



# INFINITY

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VARASTEGAN INSTITUTE FOR MEDICAL SCIENCES

NO.4 - JUNE 2024

# INFINITY

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## INFINITY:

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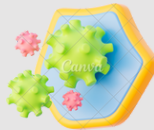
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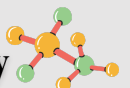
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# Director-in-Charge:

Traditional diagnostics lacked precision, relying on subjective interpretation. Technological advancements have ushered in a new era, transforming us from passive observers to active architects of health. Microscopic insights into cellular processes illuminate both disease mechanisms and therapeutic targets. This future embraces personalized medicine, a far cry from dystopian fears. We, the pioneers, pave the way with innovation, redefining human health through continuous breakthroughs.

Here, within these pages, we present the latest news, articles, and information relevant to our field, aimed at serious and inquisitive minds. This student magazine, as a first English journal of medical laboratory sciences in Iran, welcome your comments and suggestions, fueled by the desire to provide you with the most useful, efficient knowledge possible.

This is but a humble offering to join the vast and ever-evolving world of clinical laboratory science.

**Sincerely**

**Mahdieh Sadat Hosseini Nezhad**



# Editor-in-chief:

I am delighted to introduce myself as the new Editor-in-Chief of Infinity, the English student magazine dedicated to the realm of medical laboratory sciences.

When I see a new cell under the microscope, it feels like discovering a new planet through a telescope because, in the world of medical laboratory sciences, there's always a new planet waiting to be discovered and this infinite world plays a pivotal role in healthcare, encompassing disciplines such as clinical biochemistry, microbiology, hematology, immunology, genetics, and medical biotechnology. Each article featured in this magazine represents a critical exploration of disease mechanisms, diagnostic techniques, therapeutic strategies, and advancements in medical technology.

I invite you all to join us in this endeavor. Whether you're a student researcher eager to share your findings or a reader curious about the latest breakthroughs, Infinity is here to inspire and inform. Let's embark on this journey together, where curiosity meets discovery and where each page of Infinity brings us closer to unraveling the mysteries of laboratory sciences.

**Thank you to our dedicated authors and reviewers for their invaluable contributions.**

**Nazanin Zeinab Arefipour**





# **Sensor array for early diagnosis of Alzheimer**

Alzheimer's disease (AD) stands out as one of the prevalent neurodegenerative disorders characterized by a multifaceted pathobiology resulting in permanent memory loss and profound cognitive impairment. The onset of AD typically manifests in patients following years of pathological transformations. Timely identification and surveillance of AD hold significant value as prompt intervention and treatment are likely to yield optimal outcomes.

One of the most promising biomarkers that offer insights into pathways is the levels of  $\beta$ -amyloid and tau levels in cerebrospinal fluid (CSF) in the brain, in conjunction with neuroimaging and immunological detection for the diagnosis of Alzheimer's disease (AD). Traditional methods for detecting AD biomarkers ( $A\beta$  peptides and tau proteins) primarily depend on neuroimaging and immunological assays. Nevertheless, the practical application of these methods has been constrained by factors such as the radiation exposure associated with positron emission tomography imaging, high costs, and the intricate and time-consuming nature of low-sensitivity immunosorbent assays.

The association between tau proteins and  $A\beta$  peptides in the development of Alzheimer's disease is a topic of ongoing debate. Consequently, the identification of a singular biomarker for achieving an early and precise diagnosis of AD is constrained. Pattern recognition-based optical and electrochemical sensor arrays offer the capability to differentiate between various analytes in intricate settings, making them advantageous for diagnosing AD using multiple biomarkers.

Some of the techniques are displayed in Table 1.

**Table 1.** Techniques for AD diagnosis and their limitations.

Technique	Limitations
MS	Expensive Strict low-pressure requirements Depend strongly on energy, collision gas, pressure, and other factors
MRI	Expensive Low scanning velocity Motion artifacts Insensitive to calcifications
ELISA	Time consuming and inefficient Insensitive to low level markers False positives
Western-blot	Low stability An imbalance in any step of the procedure may skew the entire process
IHC	Variable antibody reactivity Interpretation is often subjective
xMAP	Expensive The results are low to medium resolution A small number of heterozygous ambiguities
PET	Expensive Poor spatial resolution Artifacts of movements

### Fluorescent Sensor Array:

The fluorescence-based detection technique stands out as a potent method for biological and environmental analysis when compared to other analytical techniques, owing its high selectivity and sensitivity. Luo's group outlined a straightforward method for creating a label-free fluorescent sensor array using four nitrogen-doped carbon dots (N-CD) to enable the concurrent detection of multiple proteins. The Forester resonance energy transfer (FRET) principle serves as a logical and efficient design approach for constructing sensor arrays.

### Colorimetric Sensor Array:

Colorimetric detection techniques have garnered significant interest owing to their inherent advantages, including visual detection, cost-effectiveness, ease of use, minimal equipment requirements, real-time monitoring capabilities, and high sensitivity and selectivity towards various analytes.

## Multiple Spectral Sensor Array:

The limit of detection (LOD) for analytes plays a crucial role in biological analysis as it indicates whether a probe can fulfill practical requirements. Hence, an approach with a high LOD is essential.

A sensor array was developed by Chen and colleagues using a multifunctional metal-organic framework (MOF) for the purpose of detecting phosphoproteins. In contrast to conventional analytical techniques, research team created a sensor array that utilized multiple signals including absorbance, fluorescence, and resonance light scattering (RLS), rather than a multi-element sensor array a congeneric multi-channel sensor array. changes in spectral properties were triggered by the binding of phosphoproteins to the MOF hybrid surface, enabling the differentiation of various phosphoproteins with high sensitivity. This study highlights the of the sensor array in distinguishing tau peptides or related to phosphoproteins through a multidimensional signal approach.

Multiple spectral sensor arrays offer the benefit of a decreased number of sensor elements and enhanced detection efficiency. Continued research and advancement in biomolecule detection, combined with the streamlined components and heightened efficiency, have the potential to elevate this sensor array to focal point of research interest

A critical aspect of the detection system lies in selecting the most appropriate electrochemical measurements. Among the most prevalent electroanalytical techniques utilized for detecting AD biomarkers are differential pulse voltammetry (DPV), cyclic voltammetry (CV), and electrochemical impedance spectroscopy (EIS). EIS stands out as a favorable technique as it offers insights into the biomolecular interaction by affecting the electron transfer resistance ( $R_{ct}$ ) and serves as a potent tool for characterizing the surface interface and identifying minute alterations occurring on biosensor surfaces.



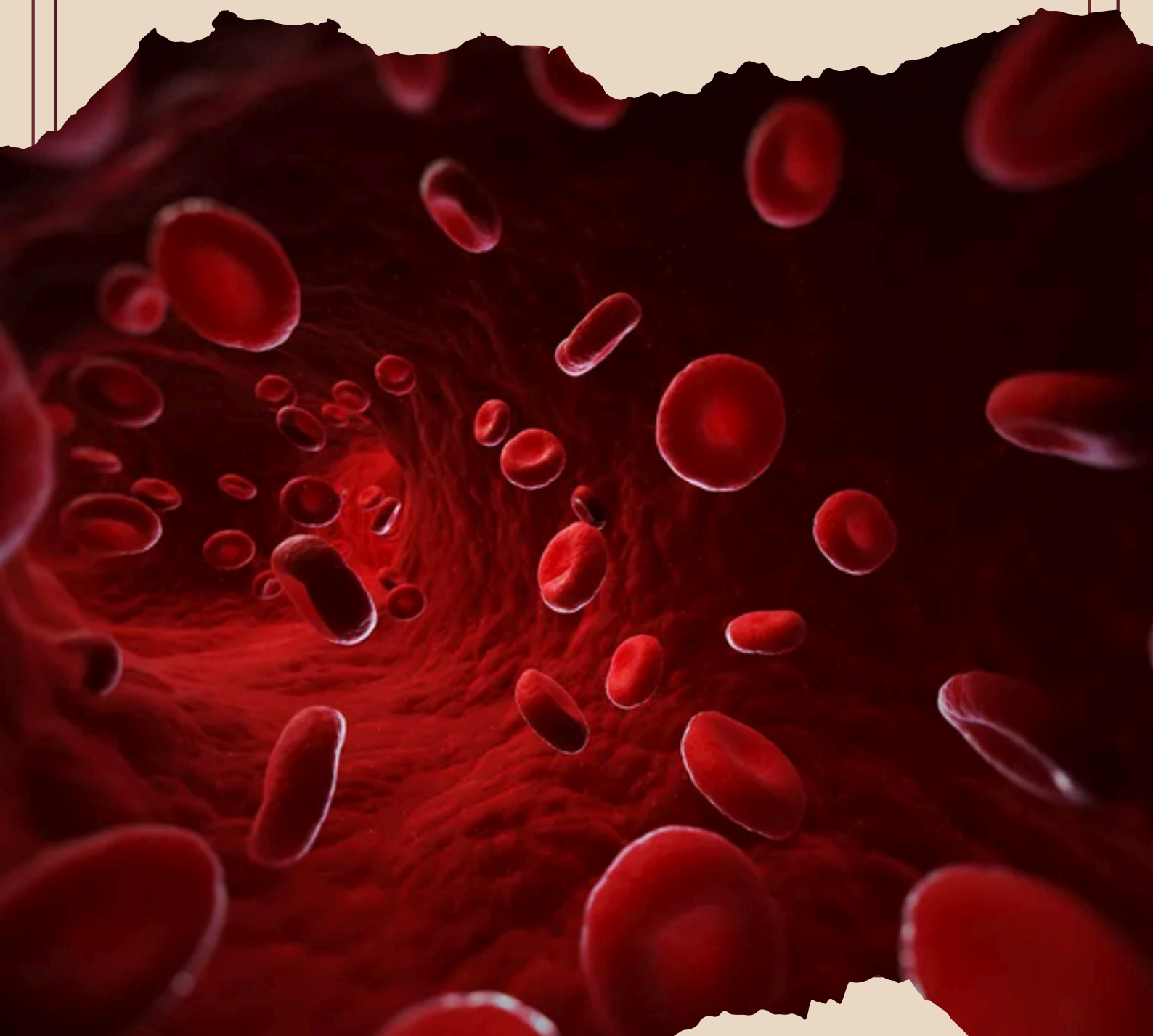
## Electrochemical sensor:

Electrochemical biosensors have garnered significant attention over an extended period. The detection of Alzheimer's disease (AD) has been linked to electrochemical transducers due to notable attributes such as high sensitivity, specificity, user-friendliness, and prompt response to the target analyte. Electrochemical biosensors are capable of converting chemical signals into quantifiable amperometric signals through potentiometric, amperometric, and amperometric transducers.

Aisan Alabaf Sabbaghi<sup>1</sup>



# **Current status of beta-thalassemia and its treatment strategies Introduction**



Thalassemia is a common hemoglobinopathy with two types: beta and alpha. Gene mutations cause dysfunctional  $\alpha$  and  $\beta$  globin proteins, leading to hemolysis and obstructing erythropoiesis. Alpha thalassemia can cause hemolytic anemia or hydrops fetalis, while beta thalassemia major results in early infancy skeletal abnormalities, growth retardation, and hemolytic anemia.

There are around 200 known mutations in the beta-globin gene that cause beta-thalassemia. Beta thalassemia has three types: mild, moderate, and severe. Beta thalassemia minor has no significant impact on hemoglobin protein functioning, while beta thalassemia intermedia causes severe anemia and major health problems. Beta thalassemia major, or "Cooley's anemia," is characterized by a lack of beta-globin synthesis, causing extreme microcytic hypochromic anemia, bone marrow hypoxia, hyperplasia, and extramedullary hematopoiesis. Frequent blood transfusions have reduced the incidence of thalassemia and bone marrow transplantation, improving life expectancy and normal childhood development. Recent advances in clinical and genetic research have led to the development of allogeneic hematopoietic stem cell transplantation (HSCT), but factors like age, iron overload, and HLA matching affect the disease-free survival rate.

## Diagnosis

Numerous laboratory tests, including DNA analysis (genetic testing), complete blood counts (CBC), blood smears, prenatal testing (genetic testing of amniotic fluid), iron studies, and hemoglobinopathy, can be used to identify and diagnose thalassemia.

Mutations in the  $\beta$ - and  $\alpha$ -globin chain genes can be found with the aid of DNA analysis tests. Hb concentrations between 7 and 10 g/dl, mean corpuscular volume between 50 and 80 fl, and MCH between 16 and 24 pg are used to classify thalassemia intermediate.

## Treatments

Those with thalassemia characteristics do not require treatment. Given that mutant genes may be passed on to family members, they may be intentionally engaging in genetic consultation. . People who have intermediate  $\beta$ -thalassemia will always have moderate anemia. While they could be conscious like other individuals, constant observation and the occasional blood transfusion will be necessary. While folic acid supplementation is frequently advised, iron supplementation is not provided.

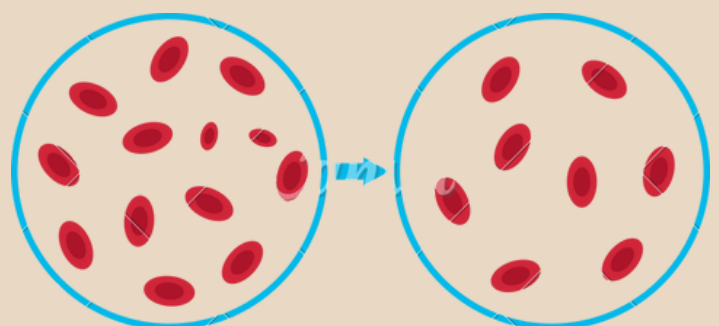
## 1. Splenectomy

Hypersplenism in people with thalassemia intermedia can lead to splenomegaly, which can aggravate anemia, stunt growth, and create a number of other mechanical problems. Although thalassemia intermedia is a symptomatic illness, when it is acute, splenectomy is the recommended course of therapy.

## 2. Transplanting bone marrow

Bone marrow transplantation is the most effective therapeutic option for thalassemia patients.

The most successful bone marrow transplants were conducted in the 1980s. The findings in young patients are 3% mortality and 87% thalassemia-free survival. However, BMT has a few disadvantages, including as the need for a suitable donor who matches the human leukocyte antigen.



### 3. Transfusion of blood

The average amount of blood transfusion is determined by a variety of factors, including the patient's hematocrit and Hb levels, as well as their weight . Multiple transfusion treatments have been predicted throughout the years; nevertheless, the most widely established objective at pre-transfusion hemoglobin near to 9 to 10 g/dl and a post-transfusion level of hemoglobin should be 13 to 14 g/dl. RBCs should not be transferred more than 15 to 20 ml/kg per day during blood transfusion therapy in order to prevent an unnecessary increase in blood volume.

### 4. 1. Gene therapy

Patient stem cells are used in gene therapy to treat  $\beta$ -thalassemia major permanently. Initially, patient hematopoietic stem and progenitor cells (HSPCs) are extracted from bone marrow, peripheral blood, or umbilical cord blood. Following that, the tissues/cells are vulnerable to a treatment that changes the DNA's design. A lentiviral vector is used to insert the normal  $\beta$  or  $\gamma$  gene into the genome of a host cell. Humans are also purposefully transferring the hemoglobin genome into pluripotent hematopoietic cells. Once more, patients receive the appropriate gene-containing cells, which proliferate in the bone marrow.

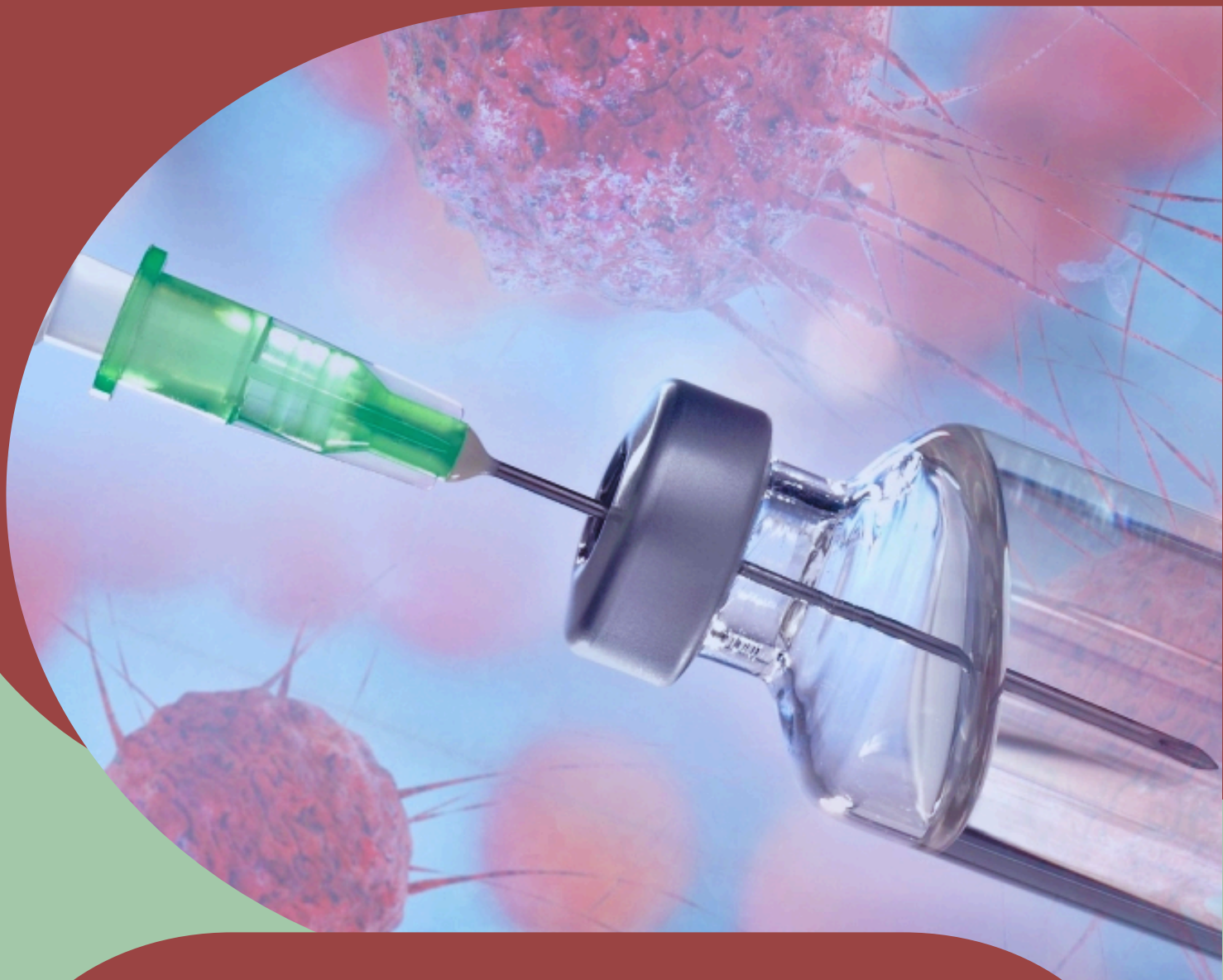


Arefeh Roudi <sup>1</sup>



Negar Hamidfar <sup>1</sup>





**AE37, HER2-targeted  
vaccine in the prevention of  
breast cancer**





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## BREAST CANCER VACCINE SAFELY GENERATES ANTI-TUMOR IMMUNITY

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### INTRODUCTION

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Breast cancer is a common type of cancer affecting both women and men, with early detection and understanding of risk factors being crucial for better outcomes. Treatment options include surgery, chemotherapy, radiation therapy, hormone therapy, and targeted therapy. Awareness and timely medical attention for any changes in breast health are essential. Challenges in breast cancer management include treatment resistance and disease recurrence, with approximately 20-30% of global cases involving human epidermal growth factor receptor 2 (HER2) positivity.

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### HER2

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HER2, a growth factor presents in various cancers, notably breast cancer, is a target for immunotherapy, particularly vaccine development. Immunotherapy for HER2-positive breast cancer includes passive strategies utilizing monoclonal antibodies like trastuzumab and pertuzumab, as well as active approaches aiming to enhance antitumor immunity through vaccines. Peptide vaccines derived from HER2, such as E75, AE37, AE36, and GP2, have shown efficacy in clinical trials by activating T cell responses. Whole protein and DNA vaccines targeting HER2 domains have demonstrated potential in animal studies. Dendritic cell vaccines loaded with HER2 antigens have induced tumor immunity in preclinical models. Combination therapies with vaccines and checkpoint inhibitors or standard treatments may help combat immune resistance.

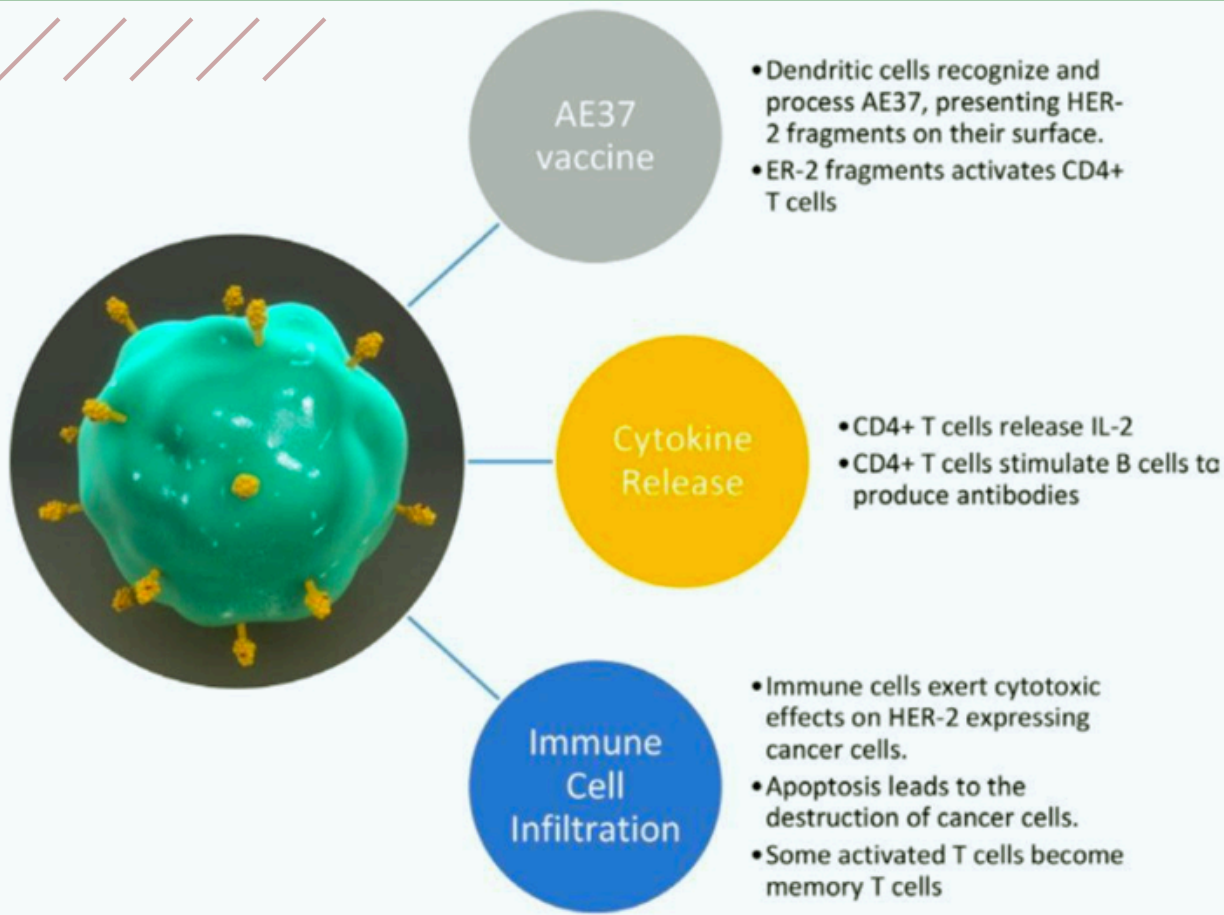
An experimental DNA vaccine targeting the HER2 protein in breast cancer patients demonstrated promising results in a phase I trial by stimulating a cytotoxic immune response crucial for cancer treatment. The study involved 66 women with metastatic cancer, showing safety and efficacy over a 10-year follow-up. Different vaccine doses were administered, with the middle dose eliciting the strongest immune response. The vaccine successfully generated the desired immune response without severe side effects, with high survival rates observed. Positive outcomes may pave the way for further trials for breast cancer treatment.

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### AE37 HER2-TARGETED VACCINE IN THE PREVENTION OF BREAST CANCER RECURRENCE

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The text discusses the AE37 human epidermal growth factor receptor 2 (HER2)-targeted vaccine as a potential immunotherapy for breast cancer. It highlights the vaccine's mechanism of action, which involves stimulating CD4+ and CD8+ T cells to generate a cytotoxic immune response against tumor cells expressing the HER2 antigen. The innovative peptide-based approach of the AE37 vaccine stimulates the immune system without directly targeting the HER2 protein, showing promise in inducing memory cells and cytotoxic T cells for an effective immune response against breast cancer. Various studies have shown that the AE37 HER2-targeted vaccine has a favorable safety profile and is well-tolerated by patients. The vaccine has demonstrated potential efficacy in specific patient subgroups, such as those with advanced-stage, HER2 under-expressed, and triple-negative breast cancer. Overall, the vaccine shows promise as a therapeutic option for breast cancer patients, with minimal adverse effects reported across multiple studies.



## CONCLUSION

In conclusion, AE37 emerges as a promising and reliable solution for reducing disease recurrence in specific breast cancer patients; and the future holds further investigation of its use in multi-modal therapy and alternate delivery vectors. The vaccine offers a rapidly produced therapeutic that has the potential to decrease cancer recurrence, and possibly decrease tumor burden. With clinically proven efficacy, AE37 has the ability to become a standard of care therapy for breast cancer patients. The use of the li-key peptide in other malignancies, viral infection, and auto-immune processes is just beginning and will undoubtedly generate new knowledge about the immune system along the way.

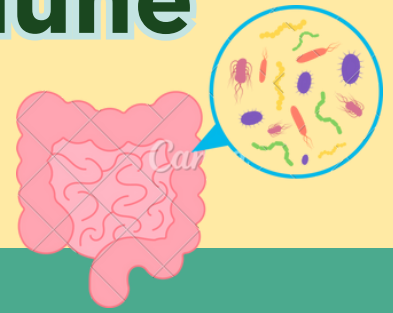
Melika Hosseinpour<sup>1</sup>



Zeynab Mirnezhad<sup>1</sup>



# The role of gut microbiome in modulating immune responses



The human microbiome consists of various organisms such as bacteria, viruses, and fungi that live on all surfaces of our bodies. Microbiomes are found in the nose, mouth, lungs, skin, stomach, genitals, and, of course, the intestines. The gut microbiome contains a rich and diverse microbial community consisting of more than 100 trillion microorganisms. This means the production of thousands of metabolites that are critical to the symbiotic relationship between humans and microbes and contribute significantly to the maintenance of homeostasis. Important links between disturbances in the gut microbiome and various diseases have been discovered. A common feature of many of these diseases is that they are mediated by disorders of the human immune system. Recent studies have shown that the gut microbiome plays an important role in the development and modulation of host immune responses. Here are some ways the gut microbiome affects the immune system:

## 1. Immune organ maturation

The gut microbiome plays a vital role in the development and function of immune organs. This includes central immune organs like the thymus, bone marrow, and bursa of Fabricius, as well as

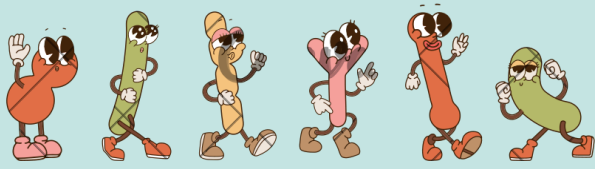
peripheral organs like lymph glands, spleen, and mucosa-associated lymphoid tissues. Research has shown that germ-free animals have underdeveloped immune organs, but microbiome colonization can promote their maturation. Additionally, the gut microbiome is crucial for the development of specific immune structures such as Peyer's patches and mesenteric lymph nodes.

## 2. Non-specific immunity regulation

The non-specific host immunity system is the first line of defense against antigens. It includes organizational barriers such as the skin and mucous membranes, as well as innate immunocytes and immune molecules. Recognition receptors, such as TLR, activate the immune response by recognizing pathogen-associated molecular patterns. The concept of colonization resistance states that certain anaerobic bacteria can form a microbial barrier in the intestines, competing with pathogens for attachment sites and nutrients. Gut microbes produce metabolites like bacteriocin and short-chain fatty acids that suppress and kill pathogens. Mucus secreted by goblet cells and mucoproteins play a role in preventing pathogen colonization. The gut microbiome can enhance non-specific immunity by maintaining the intestinal barrier function, promoting mucus secretion, and strengthening tight junction proteins. It also regulates immune cell function and cytokine secretion.

## 3. Specific immunity regulation

Specific immunity includes humoral immunity (B cells) and cell-mediated immunity (T cells). B cells convert to plasma cells and memory B cells, secreting antibodies. T cells include Th, Treg, Tc, and memory T cells. The gut microbiome regulates specific immunity through IgA secretion, T cell activation, and lymphocyte proliferation.



### 3.1. Humoral immunity regulation

The gut microbiome plays a crucial role in regulating humoral immunity. It promotes the maturation and differentiation of B cells, which are responsible for antibody production. Various gut bacteria, such as *E. coli* and *Bifidobacterium*, increase the number of B cells in the bloodstream. Short-chain fatty acids produced by the gut microbiome enhance B cell transformation into antibody-producing cells. Symbiotic strains of bacteria induce B cell differentiation through the synthesis of retinoic acid and activation of signaling pathways. The gut microbiome also influences the production of immunoglobulins, such as IgA, IgG, and IgM, which play a crucial role in immune response. Germ-free animals have impaired immunoglobulin production, but this is restored with microbial colonization. Different bacterial types can affect antibody concentration, and probiotic strains increase the concentration of SIgA. The gut microbiome also impacts antibody diversity and influences gene expression and rearrangement mechanisms involved in immunoglobulin diversity.

### 3.2. Cellular immunity regulation

The gut microbiome controls the balance between Th17 cells and Treg cells, which are involved in cell-mediated immunity. Th17 cells, specifically, are involved in the development of autoimmune diseases. The gut microbiome is necessary for the development of Th17 cells and affects their proliferation.

*Clostridium* and *B. fragilis* are two bacteria that influence the proliferation and differentiation of Treg and Th17 cells. Short-chain fatty acids produced by the gut microbiome can also affect the activity of certain immune cells. Additionally, segmented filamentous bacteria (SFB) play a role in the development of Th17 cells. The expression of forkhead/winged helix transcription factor p3 (Foxp3), which controls the development of Tregs, is influenced by *Lactobacillus* and *Bifidobacterium*.

### 4. Inflammation

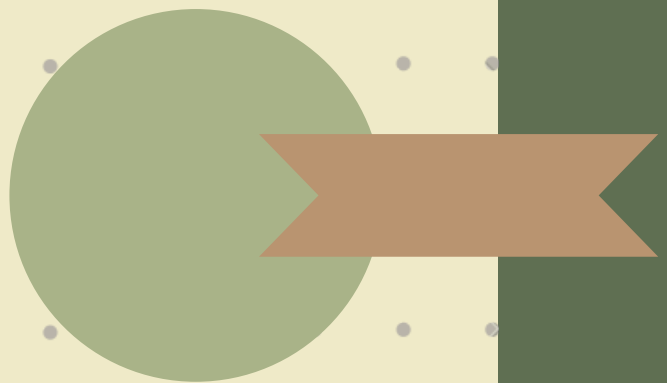
Inflammation is linked to the gut microbiome and can cause tissue damage. Autoimmune pancreatitis patients have high levels of *Bacteroides*, *Streptococcus*, and *Clostridium*, while rheumatoid arthritis patients have low levels of *Bacteroides*, *C. leptum*, and *Hemophilus*. Obesity is associated with inflammation and reduced gut microbiome diversity. Inflammatory bowel diseases (IBD) result from an imbalance in intestinal flora. *E. coli* can trigger intestinal inflammation, but butyric acid can limit it. Probiotics like *B. fragilis*, *Lactobacillus plantarum*, and *Bifidobacterium* can alleviate IBD by reducing inflammation. Certain bacteria induce the secretion of IL-17 and IL-22, suppressing intestinal inflammation. *Lactobacillus rhamnosus* reduces *E. coli* colonization and inflammation. Dendritic cells decrease TLR4 and T cell levels to limit inflammation. TNF- $\alpha$  induces apoptosis and increases intestinal permeability. Intestinal flora and short-chain fatty acids regulate immune cell activity and reduce inflammation.

In conclusion, the gut microbiome can influence the development of immune tissues, non-specific immunity, specific immunity, and inflammation. Although the mechanism of interaction between the gut microbiome and the immune system is now substantially understood, a significant gap remains. More systematic studies are needed to investigate the molecular interaction mechanism between the immune system and the gut microbiome.



Niloufar Kazemi <sup>1</sup>





# MAGIC MUSHROOM

## **Reduction of alcohol addiction by psilocybin, which is obtained from the magic mushroom:**

Psilocybin is a hallucinogenic substance obtained from magic mushrooms; This substance is prescribed to people with alcohol use disorder along with speech therapy to reduce or stop alcohol consumption. For this purpose, in a clinical trial conducted long ago, people with alcohol dependence were divided into two different groups. Doses of psilocybin or placebo were injected to test the effect of this substance. The idea of using psychedelic drugs to treat alcohol use disorder dates back to the 1960s and 1970s, when scientists used LSD (the most famous psychoactive drug in the psychedelic category) for this purpose. Although that experiment was relatively small; But it showed that this psychotropic drug can help patients reduce alcohol consumption and effectively prevent the consequences of alcohol abuse compared to pills or placebo stimulants such as ephedrine with amphetamine, but ultimately political pressure quickly stopped such research.

## **A new experiment investigating the role of psychoactive drugs in the treatment of alcohol use disorder :**

The new trial included 93 participants aged 25 to 65 who had been diagnosed with alcohol dependence according to Diagnostic and Statistical Manual of Mental Disorders (DSM4) criteria in the 12 weeks prior to the screening, three quarters of the days in which the time period was included were they consumed alcohol on more than half of these days they had heavy drinking five or more times a day for men and four or more times a day for women was said to reduce the likelihood that participants would be discriminated against They were randomly divided into two treatment groups: psilocybin or placebo; However, more than 90% of the participants and observational therapists correctly guessed who was prescribed which drug due to the different effects of the drugs, and this somewhat limited the results of the study; because this experiment was not really double-blind as it was intended, the treatment sessions were conducted four weeks apart and under the supervision of a team of therapists and medical staff.



## **The results of the alcohol consumption test in two groups:**

Both groups reduced alcohol consumption during the 32-week trial; But this improvement was significantly greater for the group that received psilocybin. Heavy drinking in the psilocybin group was reduced by 83 percent compared to pretreatment levels, compared to 51 percent in the placebo group, and eight months after receiving the first 48% of the psilocybin group stopped drinking alcohol altogether; While this rate was 24% in the placebo group.

John Costas, one of the trial participants in the psilocybin group, told a news conference about the rapid effect of the substance that he was able to stop drinking immediately after the first session. Mild and short-term side effects such as headache, nausea and anxiety were more common in the psilocybin group than in the placebo group; But several serious side effects occurred in the placebo group, including severe vomiting and psychiatric admissions due to suicidal thoughts that occurred during episodes of heavy drinking.

According to Dr. Michael Bogenschutz, no significant safety issues have been identified with psilocybin. However, since this drug increases blood pressure and heart rate and can sometimes cause debilitating psychological effects, it is important that patients use it only under close supervision.

The participants in this experiment experienced different ranges of emotions and perceptual experiences while using psilocybin, some described it as pleasant and some described it as painful, and many patients obtained significant benefits from taking the drug under treatment following their experience.



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### The mechanism of psilocybin for this treatment:

According to Bogenschutz, the mechanism of this treatment is still unknown; But researchers have provided some possible explanations according to past research; Psilocybin, like LSD, binds to structures in the brain called serotonin A2 receptors, which are abundant in areas of the cerebral cortex involved in high-level cognitive functions such as introspection and executive function; It is thought that by activating these receptors, psychedelics can strengthen the connection between brain networks and allow signals to connect between different areas of the brain more easily than normal.

According to the latest statements by Dr. Charles Marmar, head of the psychiatry department, psilocybin can affect brain circuits that allow learning in a new way that was not possible before; take place and can improve the learning process during speech therapy.

More research is needed to fully understand the mechanism of alcoholism treatment by psilocybin. To that end, in 2023, Bogenschutz and colleagues launched a larger trial that is underway at 15 sites and is likely to last two to three years. Ultimately, the US Food and Drug Administration will determine when this substance can be widely used.

The therapeutic effects of psilocybin are significantly longer and longer than the drugs currently used to treat alcohol use disorder, and if these effects continue in future trials, psilocybin can be an important step in the development of alcohol use disorder treatment.



Zeynab Mirnezhad<sup>1</sup>



Zahra Akbarzadeh<sup>1</sup>



# Dengue vaccine: Today's weapon against break-bone fever

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## Introduction:

Dengue fever-which is commonly known as break-bone fever- is a mosquito-borne viral infection caused by the dengue virus (DENV), a single-stranded RNA virus from the family Flaviviridae, genus Flavivirus.

Dengue virus is primarily transmitted to humans through the bites of infected female *Aedes* mosquitoes, mainly *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. The issue is of great global public health importance, particularly in tropical and subtropical areas. These mosquitoes are often found in urban areas and breed in standing water, making them prevalent in environments close to human habitation. When a female mosquito carrying the virus bites a person, the virus enters the bloodstream, leading to infection. The virus can also be transmitted through blood transfusion, organ transplantation, or from a mother to her fetus during pregnancy.

The Dengue virus consists of four serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Each of these serotypes is capable of causing human infection. While the majority of individuals infected with dengue may not exhibit any symptoms, those who do may experience common signs such as high fever, headache, body aches, nausea, and rash. Fortunately, most people tend to recover within 1-2 weeks. However, it is important to note that some individuals may develop severe dengue and require hospitalization for proper care.

Upon entry into the human body, the dengue virus targets immune cells, particularly dendritic cells, and monocytes/macrophages. The virus binds to specific cell surface receptors and gains entry to these cells, where it replicates rapidly. This leads to an immune response characterized by the release of various mediators and cytokines.



Interestingly, in some cases, the immune response to the virus can lead to an excessive release of pro-inflammatory cytokines, a phenomenon known as cytokine storm. This overactive immune response can cause increased vascular permeability, resulting in a condition known as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), which can be life-threatening. If not promptly treated, DHF and DSS can result in severe bleeding, organ damage, and a decrease in platelet count.

These complications may lead to shock, organ failure, and potentially death. With no specific antiviral treatment available, the prevention of dengue through vaccination stands as a promising solution.

The development of a dengue vaccine has been challenging due to the complexities of the dengue virus itself. As mentioned earlier, the virus has four distinct serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), and infection with one serotype does not necessarily confer immunity to the others. In fact, there's evidence that secondary infection with a different serotype can lead to more severe disease due to a phenomenon known as Antibody-dependent enhancement (ADE).

### **Dengvaxia (CYD-TDV):**

The first and, so far, only licensed dengue vaccine is Dengvaxia (CYD-TDV), developed by Sanofi Pasteur. Dengvaxia is a live attenuated tetravalent vaccine designed to provide immunity against all four dengue serotypes. It has been licensed for use in several countries where dengue is endemic. However, the use of Dengvaxia has been associated with some controversy and regulatory challenges. After its initial release, concerns were raised about its safety, particularly concerning the risk of severe dengue in seronegative individuals (those who have not been previously infected with dengue).



As a result, regulatory agencies have modified guidance on the use of Dengvaxia, recommending it for individuals who have had a prior dengue infection. The vaccine should be given in three separate doses within a span of six months (at 0, 6, and 12 months) to individuals aged 9 to 45 who have a history of dengue infection or have undergone serological testing for previous dengue infection.

In general, the dengue vaccines offer a 60-80% protection against dengue infection and can prevent approximately 70%-90% of severe cases that require hospitalization. Nonetheless, it remains crucial to convey to individuals that this vaccination does not provide absolute protection. Consequently, it is still imperative to prioritize safeguarding oneself against carrier mosquitoes and not dismiss this precaution.

### Conclusion:

The quest for an effective and safe dengue vaccine continues to be an active area of research and development. The need for a vaccine is critical, given the burden of dengue fever on global health, particularly in endemic regions. To address the complexities of dengue virus serotypes and the potential for immune-mediated enhancement of infection, ongoing research aims to develop vaccines that induce balanced and long-lasting immune responses, providing protection against all four serotypes without increasing the risk of severe disease.



**Mahdiah Sadat Hosseini Nezhad**<sup>1</sup>

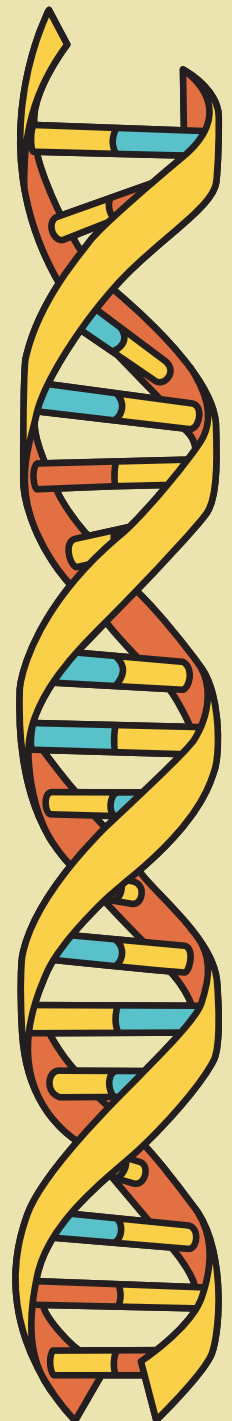


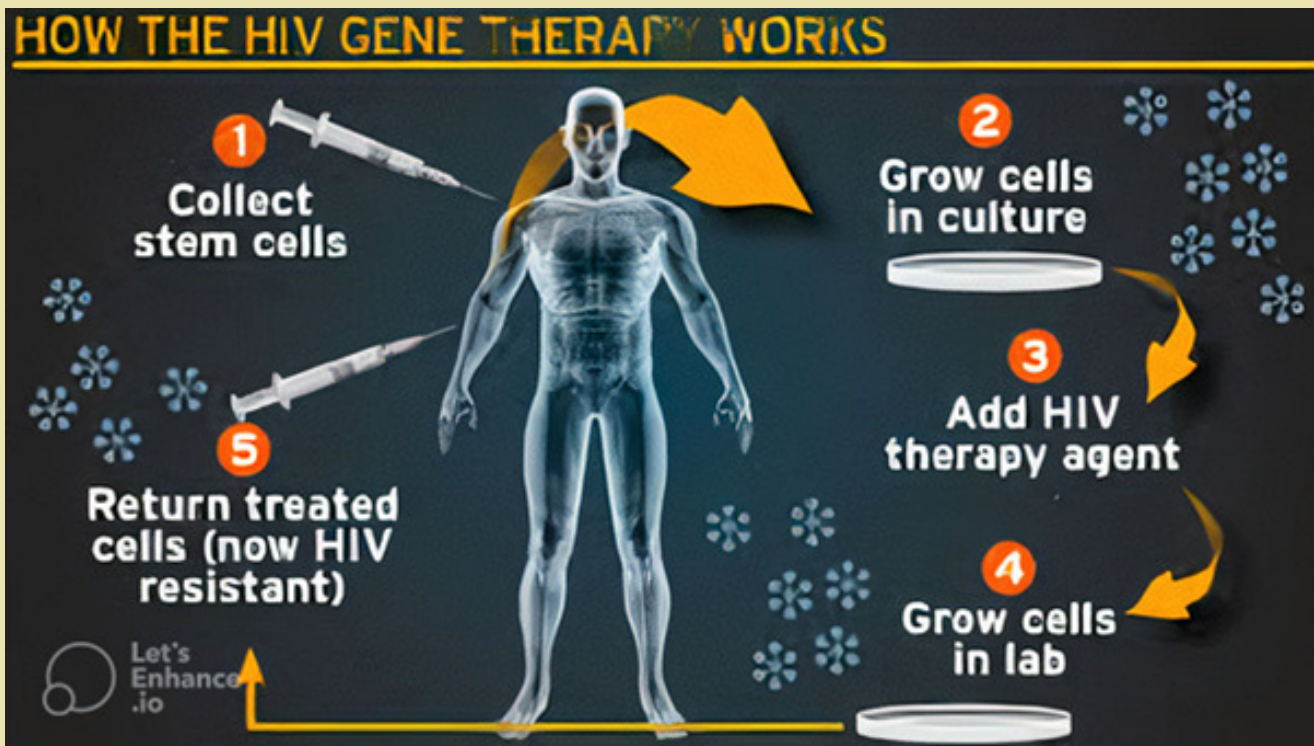
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# HIV treatment with gene therapy



HIV is a virus that attacks the immune system. If HIV is not treated, it can lead to AIDS. The HIV epidemic was first identified in 1981, posing a significant threat to human health. There are approximately 38 million people living with HIV worldwide, and more than 800,000 people die from HIV every year. HIV infection in humans originates from a species of chimpanzee in Central Africa. The only way to find out if you have HIV is to get tested. Controlling this infection is a big challenge. There is currently no effective vaccine and no cure for HIV infection. Combination antiretroviral therapy (cART) can significantly prolong the life of HIV-infected individuals, but it has significant problems and disadvantages. The use of these combinations may cause toxicities, leading to problems with adherence. However, the increase in side effects is partly due to the improved life expectancy resulting from the success of antiretroviral therapies. Furthermore, despite the risks associated with loss of immune function and viral escape, there is an increased likelihood of transmission and the creation of a larger reservoir. Gene therapy may facilitate sustained inhibition of HIV replication after a therapeutic intervention. Gene therapy for HIV involves modifying the patient's immune cells to make them resistant to the virus. One approach is to use CRISPR technology to edit the CCR5 gene, which HIV uses to enter cells. This process usually involves extracting immune cells from the patient, modifying them in the laboratory, and then reintroducing them into the patient's body. By inactivating the gene, the virus cannot infect the modified cells. Both peripheral blood T cells and bone marrow HSCs can be selected as target cells for anti-HIV gene therapy. The success of this therapeutic approach depends on various factors such as the specific gene editing technique used, the efficiency of gene delivery and the ability of the modified cells to persist in the body.





## Targeting HIV genes and their products

Several different anti-HIV-1 gene therapy methods have been tested in hematopoietic cells. The most direct gene therapy approach aims to inactivate or remove integrated provirus DNA from the host genome. These approaches can be further classified into two categories: RNA-based agents and protein-based agents.

### RNA-based inhibitory agents:

Small interfering RNAs (siRNAs) and HIV-1 specific antisense oligonucleotides can target viral RNA to inhibit replication or modulate host cell factors involved in the viral life cycle. These agents show promise in suppressing HIV replication and overcoming drug resistance.

### Protein-based inhibitors:

Protein-based agents used in HIV treatment include fusion inhibitors such as Enfovirtide, protease inhibitors such as ritonavir, and monoclonal antibodies such as Ibalizumab. These agents target different stages of the HIV life cycle to prevent viral replication and help manage the infection.

Gene therapy for HIV treatment is a promising area of research that aims to modify a patient's immune cells to make them resistant to the virus. While this approach is still in its early stages, it shows potential for long-term control or even eradication of HIV.

Therefore, gene therapy is a rapidly developing field promising a revolution in HIV management and improving the quality of life of patients worldwide.

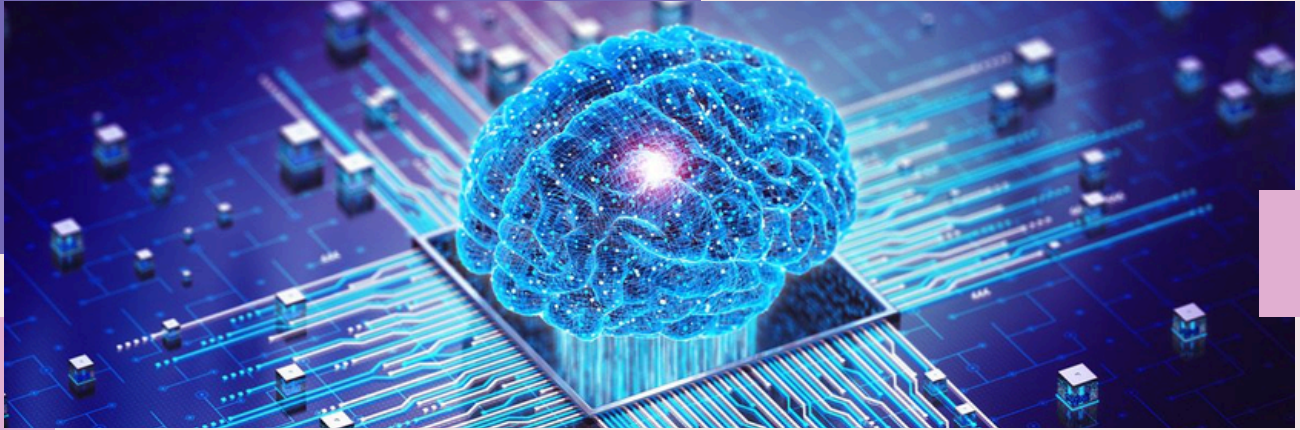


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# Trends in artificial intelligence for Biotechnology



In today's era, Artificial Intelligence (AI) has emerged not only as a technical tool but as a powerful companion in advancing scientific frontiers, particularly in the realm of medical biotechnology. This advanced technology offers extraordinary capabilities in analyzing complex data, accurately diagnosing diseases, designing targeted drugs, and even enhancing therapeutic methodologies.

The European In Vitro Diagnostics Regulation (IVDR) includes AI algorithms under its requirements, which presents challenges for companies in the in vitro diagnostics (IVD) sector utilizing AI for data analysis and decision support. Addressing ethical and legal concerns adequately, however, reveals significant potential for AI to transform medical biotechnology. AI can expedite and enhance the accuracy and cost-effectiveness of drug discovery, particularly in identifying therapeutic targets through analysis of genomic and protein interaction data using machine learning algorithms. Additionally, AI facilitates drug screening by evaluating drug activity against targets and enhances medical imaging analysis to detect anomalies and diagnose diseases using deep learning algorithms. Furthermore, predictive modeling with AI, drawing from diverse data sources such as electronic health records and wearable devices, enables forecasting of disease onset or response to treatment.

AI is a widely encompassing term used today across various domains where digital systems process data. The foundation of any AI application lies in digitization and digital transformation. The availability of vast, high-quality datasets and the rapid advancement of computing power are pivotal and ongoing factors driving AI's evolution. Moreover, robust AI ecosystems are being established, capable of self-renewal and further innovation.

Looking forward, aspirations include ensuring AI fairness, promoting open science, and advocating for open data policies. These initiatives aim to harness AI ecosystems for the collective benefit of all individuals worldwide.



Nazanin Zeinab Arefipour<sup>1</sup>

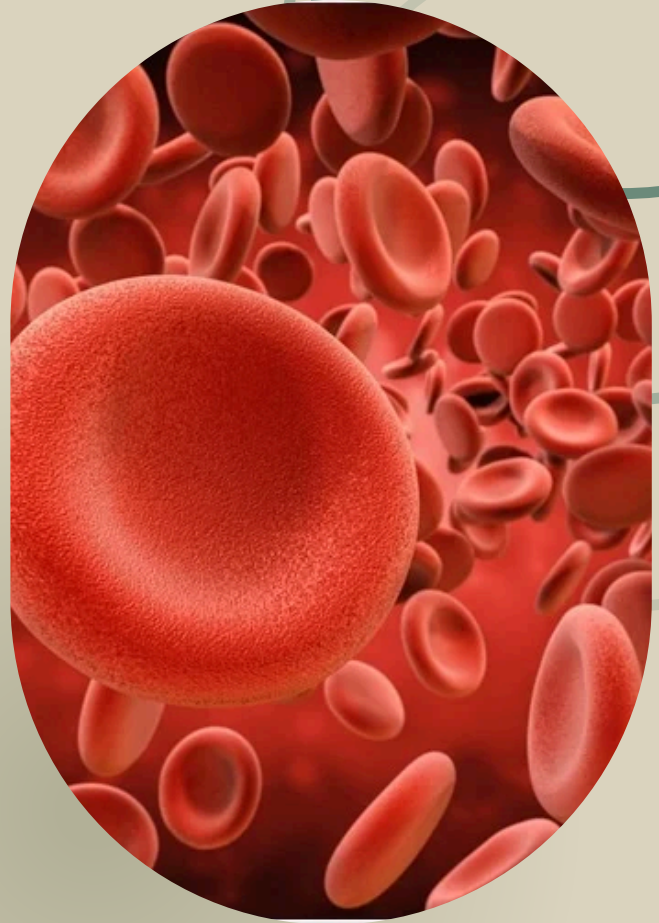


## **First Report of Known Rare Rhnull Phenotype Individuals in Iran, Sistan and Baluchistan:**

The Rhnull phenotype is a rare blood group with a frequency of approximately 1 in 6 million that is inherited in an autosomal recessive manner. This condition is characterized by weak expression (Rhmod) or absence (Rhnull) of all Rh antigens in red blood cells. The clinical significance of its assessment lies in the fact that patients with Rhnull syndrome often experience chronic hemolytic anemia to varying degrees. Another important aspect is that these individuals tend to produce alloantibodies when exposed to Rh antigens.

The general director of blood transfusion in Sistan and Baluchistan stated that the blood group of a young man who donated blood for the first time was diagnosed as O Rh Null.

This blood group lacks any antigens that could trigger an immune system response. Consequently, this blood group has a high compatibility for blood transfusions.



## **Kidneys Grown With Human Cells in Pig Embryos:**

Chinese researchers have recently succeeded in growing kidneys with human cells in pig embryos using the CRISPR system and powerful stem cells. This breakthrough could potentially help alleviate organ donation shortages worldwide. In the study, researchers first eliminated genes related to the pig embryo's kidney development using the CRISPR genome editing system to minimize competition between pig and human-created cells. They also created a cavity within the kidneys to facilitate cell growth. Subsequently, this cavity was filled with pluripotent stem cells, resulting in a combination of pig and human cells. These hybrid cells are cultured in containing before being implanted into the pigs' bodies. Finally, 1820 hybrid embryos were transferred to the uterus of 13 pigs, and after 28 days, it was determined that about 60% of the cells grown in the kidneys of pig embryos were of human origin.

In addition, the results showed only a small number of human cells were differentiated in the brain and spinal cord of pigs. While this new study marked a significant milestone for creating a complete organ of human origin in pigs, the quantity of human cells in the pig kidney remains insufficient for human transplantation. Consequently, further research is required in this area.

## Insulin producing cow:

A genetically modified cow produces human insulin!

For this study, the researchers investigated whether specific genetic alterations in cows could lead to the production of proinsulin in their milk.

The researchers used a process called reliable source somatic cell nuclear transfer to create specialized embryos. The ultimate goal was to manipulate the mammary glands of the resulting offspring to produce specific proteins in their milk. The researchers were able to produce very specific transgenic embryos, which were implanted into cows to create a transgenic cow. Subsequent attempts to impregnate the transgenic cow were unsuccessful. Finally, they induced the hormonally to produce milk.

After 21 days of lactation, the researchers collected milk for the next 30 days. They then performed experiments, specifically western blotting, and mass spectrometry, to assess the proteins in the milk. The results were compared with those from non-GM milk. The analysis revealed the presence of proinsulin and insulin in the milk obtained from transgenic cows.

"We were able to produce bioactive human insulin in cow's milk," said study author Dr. Matthew B. Wheeler, professor of biotechnology.

This study aimed to create a cost-effective source of insulin for diabetic patients.

However, this new study has several limitations:

First, the genetic modification process resulted in the creation of only one cow that efficiently produced insulin. The researchers focused their analysis on a specific component of the milk, the portion containing soluble proteins. Additionally, it is essential to identify the enzymes involved in the conversion of proinsulin to insulin.

"The biggest limitation of this study was that lactation was necessary for the cows to produce insulin, and transgenic animals often have difficulty conceiving either naturally or artificially," Dr. Splenser noted. He also added that although the authors detected proinsulin and insulin markers in cow's milk using Western blotting and mass spectrometry, they did not prove whether the insulin produced in cows is physiologically active in vitro or in vivo.

Future research could replicate these findings and explore how they might be applied in clinical practice.



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