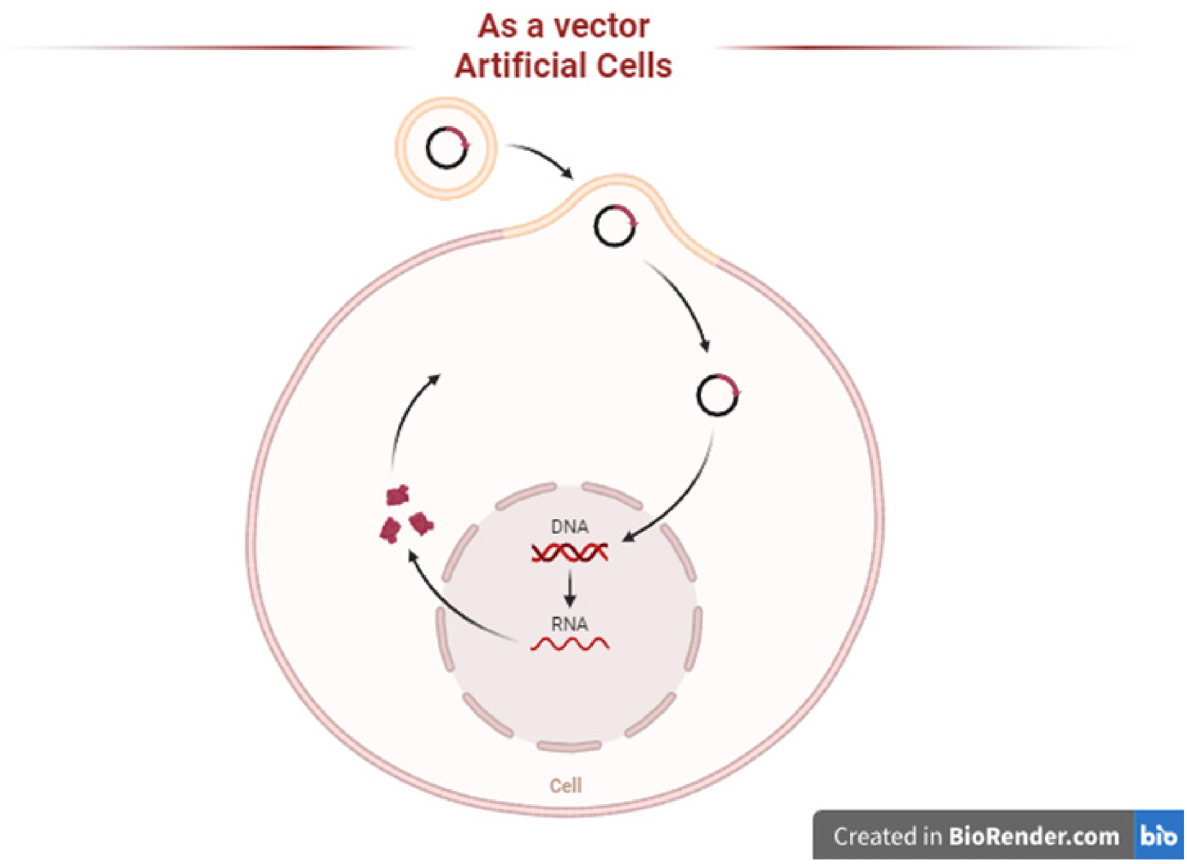

Figure 3. Artificial cells can serve as carriers for gene therapy by including vectors that transport correcting genes to cells afflicted with genetic abnormalities. This approach enables the precise delivery of therapeutic genes while preventing an immunological reaction by using an artificial cell to protect the contents from the host's immune system.

Table 1. Applications of artificial cells in the field of medicine

Application of Artificial Cells	Example(s)	Reference
Drug Delivery	-Superparamagnetic artificial cell PLGA-Fe_3O_4	38
Biosensor	-Artificial cells that alter gene expression in response to changes in osmotic conditions using a mechanosensitive channel	41
Tissue Engineering	-Artificial cells designed to produce and rele-ase bone morphogenetic protein-2 (BMP-2) to prevent or ameliorate bone loss -Functional heart tissue	43,44
Treatment of Cancer	-Artificial antigen-presenting cells (aAPCs)	48
Metabolic Diseases	-Artificial cells which release insulin	51
Neurological Diseases	-Modified T-cell therapeutics for autoimmune illnesses including multiple sclerosis	53
Synthetic Erythrocytes	-Hemoglobin-based oxygen carriers (HBOCs)	54
Microphysiological Systems	-Organ-on-a-chip" devices	55
Bioremediation and Biofuel Production	Conversion of raw materials into biofuels for biofuel production	57

velopment of artificial cells for creating microphysiological systems, also known as "organ-on-a-chip" devices. These devices aim at reproducing an entire organ's functions in a small controlled environment, providing a more physiologically relevant setting for studying drug responses and disease mechanisms. An instance of this is the development of a liver-on-a-chip utilizing synthetic cells (55). This microfluidic technology replicates the anatomical and physiological features of the human liver, serving as a powerful instrument for investigating drug metabolism and assessing toxicity. These technologies have the potential to decrease the dependence on animal models and expedite drug development processes.

Furthermore, artificial cells also find application in the field of bioremediation and biofuel production. Toxin metabolizing or sequestering processes are among the ways by which artificial cells could be used for environmental remediation (56).

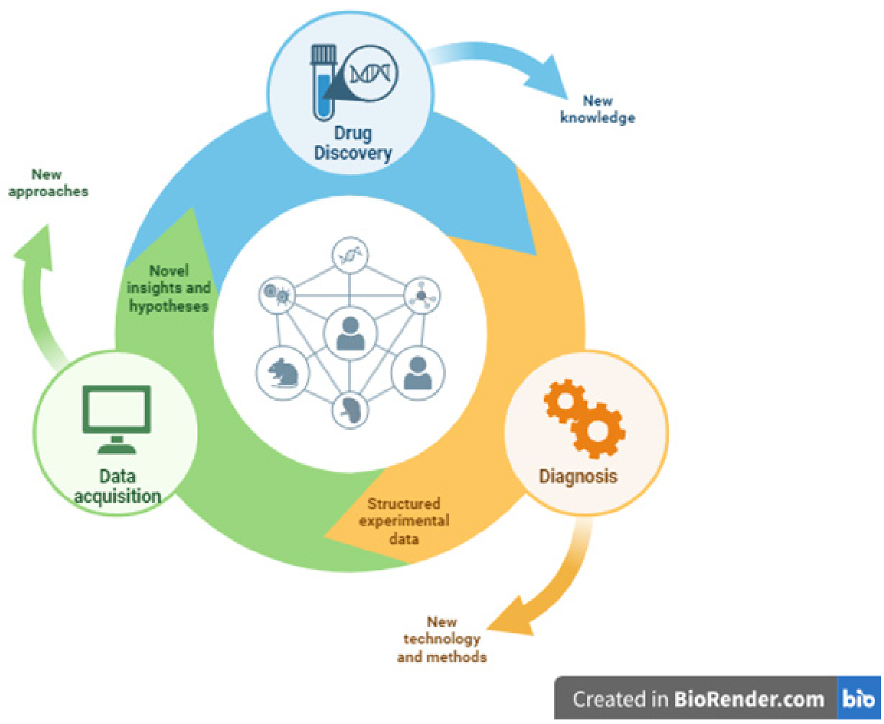

Figure 4. The ability of artificial cells to mimic natural cells has provided various gains from drug discovery to diagnosis. New discoveries are made by establishing new techniques and hypotheses with the data obtained.

The use of engineered cells with enzymatic machinery can enable efficient conversion of raw materials into biofuels for biofuel production (57).

Ethical issues in the use of artificial cells

The use and creation of synthetic cells for various purposes have ethical questions that require careful scrutiny in a number of ways. These issues involve multiple ethical dilemmas that transcend the medical laboratory to affect society as a whole.
The usage of engineered cells brings up important ethical concerns in regard to safety and risk assessment. Consequently, there is a concern about how the incorporation of such artificial constructs into living systems might lead to negative effects. Thus, unanticipated interactions with natural cells, immunological reactions, and long-term impacts must be thoroughly assessed in order to determine potential risks associated with these technologies. Therefore, there is a need for a rigorous risk assessment process and extensive preclinical studies to eradicate any possible harm.

Ethical dilemma comes from the lack of proper regulatory oversight on artificial cells. The issuance of strong regulations is important for assessing the safety, efficacy and quality of artificial cell therapies (58,59). If there is no proper supervision, these technologies can be implemented early or in an unsafe manner, making patients vulnerable and causing loss of credibility among public.

Informed consent and autonomy are essential for the proper usage of modified cells. All participants in trials / therapies involving genetically modified cells should understand that they are experimenting, risks and benefits therein, and also uncertainties. Ethical considerations must therefore include: maintaining people's independence, ensuring informed consent and decision making as well as respecting their right to refuse or withdraw from such treatments.

The availability and accessibility of artificial cell-based therapies create equity and justice issues. Additionally, concerns about cost and fair distribution may render healthcare provision more unaffordable and unevenly distributed across different socioeconomic statuses or geographical regions (60–62). This thus calls for addressing and remedying these disparities to ensure that everyone has an equal access to affordable artificial cell therapies in the spirit of justice and fairness.

The concerns arise from the diverse capabilities of genetically modified cells (63). Therefore, while trying to be helpful, biosafety hazards occur due to misapplication of technologies. It is necessary for there to be regulations in place so as to avoid unauthorized alteration and other illegal uses on ethical grounds.

The long term effects on ecosystems can be understood by conducting a thorough assessment of the impacts of introducing genetically modified cells into the environment. In addition, their continual interaction with natural biological systems should be examined in order to prevent unintended disturbances or imbalances and evaluate their future ecological ramifications towards ecosystems and environmental stability.

The future of artificial cell technology

Currently, biomedical research and development (RD) efforts are focused on refining modified cell technologies for personalized medicine and targeted therapeutics (64,65). These little cellular structures serve as a foundation for accurate drug administration, allowing for customized therapy based on the specific needs of each patient (66). This has created new opportunities in the medical field where synthetic cells can perform cellular functions and respond to specific biological signals thus improving medicinal interventions (67). Currently researchers are investigating ways of engineering cells in regenerative medicine to make functional tissues or organs (30, 68–70). In essence, the aim is to end the scarcity of organs for transplantation by revolutionizing transplant therapies.

Artificial cell research has seen the development of artificial intelligence (AI) as a growing field (71). Incorporating AI and machine learning algorithms into artificial cells has greatly improved their real-time monitoring skills, adaptive reactions and predictive modeling (72). As a result of this merging, artificial cells can adjust independently to the changing settings, thus increasing their efficiency in disease diagnosis, drug optimization and treatment alternatives.

The progress of artificial cell research depends on nanotechnology and biomaterials innovations (73). The nanoscale manipulation of biomaterials allows for the precise construction and arrangement of synthetic cells with tailored functions (74). Biomimetic materials and nanostructures are used to develop synthetic cells that imitate natural ones in shape and function, thus making them more compatible with biological systems and enhancing their performance.

Creating artificial cells is one way of expanding the possibilities in the ever-progressing field of synthetic biology and genetic engineering. Artificial cells with a certain functional specialization are being developed using genetic elements manipulation, cellular pathway engineering, and tailor-made biological system construction 35. This has helped to create more advanced versions of artificial cells that have a capability of performing complex duties such as targeted drug synthesis, metabolic tweaking, bio-sensing.

Recognition of artificial cells for their potential in environmental applications is growing, and this has contributed to the increase in research and development activities. These structures have been found useful in dealing with environmental problems, monitoring pollution as well as bioprocessing sustainably. These special cells can be used to identify and eliminate contaminants from the environment thereby contributing towards cleaner ecosystems. Alternatively, they are being tested as potential catalysts in bioenergy production and waste management providing ecological solutions that are friendly to the environment.

In future research and development, biopreservation needs to integrate biosafety and ethics in relation to modified cells. As these technologies continue to evolve, it will be crucial to incorporate biosecurity controls to prevent misuse or unintended consequences. For ethical considerations on the way forward and the implementation of artificial cell technologies, there is a need for ethical issues, regulations and public participation.

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Conclusion

Artificial cell research challenges are not easy to understand because such issues as optimizing communication between cells, creation of cell networks that are complex, increasing replication and division capacities, and bettering food uptake and movement must be encountered. The difficulty that remains is how can synthetic cells communicate with each other efficiently like natural cells do through signaling pathways? It is a very tough problem to make complicated cellular networks which reproduce the real biological connections at the same time as enhancing replication and division capacities in order for artificial cells to proliferate themselves independently. In additon, nutrient uptake in dynamic media must be improved and they should be able to move in order to keep artificial cells alive just like their natural counterparts.

Artificial cells are highly promising in the scientific world, with unparalleled prospects. By simulating life, they help us understand how it originates and evolves. This process shows how what is not alive changes into what is alive by connecting the worlds of motionless and animated things. Moreover, they can be used in pharmaceutical and fuel industries thereby facilitating creation of new drugs and biofuels. Personalized artificial cells in biomedicine advocates also enable targeted drug delivery and other treatment strategies. Consequently, this versatility leads to innovation in various technological areas through the development of new skills.

Declarations

The authors have no conflict of interest.

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