INFINITY

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INFINITY

The first and only English student magazine for medical laboratory sciences

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Director-in-Charge

Years have passed since the first day the microscope was invented. Many days passed in a row, and slowly centrifuges, cell counters, and auto analyzers replaced manual and time-consuming methods and helped us get accurate results. We stayed, we fought COVID-19, and we are still strong and stable. We stayed and fixed our eyes on the screens, understood the patients' condition with our hearts, and made decisions with our intellect and knowledge. No machine could sacrifice its life to save another human life, and of course we sacrificed many lives. Many days have passed, and now we look to the future with much more hope than before, and we are always trying to help the lives of more of our fellows. In this student magazine, as the first specialized student magazine of medical laboratory sciences in the country, we intend to present the latest news, articles, and information related to our field to serious and interested audiences. Of course, in this way, we welcome your comments and suggestions, and we hope to be able to provide useful and efficient information. We hope that the infinite world of clinical laboratory science will accept this gift from us and lead us to bright horizons of success.

Yours faithfully

Mahoora Rahimi

Editor-in-Cheif

I am writing to express my interest in the publication of the first English student magazine for medical laboratory sciences in the country.Every moment, the world faces a new challenge. A child is born with a disability, someone is diagnosed with cancer, a new virus infects humans, and many people pass away. Meanwhile, all scientists and healthcare providers are trying their best to save lives by identifying the causes of diseases and finding new approaches to treat or cure patients. We all need to stay updated in this infinite world of science to fulfill our responsibilities as effectively as possible. English, as the international language, is one of the most important tools someone needs to succeed on the way to their goal. Thus, learning it can help us communicate more easily with researchers in all countries, better understand their results, and successfully put forward our own ideas. Our group made the decision to start a magazine, which might give motivation to all those who need to begin learning English and to those who like writing academically in this language. We would eagerly welcome all students in the fields of medicine, paramedicine, and biology to join us and take part in any part of this publication they would like.

Kind regards

Arefeh Cheraghchi

Vitamin D and Diabetes

Vitamin D, an essential factor for our bodies, can be synthesized from sun exposure, foods, and supplements. But this vitamin is biologically inert and needs to be activated by undergoing two hydroxylations in the body. This fat-soluble vitamin has many roles in the body, but about 30%–50% of people are recognized to have low levels of vitamin D.

According to the importance of vitamin D for health, many studies have been done to see the connection between vitamin D and diseases. Based on evidence, vitamin D insufficiency has emerged as a potential risk factor for type I and type II diabetes. Vitamin D has potential effects on autoimmune and inflammatory diseases as well as the secretion of insulin and insulin resistance. Both types of diabetes are associated with inflammation, and type I also has an autoimmune pathology. Vitamin D is thought to be related to the pathophysiology of both types of diabetes directly (through activation of the vitamin D receptor) and indirectly (via regulation of calcium homeostasis), including pancreatic beta-cell dysfunction, impaired insulin action, and systemic inflammation. Also, vitamin D protects vessels against diabetes via several intertwined mechanisms. There are also some specific putative mechanisms possibly involved in vitamin D's protective effects against diabetes, such as:

1.increasing eNOS-dependent NO production
2.reducing oxidative stress
3.enhancing vascular endothelial growth factor (VEGF) synthesis and release
4.modulating inflammation and the immune system
5.reducing transforming growth factor-B (TGF-B) production
6.regulating the activation of the complement cascade
7.inhibiting the renin-angiotensin-aldosterone system (RAAS)
8.reducing the detrimental effects of advanced glycation end products (AGEs)
9.reducing endoplasmic reticulum (ER) stress
10.regulating the apoptosis of endothelial cells

Most investigations and studies suggest a connection between vitamin D deficiency and diabetes. However, the lack of large prospective observational studies and randomized trials specifically designed to test the effects of vitamin D on diabetes limits drawing any definitive conclusions.

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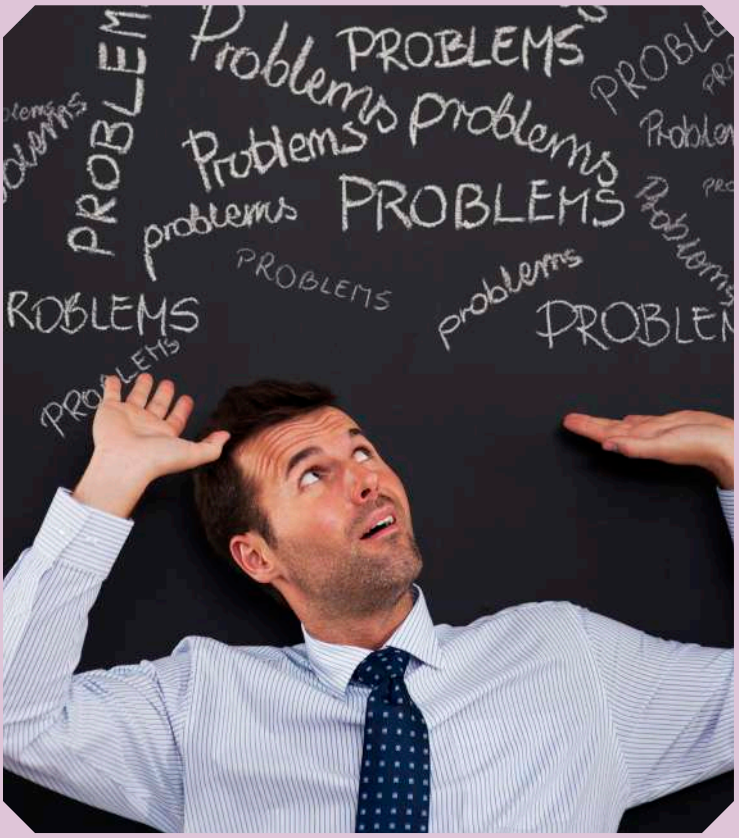
Effect of Age and Oxidative Stress on Hearing Loss

Hearing loss is a global health issue that affects roughly one in five individuals, making it the third-most significant cause of disability worldwide. This disorder has negative impacts on communication that lead to poorer quality of life and psychosocial health problems. Hearing loss is associated with tinnitus, cognitive decline, and madness. A type of this disorder is age-affiliated hearing loss (ARHL), also known as presbycusis, which affects 65% of adults aged ≥60 years, and is characterized by bilateral and symmetrical loss of high-frequency hearing (≥8 kHz) in the initial stages. The progression of the condition affects hearing at lower frequencies due to the irrevoca ble loss of cochlear hair cells and auditory nerve damage. The development of ARHL is influenced by a combination of aging, health comorbidities, environmental, and inheritable factors. These factors enhance inflammation-related processes that produce reactive oxygen species (ROS). When there is an overproduction of ROS and insufficient endogenous processes to neutralize or detoxify them, it results in a dislocation of intracellular redox homeostasis, leading to oxidative stress. This oxidative stress is believed to damage inner ear structures through membrane lipid peroxidation and denaturation of proteins, as well as DNA damage and cellular apoptosis. However, while some causes of oxidative stress are non-modifiable, there are several adjustable factors that can be managed to increase antioxidant exertion.



Mechanisms of Oxidative Stress

The main risk factor for ARHL is aging, which is characterized by chronic oxidative stress and inflammation. Generally, factors like exposure to loud noise, ototoxic chemicals, or smoking can produce stressful conditions that complicate the pro-oxidant and pro-inflammatory processes in the body.

These processes are interrelated and thus concertedly present in a number of chronic diseases, such as ARHL. When pro-oxidant activity

becomes greater than antioxidant activity, toxic levels of ROS and other free radicals are produced. This increases the chance of damaging interactions with macromolecules such as lipids, proteins, and DNA within the audile cells (e.g., hair cells, helical ganglion neurons). These relationships damage the cells' mitochondria and mitochondrial DNA and reduce the mitochondria's cytochrome C oxidase exertion. The responses lead to a curl of oxidative damage as dysfunctional mitochondria also produce further ROS, driving unseasonable metabolic ability and apoptosis, leading to the progressive and endless loss of audile cells. Also, the endothelium can be damaged by oxidative stress and inflammation. Maintaining the health of the endothelium is important for successful aging as it is responsible for releasing enzymes and/or nitric oxide to maintain vascular tone, control platelet adhesion, blood clotting, and vascular proliferation. Oxidative damage to the stria vascularis because of poor vascular health has also been linked to the ARHL pathophysiology. The stria vascularis is a structure within the cochlea that plays a crit ical role in hearing and cochlear amplification.

Modifiable Lifestyle Risk Factors and Oxidative Stress

ARHL is affected by varied factors that can be modified to reduce the progression of the condition. These adjustable factors are exposure to loud noise, an unhealthy diet, smoking, exposure to ototoxic chemicals, a lack of regular exercise, obesity, diabetes, and other cardiovascular health issues. Many studies suggest that healthy life habits like safe listening, quitting smoking, a healthy diet, and regular physical exertion have been shown to reduce the threat and progression of ARHL.

Conclusions

With the population aging, the frequency of ARHL will increase. Leading a healthy lifestyle appears to play an important role in delaying age-related oxidative damage to the inner ear and, thereby, can help to protect audile cells and inner ear function.

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THE LOSS OF SMELL IS NO LONGER A RELIABLE COVID SIGN

READ MORE ON PAGE 32

CRISPER-Cas9

A Promising Tool For Gene Editing

What is CRISPR-Cas9?

Almost the first investigation to show that directionality could be achieved using alterations in the genome of embryonic stem cells (ESC) was done in the 1980s. This process can provide pluripotency to create many other different cell types. However, the results were not reliable because the success rate was less than 10 percent. The unacceptable results of this technique led to the development of other effective and accurate techniques. such as Zinc Finger Nucleases (ZFNs), which improved in 2005, and Transcription Activator-like Effector Nucleases (TALENs), which improved in 2010. These two techniques have their own limitations. The most obvious one is the method of target recognition. These techniques use a protein-directed method to identify their target DNA. But designing proteins is a time-consuming and complex process. Therefor The search for a suitable genetic modification tool continued until, in 2012, the adaptive immune system of Streptococcus pyogenes, which is called the CRISPR-Cas9 system, started to be used as a programmable gene editing tool. This system consists of two sections: “Clustrated Regulatory Interspaced Short Palindromic Repeats” (CRISPR), which is made of RNAs and acts as a guide to identify target zones in target DNA, and “CRISPR-associated protein 9” (Cas9), an endonuclease enzyme that acts as scissors to cleave target DNA. The CRISPR-Cas9 system is a powerful RNA-guided DNA targeting tool that is used in genome modification in vitro and in vivo. CRISPR-Cas9 is not specified by protein subunits. Instead, a 20-nt guide RNA sequence is used as a targeting method and is the best of this technology in comparison to other nuclease-mediated techniques because RNA designing is much easier than the complex and difficult protein engineering process. This programmable endonuclease system enables researchers to correct genomic errors and turn genes on or off.

Molecular Mechanism of CRISPR-Cas9

The type II CRISPR system is known for its Cas9 proteins. Other types are associated with different Cas proteins. This system has two lobes: the REC lobe and the NUC lobe. The REC lobe is responsible for target recognition, and target cleavage is the task of the NUC lobe. The REC lobe contains three alpha-helical domains: Hel-I, Hel-II, and Hel-III. It has close connections with RNA strands. The NUC lobe is the functional lobe that does its task through three domains: HNH, RuvC, and CTD (the C-terminal domain). The HNH subunit cleaves the target strand, which is complementary to guide RNA, and the RuvC subunit cleaves the nontarget strand, or opposite strand, of the complementary one. The CTD subunit’s function is to recognize PAM sequences. The PAM sequence is generally NGG, where N can be every nucleotide except uracil and is located in a nontarget DNA strand. Recognition of the PAM sequence is essential for the CRISPR-Cas9 system to perform properly because it results in melting DNA upstream of the PAM region. Cas9 needs single-stranded guide RNA (sgRNA) to recognize the target site. The CRISPR-Cas9 system searches along DNA to find complementary sites to its sgRNA, ultimately leading to the cleavage of the target site. These breaks will be repaired in two different ways:non-homologous end-joining (NHEJ) and homologous-directed recombination (HDR). NHEJ causes the formation of indels, while HDR occurs in the presence of donor DNA and results in the rectification of the DNA damage.

Applications and future of CRISPR-Cas9

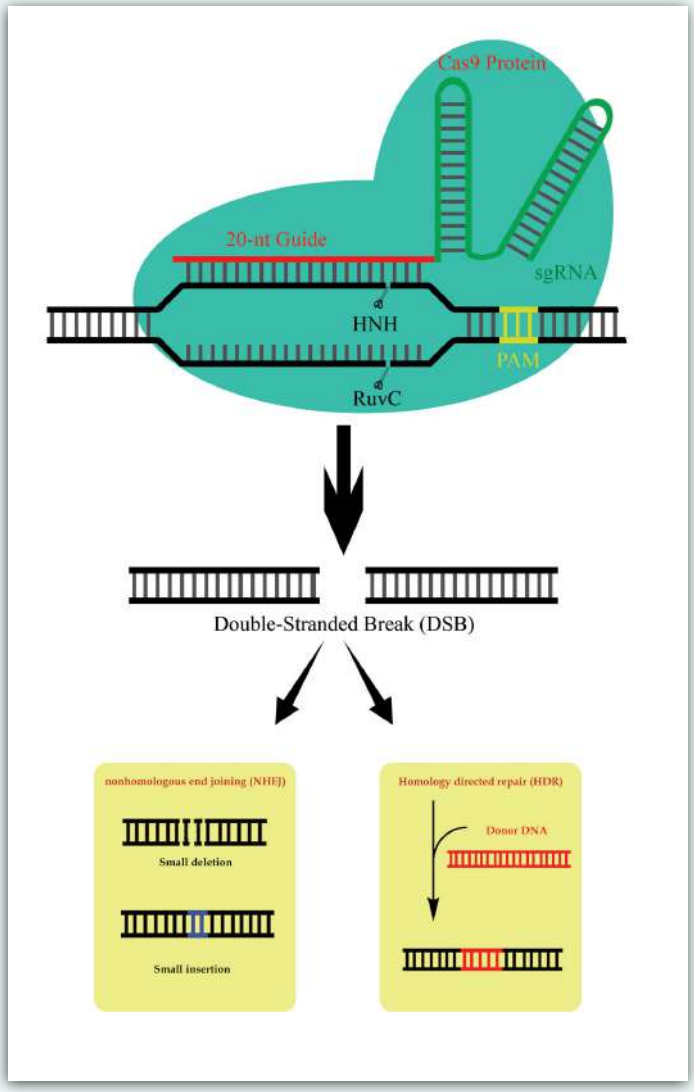
CRISPR-Cas9 enables scientists to program cells as they want. They can generate special cell lines with specific disorders to develop experimental models. Also, this system has the potential to be used in vivo to generate model animals to study diseases such as cancer. Clinical application is a major potential goal of this system. There is evidence that CRISPR-Cas9 can target the genome of viruses such as HIV and Hepatitis B. Also, it can be used for the treatment of leukemia and several other blood cancers. The application of CRISPR-Cas9 for cystic fibrosis and Duchenne muscular dystrophy treatment is noteworthy. Despite these advancements, we have a long way to go before we can use this technology clinically.

Limitations of CRISPR-Cas9

Despite its great promise, there are still many challenges left before the application of CRISPR-Cas9 as an effective therapeutic method. A particular limitation is the delivery method of sgRNA and Cas9 proteins to target cells. Adeno-associated virus (AAV) is the most widely used carrier for gene transduction. But the AAV delivery system does not have enough space to involve the Cas9 genes.

Therefore, smaller genes can be used, or another delivery method should be substituted. Furthermore, plasmids are often integrated randomly into the host genome.

So, they can be inserted in both on-target and off-target cells to avoid any harmful effect or adverse reaction. The biggest concern about this system is its off-target effects. The CRISPR-Cas9 system can tolerate up to 1–3 mismatches between sgRNA and the target site. This problem becomes more evident in clinical applications, but it can be overcome by designing sgRNAs that do not target functional proteins.



Bioethics of CRISPR-Cas9

Every technology has its own benefits and risks. Prior to a clinical trial, the ratio of risks to benefits must be assessed. Then we can answer the question: Do the risks outweigh the benefits? There are many regulatory bodies debating the balance of these two factors, including UNESCO, WHO, and the Universal Declaration on the Human Genome and Human Rights. In the United States, any manipulation of embryos for pregnancy needs permission from the FDA (U.S. Food and Drug Administration). The U.S. National Academy of Medicine (NAM) and National Academy of Science (NAS) classify genomic manipulation on the basis of purpose and heritability.

In terms of purpose, it is divided into two categories: therapeutic introversion and enhancement, and in terms of heritability, somatic cells and germline cells. The majority agrees with therapeutic applications in both somatic and germline cells. Generally, genetic modification in somatic cells is accepted ethically because of its low risk-to-benefit ratio and informed consent. However, germline modification is ethically unacceptable because of its high risk-to-benefit ratio and unforeseeable effects on future generations. Another concern is about unintended cosmetic applications of gene modification.

Many arguments show that the CRISPR-Cas9 system can be converted into a "baby designing machine". It can cause societal changes toward global inequality. Because rich people can access CRISPR technology more than other people, they will have smarter and stronger offspring.

Another cosmetic application is modifying physical traits to achieve "enhancement" of muscle or intelligence. Therefore, bioethics and ethical boundaries within which CRISPR-Cas9 can be used must be fully determined, and lawbreakers must be dealt with.

Conclusions

Jennifer Doudna and Emmanuelle Charpentier opened a new door for humanity in 2012. The door behind which was an unknown world of genetic modifications. Despite the fact that CRISPR-Cas9 can be a savior for humanity, it can also become a weapon to destroy it. And the main question remains unanswered. Do the benefits outweigh the disadvantages?

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Pharmacogenetics

Personalized Medication Design

Pharmacogenetics and pharmacogenomics are studies of how genetic diversity can affect the body's response to a medicine, the differences between the specific genes that control drug transportation and metabolization, or the genes that determine drug receptors' structure and characteristics. Pharmacogenetics studies a single gene variation, while pharmacogenomics studies genome differences that impact individuals or populations. These are methods to achieve personalized healthcare where medication is specifically designed for each individual due to their unique genetic makeup, health history, and conditions, which is important to reduce adverse reactions and improve medication function and efficiency. In studies done so far, adverse reactions were more common in the standard care group in comparison to the genotyped group. This must be taken seriously because it can be a serious issue for patients with various diseases, whether elderly or pediatric. Also, assessments in the USA indicate that treatment side effects reduction decreases healthcare system costs and healthcare workers load considerably.

Currently, in many countries worldwide, the focus is on mainstreaming genomic medicine by making genotyping technologies widely available and decreasing their cost.

Advancements in genomic profiling methods aim to enable novel patient genotyping and biobanks, which, paralleled by machine learning developments, allow us to parse the enormous mass of data and establish polygenic models and novel genetic markers for drug selection and dosing.

Nowadays, delivering pharmacogenomics into healthcare systems is a major challenge that includes an immense knowledge gap about genomic medicines and personalized healthcare among healthcare workers and the modification of standard care protocols.

Another challenge is that people are usually diagnosed with multiple diseases, and the different medicines they take may affect each other's absorption and metabolization. Besides, we should be aware that reimbursement practices and insurance coverage are also vital to mainstreaming genomic medicine.

Despite the fact that pharmacogenetics beginning dates back to the 1950s, many questions still remain, and pharmacogenetics is still not commonly utilized in clinical settings and is only used clinically in oncology. The reason is the difficulty of using the genotyping results in complex patients' conditions and delivering pharmacogenomics into health care systems.

However, pharmacogenetics is being used in clinical trials and recently in fields like cardiovascular diseases, diabetes, coagulation disorders, respiratory diseases, and especially psychiatric disorders.

In the case of psychopharmacology, molecular targets have not yet been completely identified. Available treatments exist, but only one-third of the patients respond to these treatments due to genetic variations and the fact that the medication prescription in psychiatry relies on observational study trials and a trial-and-error approach. In this method, time is a very important factor because it can be dangerous with untreated suicidal thoughts and behaviors.

Eventually, following the advantages and reasons stated above, we should mention the lack of pharmacogenomics studies in Asia and Africa, which hold 77% of the world population, by referring to a review article claiming that 104 studies out of 146 studies analyzed were conducted in North America, 26 studies in Asia, and 16 studies elsewhere (Africa, Australia, Europe, and South America).

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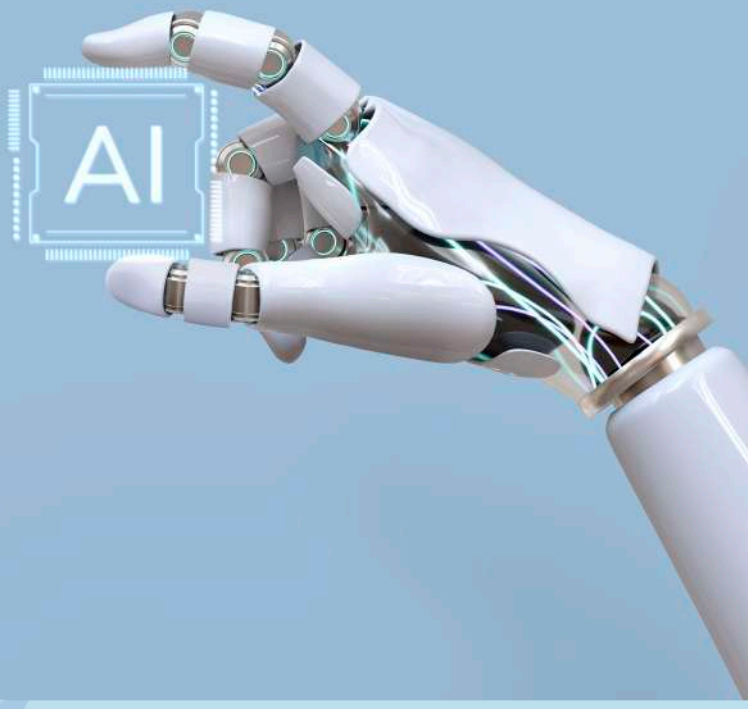
Application of Artificial Intelligence in Medical Diagnostic Laboratories

Artificial Intelligence

Artificial intelligence (AI) refers to software that, in addition to analyzing data, can make decisions and is an imitation of human intelligence. These techniques are rapidly being developed and implemented throughout healthcare systems, and laboratories will see significant growth in AI applications soon.

These information technology strategies can be adjusted either to control the epidemic or to support containment, which helps to control the spread of infection. Artificial intelligence in medical laboratories can be used to make operational decisions and automate or augment human-based workflows. Error detection, prediction of results, genomics, and image analysis are different uses of AI. It can also reduce errors and save time.



Despite the advantages, it should be noted that the specific knowledge of this technology in the field of medicine is weak, and AI training is necessarily needed. High investment costs, a lack of proven clinical benefits, a small number of decision-makers, and privacy concerns were identified as barriers to adoption. Teaching the value of AI, simple implementation and integration into existing workflows, and research to prove clinical utility were suggested as solutions needed to mainstream AI in medical laboratories.

AI in the Medical Diagnostic Laboratory During the Coronavirus Pandemic

In December 2019, the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China led to a global outbreak of the coronavirus disease. This disease spread all over the world and became an international public health issue.

The high contagion of the new coronavirus has attracted the attention of researchers toward the use of artificial intelligence to deal with this epidemic, control it, and manage crises.

During the pandemic, AI was used in laboratories not only for early diagnosis but also for screening patients, monitoring treatment stages, epidemiology, managing the pharmaceutical system, reducing the workload of medical personnel, tracking infected areas, forecasting the pandemic situation, and monitoring the spread of COVID-19. Artificial intelligence can also be used in the field of predicting mutations that may occur in viruses in the future and cause new symptoms and complications of the disease.

Conclusions

Results show that the use of AI in medical laboratories has accelerated the performance of coronavirus diagnosis tests and reduced errors, and clinical laboratories will routinely use these techniques in the near future.

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New Approaches to Treat Acute Lymphoblastic Leukemia in Children

In pediatric patients, acute lymphoblastic leukemia is the most prevalent blood cancer. The 5-year survival rate has increased significantly in recent years, rising from 57% in the 1970s to up to 96%, reflecting the significant advancements in ALL therapy. Most treatments are based on traditional techniques, such as chemotherapy and radiotherapy. Their main disadvantage is extreme toxicity, which demands dosage reduction but reduces the efficiency of the therapy. Scientists are seeking out more cutting-edge treatment alternatives, including immunotherapy and targeted therapy, for pediatric patients receiving hematological care. Chemotherapy is now combined with these techniques.

Targeted therapy

Targeted therapy identifies and kills particular cancer cells using medicines or other chemicals. Compared to chemotherapy or radiation therapy, targeted therapies typically have a lower impact on normal cells. Targeted therapy comes in a variety of forms:

Tyrosine kinase inhibitors (TKIs)

The proto-oncogene Abelson murine leukemia (ABL1) gene, which is located on band q34 on chromosome 9, translocates to the band q11 on chromosome 22, where the breakpoint cluster gene (BCR) exists to create the Philadelphia chromosome. TKIs prevent stem cells from producing more white blood cells than the body requires by inhibiting the activity of the tyrosine kinase enzyme. Dasatinib and imatinib are used to treat pediatric Philadelphia chromosome-positive ALL, and a TKI being researched for the treatment of newly diagnosed high-risk ALL is roxolitinib.

Monoclonal antibodies

Monoclonal antibodies are immune system proteins made in the laboratory to treat many diseases, including cancer. These antibodies can bind to a particular target on cancer cells or other cells that may help the growth of cancer cells.

The cancer cells can then be eliminated, their growth stopped, or their ability to spread prevented by the antibodies. Monoclonal antibodies are given by infusion. They can be employed independently or to deliver medications, poisons, or radioactive substances directly to cancer cells. Blinatumomab and inotuzumab are monoclonal antibodies being studied in the treatment of refractory childhood ALL. Standard-risk ALL is another condition for which blinatumomab is being researched. A monoclonal antibody called nivolumab is being investigated for the treatment of relapsed childhood ALL.

Proteasome inhibitor therapy

This type of targeted therapy prevents cancer cells from producing proteasomes by blocking their activity. Proteins that the cell no longer requires are removed by proteasomes. The proteins accumulate in the cell when the proteasomes are stopped, which may lead to the death of the cancer cell. A proteasome inhibitor medication called bortezomib is used to treat relapsed childhood ALL. The use of bortezomib in the care of patients at standard or high risk is being investigated.

Immunotherapy

Immunotherapy is a type of cancer treatment that activates the patient's immune system. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This cancer treatment is a type of biologic therapy.

CAR T-cell Therapy

CAR-T stands for chimeric antigen receptor T cell. This therapy involves gathering your own immune cells and modifying them to improve their ability to combat leukemia cells. The leukemia cells are then targeted by these cells. Tisagenlecleucel (Kymriah) is the brand name for the specific CAR-T treatment used to treat ALL. If other treatments have failed or if ALL returns, it may be used to treat young adults under 25 with B cell ALL. The CAR-T therapy is challenging and may result in negative side effects. Only a very tiny number of people can use it. It is only currently accessible in a small number of specialized hospitals. It might be provided to some individuals as part of a clinical trial.

Conclusions

The treatment approaches for children with ALL have changed significantly over time. Traditional treatment modalities like chemotherapy are still the cornerstone of ALL treatments. However, it has been observed that new methods such as targeted therapy and immunotherapy have had effective results. However, only a few percent of patients may receive targeted therapy. Therefore, there is a requirement for the development of novel medicines that are efficient across the broadest spectrum of patients.

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A NEW DRUG MAY ONLY REQUIRE TWO DOSES EACH YEAR TO CONTROL BLOOD PRESSURE

READ MORE ON PAGE 32

Gene Therapy in Severe Combined Immunodeficiency

Gene Therapy for Severe Combined Immunodeficiency

What is SCID?

Severe combined immunodeficiency (SCID) is a group of diseases characterized by low T-cell number and impaired T-cell function, resulting in severe cellular and humoral immune defects. If not diagnosed and treated promptly, infants with this condition can develop a severe infection that will result in death. T-Cell Receptor Excision Circle (TREC) levels are measured in newborns for SCID screening.

SCID is caused by genetic mutations that affect the function of T cells. Depending on the type of SCID, B cells and natural killer cells (NK cells) can also be affected. These cells play an important role in helping the immune system fight against bacteria, viruses, and fungi. Most affected infants who are not treated with a hematopoietic stem cell transplant in their first year of life will die.

According to reliable research reports, it has been determined that more than 12 genes are involved in the development of SCID. However, a new NIH-sponsored study shows that gene defects remain undetected in approximately 15 percent of screened SCID infants.

Gene therapy

Inherited and acquired diseases of the hematopoietic system can be cured by allogeneic hematopoietic stem cell transplantation. . This strategy is highly successful when an HLA-matched sibling donor is available, but if not, few therapeutic options exist. Gene-modified, autologous bone marrow transplantation can circumvent the severe immunological complications that occur when an HLA-mismatched donor is used and thus represents an attractive alternative. Gene therapy is a type of molecular medicine that involves adding a repaired copy of a gene to a person's somatic cells with the aim of curing or lessening his or her condition. This approach could soon lead to the development of novel therapies for a wide range of genetic disorders.

Only two cell types—accessible stem cells and terminally differentiated, postmitotic, long-lived cells can be effectively used in gene therapy at the moment. When targeting dividing cells, it is necessary to use viral vectors that can integrate into the host genome in order to ensure the replication of the transgene, whereas nonintegrative vectors can be used when transferring genes to postmitotic cells. Integrative gene transfer is mediated by RNA viruses (retroviruses and lentiviruses). On the other hand, nonintegrative methods of delivering therapeutic genes are offered by DNA viruses. Adenovirus (Ad) and Adeno-Associated Virus (AAV) have frequently been employed in clinical trials of gene therapy. These two viruses can only infect postmitotic cells since their genetic material does not integrate into cells and is not reproduced during cell division.

Two stem cell compartments, those in the hematological system and those in the skin, outperform the others in terms of their qualities for use in gene therapy. These two stem cell compartments stand out for their ability to self-renew and sustain functions over the course of an individual's lifetime. In fact, over 20 years of research on ex vivo manipulation of these stem cell compartments (in HSCT and burn repairs, respectively) has enabled rapid advances in the gene therapy field. The cell types' accessibility, capacity to survive in ex vivo cell culture, and transplantability are advantageous for their use in gene therapy.

Conclusions

Gene therapy is being used to treat a number of primary immunodeficiency illnesses due to its efficiency. However, in recent years, some of these treatments and trials have been halted due to concerns over the safety of viral vectors. As a result, many organizations worldwide are attempting to create safer gene variants and methodologies. It is hoped that safety issues will soon be resolved and that more effective gene therapy treatments will be made available to treat a number of SCID subtypes.

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Recently Developed Treatment in HIV

The HIV-1 pandemic is unquestionably the most serious health catastrophe of our time. It is a complicated mixture of various diseases that have spread inside and between different nations and areas of the world. Inhibitors of the HIV-1 integrase (IN) enzyme represent one of the most important advances in HIV care. Among the essential enzymes encoded by HIV-1, protease (PR), reverse transcriptase (RT), and IN are necessary for the integration of viral double-stranded DNA into the host cell's chromosomal DNA, a step that is critical to establishing persistent HIV-1 infection. The currently approved three drugs that belong to the class of integrase inhibitors (INIs) are termed integrase strand transfer inhibitors (INSTIs) because of their preferential targeting of the strand transfer step of integration. Due to favorable clinic characteristics, such as high antiviral potency with quick declines in HIV RNA, good tolerability, a favorable safety profile, the absence of significant drug-drug interaction, and the fact that they target a new mode of action, these new medications lack cross-resistance to other drug classes.

The three INSTIs that have received FDA and European Medicines Agency approval are raltegravir (RAL), elvitegravir (EGV), and dolutegravir (DTG), which are the newest classes of antiretroviral medications available to treat HIV infection. Despite having many qualities in common, such as antiviral potency, a common mechanism of action, and a good tolerability and safety profile, they also have important characteristics that set them apart from one another, including dosing, formulation, and resistance profiles. In several clinical situations, INSTIs have been demonstrated to be a desirable alternative for the treatment of HIV-1 due to their native and pretreated characteristics. Currently, we have enough information from clinical studies to describe how these medications differ from one another.

Raltegravir

On October 12, 2007, the FDA approved the first HIV INSTI, called raltetegravir (RAL), for people with viral resistance who have received antiretroviral therapy in the past. Due to its low side effects and few long-term safety issues, RAL is regarded as one of the best-tolerated antiretroviral medications. Lacking substantial drug-drug interactions, RAL may be helpful in treating a number of particular patient populations, including those with renal disease, cancer, tuberculosis, and co-infection with hepatitis.

Elvitegravir

The second INSTI available for treating HIV is elvitegravir (EGV). It has received approval from US and EU regulatory bodies for use as a STR to treat HIV-1 infection in individuals who have never had treatment for HIV infection. It was co-formulated with cobicistat (COBI), FTC, and TDF.

Recent twin-randomized, open-label clinical trials indicate that this may soon be expanded to be used for patients who are virologically suppressed and who are currently taking either an NNRTI or a PI-based regimen. Clinical trials show that EVG is just as effective and well-tolerated as RAL but only calls for a once-daily dosage. Most side effects were mild to moderate in severity, and substantial drug-related side effects and discontinuations due to them were infrequent. EGV must be administered along with a pharmacokinetic booster (RTV or COBI) to prevent the cytochrome P450 enzyme system from metabolizing it.

Dolutegravir

The newest INI and the first to be administered once daily without a booster is dolutegravir DTG. For use in both treatment-naive and treatment-naive patients, it has received FDA and EU approval. DTG is well tolerated like other INSTIs; however, unlike them, DGV has a favorable resistance profile. It has a favorable drug-drug

interaction profile and a greater genetic barrier to resistance. Four phase lll clinical trials, including DTG, have been conducted, and there is further week 48 data for treatment-naives from a phase lllb/lV research.

Conclusions

Due to the data on efficacy, tolerability, and safety of all three drugs (raltegravir, elvitegravir, and dolutegravir) currently belonging to this new family of antiretrovirals, INIs have become part of the recommended initial antiretroviral therapy options. Some differences in dosing, drug-drug interactions, and robustness/genetic barrier among them will lead the physician to make the best choice.

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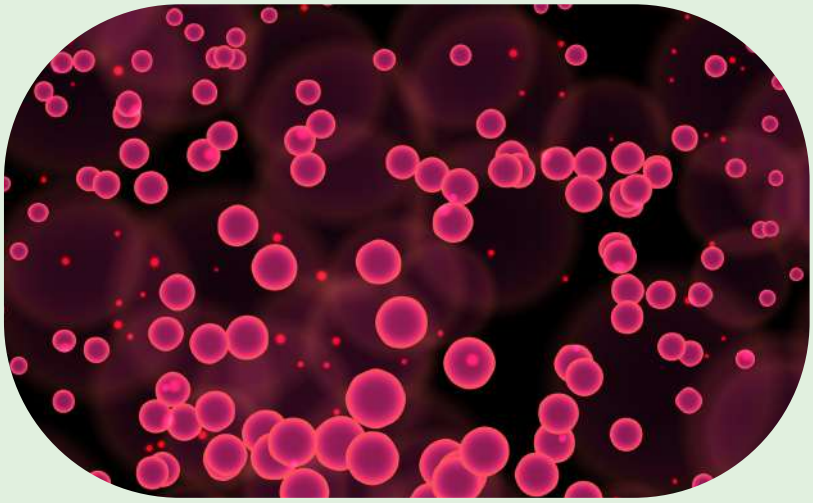
LOSING YOUR SENSE OF SMELL MAY BE A WARNING SIGN OF ALZHEIMER'S

READ MORE ON PAGE 32

Antimicrobial Peptides

Finding anti-infectives with a novel mode of action that are less prone to bacterial resistance has become more urgent because of the rapid development of microbial resistance to traditional antibiotics. Antimicrobial peptides (AMPs) are short, positively-charged oligopeptides that are present in almost all organisms. They have a wide range of forms and activities. The innate immune system's essential building block, AMPs are crucial to the initial immune response produced against both infections and injuries. Since cells of myeloid origin and epithelial cells, among the first to respond to infections, are where AMPs are largely generated and stored, AMP-mediated immune responses are quickly activated after infections. A wide range of tissues, including the skin, eyes, mouth cavity, lungs, female reproductive tract, cervical-vaginal fluid, intestines, and urinary tract, express AMPs. Antimicrobial peptides (AMPs) are one of the first immune mechanisms to get activated in vivo when several pathogens invade different organs. The human cathelicidin LL-37 and defensins are the two most well-studied AMP classes that display broad antibacterial activity in humans.



AMPs may inhibit a wide variety of bacteria, fungi, parasites, and viruses. The development of AMPs, which have a promising future in medicine, food, animal husbandry, agriculture, and aquaculture, was prompted by the advent of antibiotic-resistant microbes and growing concerns regarding the usage of antibiotics. Several AMPs are currently being evaluated in late-stage clinical trials not only as novel anti-infective drugs but also as innovative product candidates for immunomodulation, promotion of wound healing, and prevention of post-operative scars. In the upcoming years, it is anticipated that efforts to translate AMP-based research findings into pharmaceutical products will intensify due to technological advancements in several fields, such as a better understanding of the mechanism-of-action of AMPs, smart formulation techniques, and sophisticated chemical synthesis protocols. It is recognized that cytotoxicity, low metabolic stability due to sensitivity to proteolytic degradation, and limited oral bioavailability are some of the key weaknesses of AMPs. Furthermore, the pricing and reimbursement environment for new antimicrobial products remains as a major barrier to the commercialization of AMPs.Despite the difficulties in turning nonclinical candidate AMPs into therapeutic medicines, recent advances in describing their properties are anticipated to hasten the development of AMPs as therapeutic agents in the upcoming years. Scientists predict that numerous novel AMP-based medications will enter clinical use within the next ten years, with several AMPs presently undergoing late-stage clinical development. New AMP-based experimental medications entering the market and exhibiting considerable and distinctive medical value, as in many other therapeutic areas, might then have a transformative impact on firms' and funding organizations' desire to make additional investments in the AMP space.

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News

The Loss of Smell Is No Longer a Reliable COVID Sign

- According to a recent study, compared to the early stages of the pandemic, the likelihood of smell and/or taste loss from COVID-19 has dramatically decreased.
- It's not a guarantee that you have COVID if you've lost your sense of taste and smell. However, it does not necessarily follow that you are not infected just because you have not lost your sense of smell.
- It's unclear why the likelihood of COVID making you lose your sense of smell has decreased, but it's plausible that immunity from vaccinations, prior infection, and virus mutations are contributing factors.

A New Drug May Only Require Two Doses Each Year to Control Blood Pressure

- A novel RNA-targeted medicine was found to decrease blood pressure for up to six months, according to a limited clinical research.
- Zilebesarin is directly injected into the liver to have its desired effects there.
- While most drugs for treating hypertension target the hormones that raise blood pressure, this one targets the RNA that makes the hormones.
- The medicine won't be available for years, but research is still being done.

Is Air Pollution to Blame for Your Headache?

- The mechanism by which air pollutants evoke headaches is still unknown, though experts believe it has to do with inflammation and specific nervous system pathways.
- Breathing issues and headaches are only a couple of the symptoms linked to air pollution exposure.
- To monitor your risk if you suffer from migraines, follow the air quality index (AQI).

Losing Your Sense of Smell May Be A Warning Sign of Alzheimer's

- You have a high chance of Alzheimer's if you have the APOE e4 gene. According to a recent study, those who possess the gene may also be more prone to losing their sense of smell around the age of 65.
- Changes in smell can be an early marker of neurodegenerative disorders like Alzheimer's and other dementias.
- Experts think that establishing a smell test might become a standard component of Alzheimer's screenings.

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