European Medical Students' Association

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EMSA European Medical Students' Association

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European Medical Students' Association -
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(EMSA) is a non-profit, non-governmental organisation representing more than 150.000 medical students from over 90 faculties across Europe. Founded in 1990, in Brussels, it is the voice of students within the European Commission, the Council of Europe and the United Nations. The association provides a platform for high-level advocacy, projects, trainings workshops and international meetings. Its activities gather around Medical Education, Medical Ethics and Human Rights, Health Policy, Public Health, Medical Science and European Integration and Culture.

OUR VISION

Shaping a solidary and united Europe, where medical students actively promote health.

OUR MISSION

EMSA empowers medical students to advocate health in all policies, excellence in medical research, interprofessional healthcare education and the protection of human rights across Europe.

EUROMEDS CHIEF EDITOR'S NOTE

Teodora Mărgineanu
EuroMeds Chief Editor
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Dear EuroMeds Enthusiasts,

We are beyond excited to share with you the 27th issue of EuroMeds, the Spring Assembly'24 Issue.

This year, our theme of "Innovative Medicine" couldn't be more timely or relevant. As medical students, we are constantly at the forefront of groundbreaking discoveries, cutting-edge technologies, and novel approaches to healthcare. From artificial intelligence and precision medicine to telemedicine and beyond, the landscape of medicine is evolving at an unprecedented pace. EuroMeds aims to capture this spirit of innovation, to explore its implications for the future of healthcare, and to inspire our readers to think boldly and creatively.

But EuroMeds is more than just a magazine; it is a tool for advocacy, a platform for change, and a bridge between medical students and the wider healthcare community. Through our pages, we highlight pressing issues facing our generation and empower our readers to become agents of change in their own communities.

On behalf of the EuroMeds Editorial Team, I sincerely hope that you enjoy reading this issue as much as we enjoyed preparing it.

Warm regards,
Teodora Mărgineanu | EuroMeds Chief Editor

VICE PRESIDENT OF CAPACITY'S NOTE

Ayça Kahraman
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Dear EuroMeds Enthusiasts,

Welcome to the latest issue of EuroMeds, where innovation meets medicine!

As the Vice President of Capacity, I am thrilled to introduce you to first issue of the term, EuroMeds SA'24 Issue - Innovative Medicine.

I would like to thank our EuroMeds Editorial Team members, especially our dear Chief Editor Teodora for pioneering such a great EuroMeds Issue. I also want to give a special thanks to the authors for their contribution and Dr. Mert Ersan & Prof. Dr. Uğur Sezerman for accepting our invitation for the interviews.

I'm ending my words to leave you with our magazine to read this beautiful issue of EuroMeds.

Best Regards,
Ayça Kahraman | Vice President of Capacity 23-24

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INTERVIEWS

Interview with Dr. Mert Ersan

I'm Dr. Mert Ersan, born in 1990 in Izmir, Türkiye. After graduating from high school, I went to Hacettepe University, Faculty of Medicine, which took me six years to complete. In Türkiye, we enter an exam for our specialty programs. I chose plastic surgery and began my residency, which took 5.5 years. I became a plastic surgery specialist 3.5 years ago.

In Türkiye, when you become a specialist, the government assigns you to a location that lacks doctors. I worked in a city called Yozgat for two years as a plastic surgery specialist. During that time, I passed the EBO examination, becoming a fellow of the European Board of Plastic, Reconstructive, and Aesthetic Surgery. I then pursued a fellowship program with ISAPS, the International Society of Aesthetic Plastic Surgery, which is the most renowned aesthetic surgery society in the world. I went to the Netherlands, where I completed my fellowship in various private plastic surgery clinics. Afterward, I returned to Istanbul, Türkiye.

Now, I work at Yeditepe University, performing surgeries and serving as an academician. I have been giving lectures to students and recently became an assistant professor. It’s good to be here in Istanbul. That's a brief overview of my plastic surgery career.

Melika Nejati Afkham
Content Creator

How do you manage being a surgeon, an academic professional, and having an online presence?

It wasn't difficult for me because my father was a doctor, a surgeon, but he was an oncologist. Being a doctor and a surgeon felt natural to me since my childhood. Plastic surgery, however, stood out to me because it deals with all age groups and all organs of the body. We handle everything from hair to face, breasts, arms, abdomen, legs, and the genital area. The field's broad scope is fascinating. Additionally, we use a lot of Mathematics in plastic surgery for calculations, ratios, and angles, which I enjoy. I also have an interest in arts, sculpting, and painting, which are related to plastic surgery. These diverse interests led me to choose plastic surgery for my future.

The general population probably thinks plastic surgery is just about the face or the upper part of the body. What do you think about this?

Our specialty, plastic, reconstructive, and aesthetic surgery, covers a lot. For aesthetic purposes, we deal with everything from hair, eyebrows, eyes, nose, and ears to breasts, abdomen, thighs, and more. It’s a comprehensive field.

What are the most cutting-edge technologies currently used in plastic surgery?

Innovation is crucial because it allows surgeons to perform more precise and effective interventions, speeding up patient recovery. Key advancements include stem cell therapies, 3D surgical simulation tools, and 3D-printed implants.

In the past few years, there has been an increase in artificial intelligence and machine learning. How do you think this will affect your field in the future?

Artificial intelligence and machine learning are becoming integral to our daily lives, including plastic surgery. We’ve been using AI for two to three years now. It will play a significant role in surgical planning, education, and patient-doctor relationships, enhancing both the process and outcomes.

Do you think AI will just be a tool to help people, or will it change how surgeons and patients interact?

It will do both. It will change doctor-patient relationships and improve doctors' abilities to perform better surgeries.

Could you elaborate on how these advancements will help the field of regenerative medicine, particularly for patients with severe burns or scars?

Stem cells are a significant innovation in plastic surgery. They have the ability to regenerate themselves and differentiate into many cell types. Stem cells can be found in places like the placenta, blood, bone marrow, and adipose tissue. We often use fat, which contains stem cells, from liposuction procedures. Instead of discarding the fat, we now use it for its regenerative properties. Stem cells produce collagen and elastin, thicken the dermis, and improve blood flow, aiding in skin rejuvenation, hair loss treatment, wound healing, and scar reduction.

How do 3D printing and bioprinting technologies play a role in personalized treatment plans for plastic surgery patients?

3D printing is crucial for producing custom-made implants and surgical applications. We use it for facial reconstruction, tissue regeneration, and creating implants tailored to a patient's anatomical needs based on their CT images. This technology is improving and becoming more widely used, despite some ethical dilemmas.

Can you share insights on the use of nanotechnology in plastic surgery for targeted drug delivery or tissue regeneration?

Nanotechnology plays a role at the molecular level, with applications like stem cells being considered a nanotechnology product. Although we use these innovations, much of the fundamental research happens in laboratory branches like physiology, biochemistry, and genetics. We apply the findings from these studies to clinical practice.

What are some emerging trends in non-invasive cosmetic procedures?

Exosomes are a significant advancement. They are nanovesicles that facilitate cell communication and regeneration. Unlike stem cells, exosomes don't require a donor area and are produced in a lab. They help in wound healing, hair regeneration, and anti-aging, representing the future of non-invasive treatments in plastic surgery.

The focus is shifting towards biological treatments that use the body's own products for more permanent solutions.

The medical field is moving towards non-invasive approaches. Preventing issues is easier than treating them. While surgeries are sometimes necessary, non-invasive treatments can prevent problems like wrinkles, making them valuable.

Do you have any advice for students who would like to pursue a career in plastic surgery?

Work hard and stay curious. Be interested in different fields, have a good command of foreign languages to keep up with international developments, and attend important conferences. Embrace new technologies like VR and AI, and cultivate hobbies like art and sculpting to enhance your creative thinking. Studying hard and staying informed will open all doors in plastic surgery.

Interview with Prof. Dr. Uğur Sezerman

Since your background is in electrical engineering, why did you choose to work in the field of medicine? What made you transition from computer science to bioinformatics?

I studied electrical engineering as an undergraduate. The reason I studied it is that I was a good student. I had high marks and the highest-scoring department that you could go into after the university entrance exam was the electrical engineering department of Bosphorus University. I didn't want to waste my score. I wanted to undertake the best degree. I didn't even question whether it fits me as a person or as a job. As a result, as soon as I started, I didn't like it. I wanted to do something close to people; I am a more social person. I like doing things for people, but in electrical engineering, you develop circuits, write algorithms, etc., but it's not tied to people much. That's why I didn't like it. But I was a good student, and I got good grades.

For my graduate program, I have decided to change it. I switched to biomedical engineering, where I designed devices for accelerating the healing process of bone fractures using electromagnetic fields. It was still electrical engineering but applied to human research.

And still, that was not enough for me!

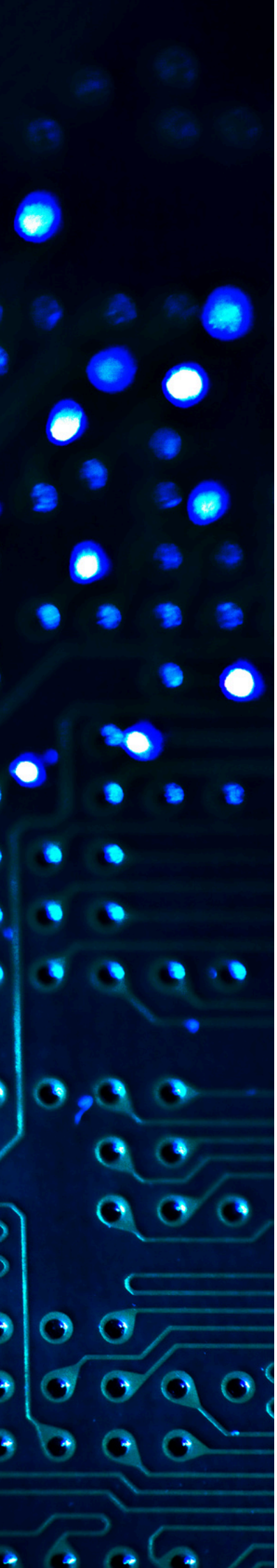
Begüm Yılmaz
Content Creator

I did my PhD at Boston University with the person who initiated the Human Genome Project (HGP), Professor Charles DeLisi. He said that we need engineers, we need computer scientists, and people from different disciplines to analyze the data coming from the HGP to turn it into valuable information for diagnostics and therapeutics. They needed people with an analytical way of thinking to approach the data analytically, find new solutions, and add more value to the data generated from the HGP. I was quite intrigued by this, and I switched my field to bioinformatics. We were one of the first bioinformaticians!

I started to work on analyzing the sequencing data. This could be any kind of sequencing application and building models, artificial intelligence models, or machine learning models for interpreting this data and using it for therapeutic or diagnostic purposes. That has made me switch my field, and I'm quite happy. The reason why I'm in medical school is because I want future doctors to learn these subjects. In the classical way of medicine, there is a lot of memorization and you don't use your analytical sight much. You memorize a lot, unfortunately. But there is a lot of data coming in with “omics” technologies. You have next-generation sequencing data, proteomics data, metabolomics data, microbiome data, and lipidomics data. Lots of “omics” data are coming in, and future doctors should learn what they mean, and how they can use it in their diagnostics and therapy decisions.

All around the world, the best students go to medical schools, which means they have the intelligence capacity and the analytical ability, but they don't use it to the full extent. That's why I positioned myself in the medical school to give this opportunity to students so that they can learn programming algorithms. All these “omics” technologies have to incorporate this in their decision-making criteria.

Therefore, they are learning lots of subjects on this topic. And they are doing lots of hands-on projects as well. I think they will be the doctors of the future, where they can incorporate such multi-omic data in their decision-making criteria.



Could you talk about your involvement in the HGP and how such an incredible project changed the course of humanity over the past 20 years?

One genome project took years to conclude. The goal was to obtain the human genome of the whole, almost 3 billion letters, and then interpret it afterwards. Once we have the genome, it's not resolved, then you have to find where the genes are. Then one has to find the protein sequences; you have to understand and interpret the mutations in the genes. What do they mean? How does this reflect the protein sequence? What's the impact of those mutations? Are they pathogenic mutations, benevolent mutations, or accepted mutations? And can it explain the disease phenotypes of the individual? There are many challenges that one has to solve once one gets the genome and the exome. An exome is a shorter version of a genome; only the exomic regions are sequenced. How to interpret this data and how to turn it into a form where you can use it for diagnostics and therapy decisions.

There were many challenges involved in the HGP involving obtaining the human genome from the sequencing technology. It's called a “fragment assembly problem". There were short sequences because they could sequence up to 1500 long sequences, and they broke the genome down into smaller pieces. Then they had to bring those pieces together to get the whole genome.

Many computational methods are used in this. Most of them are like the traveling salesman problem, which is a common problem in the computer science domain, where you find a solution that contains all the fragments that are sequenced with the maximum confidence, that you are sure of the sequence that you are getting and of the order of the fragments that you obtain.

Many non-computational algorithms are adapted for the Human Genome Project. But there were other challenges. As I said, you had to find the genes. To find the genes you look for certain signal motifs. One of the common motifs is the promoter sequence, “TATA box” was one of them. But there are other promoter sequences as well. Then they saw that that was not efficient enough to explain the regulation of the transcription as there were other mechanisms at play. Then they found out about epigenetic mechanisms and methylation, and other epigenetic mechanisms that play a key role in transcription regulation, the post-translational modifications after the protein synthesis. How it's activated, what's phosphorylation, acetylation, methylation and what's ubiquitination? Various post-translational modifications take place at the DNA level and protein level. What are “the rules” that are conducting these things; are there any motifs? Motif-finding algorithms are the next steps for bioinformatics, and then with the advancement of technology, we got transcriptome data.

We know how many transcripts are there, we can count them, and then we can tie it to the disease mechanisms by controlling the disease and individuals and finding the differences, for example, certain genes are overexpressed in certain cancer patients, and some of those genes are oncogenes. Oncogenes have a specific function - they are normal genes. But after a certain mutation, they become constitutively active. Then they turn into an oncogene. They have a normal function, which is required for the body. But after certain mutations and changes, these genes are overexpressed, and they turn into oncogenes, causing uncontrollable growth. And there are tumor suppressor genes, that's the check system. If the cell is growing too much, then the suppressor gene turns on. The tumor suppressor genes initiate the mechanisms that cause the cell to undergo apoptosis so that you don't have the overgrowth of the cell. All these mechanisms are mostly found as a result of computational approaches, mostly.

There were also other experimental methodologies with the advancements in sequencing technologies and other “omics” technologies. We started to get lots of data about all kinds of omics. Each of these "omics" shows us different aspects of that individual's health status. The goal is to combine all of them to have a snapshot of that person's health. And then what problems are, what are the mechanisms that are involved? And how you can stop that overgrowth signal, for example. And that's personalized medicine. And that's the field that I'm working in today.

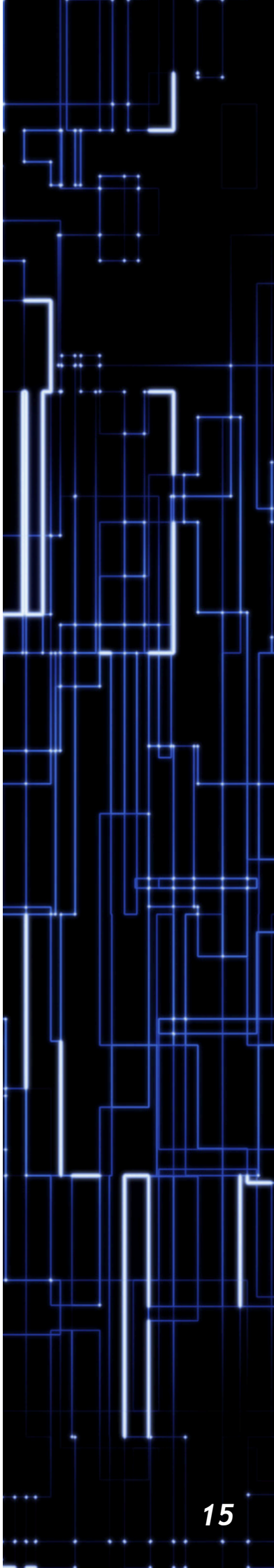
With the rise of artificial intelligence and machine learning, the general population might be scared of these changes and how they will affect doctor-patient interactions. What are your thoughts on how the future will look like with these technologies?

There's nothing to be afraid of, in terms of AI, for example, that robots will control us, or they are going to take over. And of course, with this big amount of data coming in - “omics” data, the human mind is not sufficient enough to understand the intricate relationship between these different omics data, the phenotype, and the medical data.

We have variable sensors everywhere. We are being traced by every device. It's impossible to integrate all of them and understand the health status of the individual by the human mind. But if you train the computers, they can understand this intricate relationship.

For example, you're consuming too much meat. Because of meat consumption, the microbiome and bacteria data levels are very high, which means there's a good association between meat consumption and bacteria data. This causes these metabolites to increase, and we see that in your metabolic data that triggers this event, and that causes an increase in your creatinine levels, for example. You can get this kind of reasoning and intricate relationships from this model and understand the causality, and then once you know the causality of your symptoms, your measurements, and if you know the cause of it, then you can intervene, and you can change your lifestyle.

For example, you can lower your meat consumption, or you can increase your fermented food intake. You need certain types of bacteria to increase so that they can auto-regulate your immune system.



There are many intricate relationships we know very little about. But all these relationships can be deduced as part of the models. AI can do machine learning but as I said, it has to be controlled by people because the input data is provided by people. This data has to be annotated and corrected. The phenotype should be correct. Otherwise, we have a saying "Garbage in, garbage out". So if you tell a control person a cancer patient by mistake, if the notation is wrong, it will try to predict that person as a cancer patient, and that will tweak the model, and it will be a wrong model as a result, so it will be garbage as a result. The data should be checked carefully. We have to be sure of the annotation, phenotyping information, and all the other types of information.

It will not replace the human; it will not replace the doctor. It will give recommendations to the doctor, the doctor will make the final decision, and it will say: "I think this person has such and such disease because of such and such changes." look at a person with this much microbiome change to this bacteria in the past 20 examples show this kind of symptoms. And the person with this much change in the Creatinine level and having lots of meat consumption had these kinds of symptoms. And because of those reasons, I think this person has this disease. The best treatment is this because 98% of the people in the past responded to this treatment, showing similar symptoms. That is a lot of information for the doctor. It will reduce to a minimum the amount of mistakes made in the diagnostics and the therapy decisions. But the final decision will depend on the doctor. So we are seeing not artificial AI - but augmented.

Augmented intelligence is artificial intelligence. Models give you the reasoning and some predictions, and you bring it all together and make the best decision for your patients. I think that's the way I see the future of medicine. But you need this information, as you cannot process it on your own. With so much data coming in as a physician, you cannot process it on your own.

There is one aspect of your lectures that particularly draws my attention. You come with a smiling face, and you love to present the lectures. And it's obvious that you love your job and your work field. What is the secret?

I like touching people's lives. And I think I'm doing the right thing, educating future doctors in the right way. I think this is the way it should be all over the world. I believe you guys will be the first examples where bioinformatics, omics, and AI are integrated into medical education. And with your success, I think many other countries will change their curriculum, and we'll take these subjects into their curriculum as well because it's going to make a difference when they make the right decisions early on and apply the correct therapy early on.

I believe if you do something that you strongly believe in, you will enjoy it. I enjoy seeing bright and smiley faces, students hungry to absorb more information and more knowledge. And that always stimulates the teacher as well. I enjoy it when you enjoy it!

You asked me questions, you participated in the lecture, and that has made me even happier and more enthusiastic about teaching. So that's why and I also believe in what I do, that this is the future of medicine.

I think it's going to make a difference. And with your upbringing and your knowledge, you're going to make a difference in patients' lives. And you're going to pass this information on to others as well. So I think it's going to propagate everywhere. And in the end, we are all here to make a difference.

If I can touch ten people, that's a big difference for me. And if I can contribute to making the right decision for patients, the right diagnostics, the right therapy, that makes me a very, very happy person.

These are the things that drive me most of the time. That's why I'm a very happy person.

Do you have any advice for students who would like to pursue bioinformatics or a career in research?

Yes, learn programming. There is easy programming, and there are many online courses and resources for programming. Start with R which is very good for bioinformatics data that has been in libraries and resources, it's easy to learn. And there are many online courses on “Coursera”, you can attend and try to take as many courses as possible on these topics.

It's a very wide field, and there are new concepts coming in all the time, the things I was teaching five years ago, and now teaching completely different things. It's very exciting to be in such a good field because there's always new data, and a new dimension coming in. It's never a dull moment, you always have some excitement going on. So then I think, even though you're gonna be a doctor, but be a doctor with a different point of view, try to look at the individual from different perspectives.

I think we should go back to the soul of medicine. There is no disease, there is the patient, and every patient is different from each other. So you cannot generalize everyone. Every breast cancer patient has their own way of driving the cancer mechanism. That should be taken into account and understood, and then a proper treatment should be provided to that patient. All these approaches can be gathered by studying bioinformatics, algorithms, and omics data.

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THEME ARTICLES

Harnessing the Power of siRNA: Advances and Challenges in Therapeutic Development

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Medical science has made significant advancements in gene therapy, by transferring genetic material to patients for disease treatment. In 1990, the first clinical study involving a rare immunodeficiency disorder commenced, despite decades of discussion in the scientific community. Thousands of clinical studies have been initiated since then, which indicates rapid growth in the field. Studies on these topics range from addressing monogenic diseases to tackling infectious diseases, complex neurodegenerative disorders, and even cancer. [1]

The categorization of gene therapy involves multiple factors, such as the kind of disease (genetic or acquired), the nature of gene delivery vehicles (integrating or nonintegrating), and the mode of administration (in vivo or ex vivo). The main goal of augmentation gene therapy, generally known as sustained expression of the transferred gene at therapeutic levels, is to treat hereditary disorders. A functioning copy of a mutant gene is usually what is transmitted. As an alternative, genome editing, or RNA interference techniques can be used to reduce harmful gene expression. Although the use of genome editing techniques to fix faulty genes is still speculative, it has potential use in clinical trials down the road. [2]

REFERENCES

The selection of vectors is crucial when considering in vivo versus ex vivo gene therapy. To introduce genetic material into stem cells and ensure stable integration into the genome for transmission to daughter cells during division, vector integration is essential. On the other hand, because they can maintain long-term gene expression, vectors such as adeno-associated viral vectors are favoured in long-lived postmitotic cells that are the aim of in vivo gene therapy. For ex vivo gene transfer into hematopoietic and other stem cells, lentiviral vectors are preferred. [3]

Gene expression can be corrected, enhanced, or decreased by introducing particular nucleic acid molecules into the patient's targeted tissue. To limit gene activity, molecules like inhibitory antisense oligonucleotides (ASOs), microRNA (miRNA), piwi-interacting RNAs (piRNAs), and small interfering RNA (siRNA) are frequently employed. However, to increase or correct the target gene's expression, plasmid DNA, messenger RNA (mRNA), small activating RNA (saRNA), splicing modulatory ASOs, and CRISPR/Cas systems are usually used. [4-6]

Three primary types of small RNAs with different biological activities have emerged: piRNAs, siRNAs, and miRNAs. Double-stranded RNA (dsRNA) initiates RNA interference (RNAi), a novel mechanism that silences genes by breaking down complementing mRNA. RNAi has revolutionised gene function research and treatment techniques. While there are still obstacles in the way of creating effective delivery methods, siRNAs hold great promise as nucleic acid medications for the treatment of diseases such as cancer. This restriction impedes the therapeutic implementation of siRNA, despite its great potential. [7]

On the other hand, the identification of RNAi offers chances to bring new treatment modalities into clinical settings. Numerous diseases are associated with disruptions in RNAi pathways, indicating a major change in the way cellular networks are managed. [7]

First, larger dsRNA is processed and cleaved into shorter segments called siRNAs in the RNAi pathway. A 2-nucleotide overhang usually appears on the 3′ end of each strand of these siRNAs. One enzyme that does this processing work is called Dicer, and it works similarly to an RNase III-like enzyme. After siRNAs are produced, they attach to a group of proteins known as the RNA-induced silencing complex (RISC). The siRNA strands separate within the RISC complex, and the strand with the more stable 5′-end typically integrates into the active RISC complex. The antisense single-stranded siRNA part then moves the RISC complex in the direction of and aligns it with the target mRNA. The mRNA is cleaved under the catalytic activity of a RISC protein, usually an argonaute family member (like Ago2). [7]

A natural defence mechanism against the introduction of foreign genes is RNA interference, or RNAi. By preventing mRNA translation in the case of miRNA and triggering targeted mRNA degradation in the case of siRNA and miRNA, respectively, RNA interference methods such as these can selectively lower the expression of target genes. A single miRNA can affect the expression of several target genes at once, even though siRNA is typically more efficient and selective at silencing genes than miRNA. As a result, in pharmaceutical applications, siRNA and miRNA have different functions. [8]

siRNA therapies have advanced significantly since the RNAi idea was introduced in 1998. Research on the topic exploded in 2001 after Tuschl et al. used chemically synthesised siRNA to successfully mute particular gene expression in mammalian cells. Although stability, specificity, and distribution remain obstacles, recent developments in chemical modification and delivery techniques have brought new life to the area. As the first commercial RNAi-based treatment for treating adult patients with familial amyloidogenic transthyretin amyloidosis with polyneuropathy, ONPATTRO®'s approval in 2018 was a significant milestone. The FDA subsequently approved GIVLAARITM to treat acute hepatic porphyria. [9]

Because siRNA can bind to mRNA accurately, it has intrinsic benefits over monoclonal antibodies and small molecule therapies. By choosing the right nucleotide sequence along the target mRNA, siRNA can potentially target any gene, whereas small molecule and antibody medications are dependent on identifying intricate protein structures. However, stability problems, off-target effects, and immune system activation pose challenges for siRNA in clinical applications, despite its encouraging potential. [10]

Scholars have investigated diverse chemical changes and delivery mechanisms to optimise the therapeutic efficiency of siRNA while mitigating associated adverse effects. This entails assessing patterns of alteration and creating delivery systems made of polymers, peptides, lipids, lipoid-like materials, exosomes, and inorganic nanoparticles. There are continuous efforts to advance siRNA therapies, as seen by the progression of several alteration patterns and delivery systems to clinical investigations. [9]

Compared to small compounds, monoclonal antibodies, and proteins, siRNA's method of action enables it to target almost all disease-related genes of interest, allowing for a shorter timeframe for medication research and development. Excellent phase 3 data from InclisiranTM clinical studies highlight the potential for siRNA therapy to soon reach another milestone by treating common disorders like dyslipidaemia, following the successful commercialization of ONPATTRO® and GIVLAARI™ for uncommon diseases. [9]

In summary, gene therapy has advanced the treatment of many diseases by allowing patients to receive genetic material. With thousands of clinical investigations conducted since its founding in 1990, its scope has expanded to include a wide range of ailments. Innovative delivery methods, particularly those that make use of siRNA, and augmentation gene therapy hold promise for focused medical intervention. Notwithstanding several obstacles, such as stability problems, siRNA therapies have the potential to revolutionise medical care, and their recent results are opening new avenues for research and development.

Unveiling the Frontier of Innovative Medicine: Shaping Healthcare with Innovation

Bibek Shrestha

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REFERENCES

Introduction

Innovation is a primer for quality improvement practitioners and physician leaders who play a key role in creating innovation and environments for innovations to flourish. [1] Innovative medicine revolves around different topics such as transformative technology, digital health, and novel approaches that redefines the boundaries of existing medicine. The main motive of Innovative medicine is to revolutionize the diagnostic care, which helps in the upliftment of the patients' care. Medicine is one area that definitely needs to be modernized. Health care is chaotic, inefficient, and frequently ineffective; it is desperate for innovation. Medicine and innovation go hand in hand. Medical technology innovation is poised to explode in the modern era. The health care delivery system will undergo a fundamental transformation in the coming years due to advancements in medical technology. [2] In this article, we will go through the different domains of Innovative medicine, know the latest trend, breakthrough and their use in the future.

Discussion

The science of identifying, treating, or avoiding illness and harm to the body or mind is what is known as medicine. [3] Change is required because our society depends on the upcoming generation of doctors to be innovative and tech-savvy. In order to start developing standards for the responsible use of technology, medicine must accept and embrace modernization given the growing frequency of portable electronic devices in daily life and the rise of social media. [2] The development of the artificial heart was one of the greatest technological advances in medical history. The earliest known patent for an artificial heart was obtained by Dr. Paul Winchell in the middle of the 1950s. [3] There are different domains of Innovative medicine which includes Precision Medicine, Digital Health and Telemedicine, Artificial Intelligence and Machine learning in Health care, Regenerative Medicine.

Precision Medicine

Precision medicine aims to optimize healthcare quality by tailoring the medical procedure to each patient's particular, constantly changing state of health. This project encompasses many scientific fields, including as medication development, genetics and genomics, health communication, and causation inference all in favor of data-driven, or evidence-based, decision making. [4] This facet of medicine states paradigm shift in health care which involves genomic insight, molecular diagnostic methods, and different statistical and analytical methods to personalize treatment methods. This medicine has the potential to increase the therapeutic efficacy with minimizing the adverse and side effects. Some of the examples are; Hemophilia can now be treated using recombinant biologic medicines as replacement therapy. Additionally, electronic health records have produced a comprehensive and easily available library of clinical data that can be utilized for clinical care guidelines and research. Perhaps the most significant effects are being seen in gene therapy, genetics, and next-generation DNA sequencing techniques; they will continue to progress as costs come down. [5]

Digital Health and Telemedicine

Digital health is the use of information and communication technologies in medicine and other health professions to manage illnesses, health hazards, and promote wellbeing. [6] Telemedicine is derived from the Latin "medicus" and Greek "tele," which literally means "healing at a distance." [7] The integration of digital health technologies and telemedicine platforms is transforming the healthcare environment by enabling remote consultations, monitoring, and patient interaction. It has provided improved access to health care, reduced any inefficiencies in the health care system, improved the quality of care, lowered the cost of healthcare, and provided more personalized health care for patients. There has been some research which shows that the use of digital medicine has made them able to better track their own health and wellness such as smartphone, blood pressure monitoring devices. People's definitions of digital health vary. Here are the major subcategories: Remote sensing and wearables, Telemedicine and Health Information Data analytics, intelligence, and predictive modeling, Tools for modifying health and wellness behaviors, Bioinformatics Tools (-omics), Medical social media, Digitized health record platforms, Patient-physician-patient portals, DIY diagnosis, compliance, and therapies, Decision-support systems Imaging. [7]

Artificial Intelligence and Machine learning in Health care

In the field of medicine, treatment and diagnosis should be given properly and on time. If there is a slight delay in the diagnosis, then that can be fatal for some people. For this, there have been developments of different technologies which help in diagnosis and treatment. The application of AI can be divided into three broad areas. The first is the early detection and prediction of a medical issue. The second step is to treat the disease, and the third is to evaluate and anticipate the outcomes. [8] Artificial intelligence has been utilized for the diagnosis of stroke in which movement detecting equipment was developed for the prediction of stroke in patients. Through machine learning as well, patients can be categorized into high risk and non risk with the help of the Markov model. [9]

Regenerative Medicine

Advances in regenerative medicine, such as stem cell therapy and tissue engineering, hold the promise of repairing or replacing damaged tissues and organs, potentially transforming treatment of degenerative diseases and accidents. Regenerative medicine offers the ability to address the issue of a scarcity of organs available for donation relative to the number of people who require life-saving organ transplantation. [10] Regenerative medicine is an interdisciplinary field that promotes regeneration by applying engineering and life science principles. Regenerative medicine promotes the treatment of chronic diseases and acute injuries. [11] Cell treatments (the injection of stem cells or progenitor cells), immunomodulation therapy (regeneration by biologically active chemicals supplied alone or as secretions by infused cells), and tissue engineering (the transplantation of laboratory-grown organs and tissues) are some examples. While the latter word encompasses a wide range of applications, it is most commonly linked with procedures that repair or replace sections or entire tissues (for example, bone, cartilage, blood vessels, bladder, and skin). [12]

Challenges and Opportunities

While the potential benefits of transformative medicine are great, there are some issues to overcome. These include legal challenges, ethical concerns, and fair access to new treatments and technologies. But by collaborating and advocating for policies that promote health care innovation, we can overcome these barriers and fully realize the potential of new medicine to improve patient care.

Conclusion

Medical innovation is not a luxury, but a necessity for our efforts to solve the health problems of the 21st century. As medical students, we need to embrace the concept of medical innovation, stay on top of new developments, and actively contribute to the advancement of medical science. By doing so, we can help shape the future of healthcare and improve the lives of people.

Illuminating New Paths in Cancer Treatment with Oncolytic Viral Treatment

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The accumulation of genetic and epigenetic changes that result in antigens specific to cancer characterises the intricate process of carcinogenesis. These antigens are broken down by antigen-presenting cells (APCs), such as dendritic cells, and then presented to T lymphocytes in lymph nodes. T-cell activation and proliferation require antigen stimulation and costimulation signalling, which are typically facilitated by molecules like CD28. Cytotoxic lymphocytes (CTLs) are introduced to the tumour after priming and employ direct contact to kill cancer cells. [1,2]

However, because factors like hypoxia, acidity, and immunological suppression impair immune cell activity, the tumour microenvironment (TME) presents challenges for cancer immunotherapy. The TME is composed of several cell types, including tumour cells, stem cells, and immune cells such as T-cells and macrophages. Immune checkpoint molecules obstructing CTL function further complicate the treatment process. [3,4]

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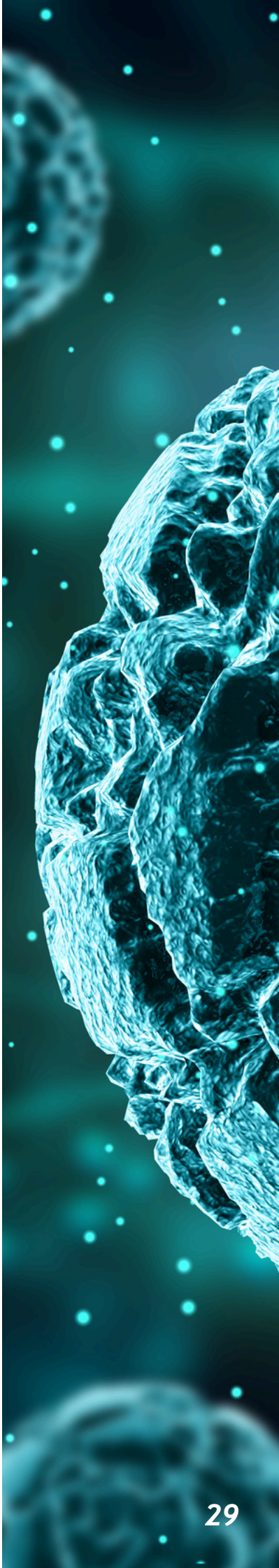
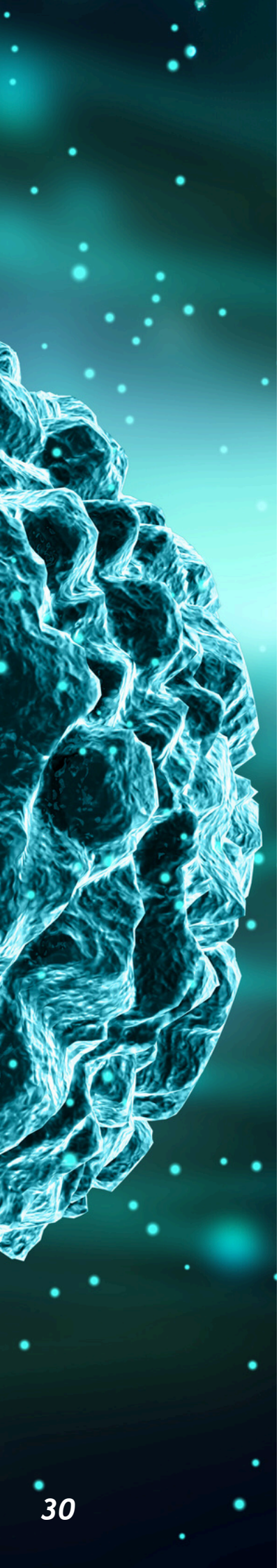
A few strategies utilised in cancer immunotherapy to increase T-cell activity are immune checkpoint inhibitor medications, cancer vaccines, and adoptive cell therapies. Despite these advancements, immunotherapies are often not well received by patients for two main reasons:
immune system suppression and limited T-cell activation. [5]

There has been research on the possibility of using some viruses as potential cancer treatment agents since they have been altered to specifically infect and kill tumour cells. These oncolytic viruses (OVs) have shown promise in immune activation against tumours and TME regulation. Many OVs have been granted licences for use in cancer treatment, and ongoing research is investigating their potential to enhance antitumor immunity in conjunction with other immunotherapies. [6]

Oncolytic viral treatment (OVT) is a unique form of immunotherapy that targets and kills cancer cells while sparing healthy cells. It works by using naturally occurring or genetically produced viruses. Over the years, OVT's progress has reached many significant turning points. [7,8]

Natural viruses were investigated as a possible cancer treatment in the early 1900s; after contracting a virus, some patients had a brief remission of their tumours. By the 1950s and 60s, OVs could be tested in vivo on patients thanks to developments in cell and tissue culture techniques, which produced encouraging outcomes. When viral serotypes in patients with cervical carcinomas were investigated in 1950, significant tumour necrosis was found. [9] The development of virotherapy was significantly aided by using biotechnology to genetically alter viruses. Martuza et al. found the first herpes simplex virus-1 thymidine kinase-negative mutant in 1991, and it caused animals with gliomas to live longer. Oncolytic viruses, such as ONYX-015, an attenuated adenovirus that cytolyzes tumours selectively, were created because of further modifications intended to increase safety and tumour selectivity. [6]





In 2004, Latvia approved RigvirTM, the first oncolytic virus to be used in the treatment of melanoma. Subsequently, oncolytic adenovirus H101 became the first OV approved for the treatment of head and neck cancer in China in 2005. The engineering of OVs with transgenes led to more advancements, such as T-VEC which encodes the human granulocyte-macrophage colony-stimulating factor (GM-CSF). When the US FDA authorised T-VEC in 2015 to treat melanoma, OVT received a lot of attention. [6] The list of authorised OVs was further expanded in 2021 when DelytactTM, a modified herpes simplex virus, was licenced in Japan for the treatment of malignant gliomas. Numerous viruses, such as the measles virus, herpes simplex virus, adenovirus, and others, are still being investigated as possible OVs, opening new possibilities for OVT-based cancer treatment. [6]

Antiviral defence mechanisms in tumour cells are frequently aberrant, which permits viruses to live and multiply there. There are two types of OVs: naturally occurring and genetically modified. Genetically altered OVs are designed to specifically target the compromised antiviral pathways found in tumour cells. This allows them to infect, multiply, and kill cancer cells while avoiding damage to healthy cells. By releasing infectious OVs from lysed tumour cells, this targeted method increases the therapeutic efficacy of the OVs by spreading their oncolytic activity to nearby uninfected tumour cells. According to recent research, exosomes originating from tumours that are released following infection contribute to the enhancement of anticancer efficacy. The OV is present in these tumour-derived extracellular vesicles, which also have a strong affinity for tumour cells and initiate the antitumor response. [10,11]

Upon injection, OVs reveal pathogen-associated molecular patterns (PAMPs), to the host immune system. Numerous forms of immunogenic cell death, such as immunogenic apoptosis, necroptosis, and pyroptosis, are triggered by these PAMPs. Viral capsids, DNAs, RNAs, and proteins are examples of these PAMPs. Heat shock proteins, ATP, and high mobility group box 1 protein are among the immunostimulatory damage-associated molecular patterns (DAMPs) that are released when endoplasmic reticulum stress is induced. [6]

Pattern recognition receptors (PRRs) on immune cells detect these PAMPs and DAMPs. PRRs include stimulators of IFN genes (STING), Toll-like receptor (TLR) adaptor molecule 1, and TLR3. Consequently, they generate chemokines such as CCL2, CCL3, and CXCL10, as well as cytokines such as type I IFNs, interleukins, and TNF-α, which initiate a proinflammatory environment. Through this process, "cold" tumours become "hot" tumours, creating an environment that is friendly to the immune system. [6]

Chemokines like CCL3 and CXCL10 attract neutrophils and macrophages to the infection site, where they initiate a potent antitumor response. Moreover, PAMPs that bind to the virus-recognizing receptors on natural killer (NK) cells induce an early influx of NK cells, which can eliminate virus-infected cells and trigger the production of TNF-α and IFN-γ, which in turn activates T cells, DCs, and macrophages. This sequence of events reinforces the initial innate immune response and aids in the activation of adaptive antitumor immunity. [12]

Tumour-specific T-cell activation is the primary mechanism via which the adaptive immune response against tumour cells is mediated after OV infection. Three signals from APCs are needed for this process: costimulation, cytokine signalling, and antigen presentation through major histocompatibility complex (MHC) molecules. [6] Tumour-associated antigens and neoantigens (TAAs and TANs) are released when OV-induced oncolysis of tumour cells occurs. These antigens are processed by APCs to create antigen epitopes, which are then presented on the surface of the APC together with MHC molecules. After exposure to OVs, type I interferons boost the production of MHC class I and II molecules on the surface of DCs in the cytokine milieu, along with costimulatory molecules such as CD40, CD80, and CD86. [13]

OVs have been demonstrated in multiple studies to activate costimulatory molecules and molecules connected to the MHC class I pathway. Furthermore, OV-infected cells' and mature APCs' production of cytokines and chemokines aids in the recruitment and reactivation of T cells. Activated antitumor CD8+ T cells and B lymphocytes can eliminate distant or newly transplanted cancers without requiring OV. They also promote tumour regression. [14]

OVs, including herpes simplex virus-1 (HSV-1), vesicular stomatitis virus, measles virus, and oncolytic adenovirus (OAd), are known to elicit effective and specific T-cell immunity, which is then used to combat tumours in an antigen-specific manner. [6]

A large amount of the solid tumour mass is composed of an extracellular matrix, a noncellular substance produced by activated cancer-associated fibroblasts (CAFs). The high concentration of hyaluronan, collagen, and proteoglycan surrounds the cancer cells, creating a strong, dense barrier that prevents OVs from effectively entering the tumour. [15,16] Studies have demonstrated that interactions between antigen-presenting factors and cancer cells can enhance the therapeutic efficacy of OVs-based therapy. While transforming growth factor-beta 1 generated by cancer cells enhances OV infection of CAFs, large levels of fibroblast growth factor 2 render tumour cells more susceptible to viral infection. Moreover, OAd has demonstrated efficacy in addressing glioblastoma cells and stromal fibroblasts associated with glioblastoma. [17, 18] Viral endothelial cells (VECs) are infected and lysed by OVs, which impacts tumour blood vessels. Vascular endothelial growth factor promotes viral infection in the tumor's blood arteries while suppressing the immune system's ability to fight back, so allowing the virus to multiply inside the bulk of the tumour. Modified OVs have been demonstrated to be able to completely destroy systemic malignancies in clinical settings by precisely targeting and disrupting the existing blood arteries in the tumour. [19,20] OVs are a promising new therapeutic option for the treatment of cancer since they effectively target and destroy tumour cells. To improve their selectivity and effectiveness, a variety of strategies have been devised. [21, 22]

One approach to improve the tumor-specificity of OVs is through genetic modifications. Viral replication is maintained through the downregulation of proapoptotic pathways, virulence gene deletion, or alteration of viral components. For example, the HSV-1 T-VEC was altered by deleting non-essential viral genes. As a result, the presentation of antigen infected cells was suppressed and tumor-specific lysis was enhanced. Similarly, the oncolytic adenovirus oncorine was created by deleting the E1B gene, enabling selective replication in tumours devoid of p53. Additionally, essential viral genes, such as those involved in adenoviral replication, have been stimulated to express through the use of promoters specific to tumours. hTERT and HRE are two promoters that enhance the specificity of viral replication in cancer cells. [23] To identify cancer cells, new gene circuits combining tumor-specific promoters and microRNAs (miRNAs) have been created. Through regulation of gene expression, miRNAs can enhance oncolytic selectivity. OVs containing tumour suppressor miRNA effectively halt tumour growth and initiate apoptosis. [24]

In the end, OVT provides a promising new approach to cancer treatment. This therapy is targeting and delivering significant antitumor effects with minimal harm to healthy tissues. Prolonged research and development in this field present an important potential to improve patient outcomes in the ongoing fight against cancer.

Digital Pills

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THE JOURNEY OF DIGITAL PILLS

In this concise article, we will review the topic of digital pills: the most popular ones, what they bring to the table, and **spoiler alert**, what caused their downfall.

What are they?

In the era of everything being ‘’smart’’ and digitized, the term digital pills is understandable from the get-go, and yes, it has something to do with the intake of pills and technology. In a nutshell, they are medications that contain embedded sensors or tracking devices. The sensors are designed to monitor various parameters related to medication intake, such as when the pill is ingested, its absorption rate, and sometimes even physiological responses within the body. [1]
But with technology like this, what are the prospects? Keep reading to know the good, the bad, and the ugly of digital pills.

When did it all start?

The idea of digital pills is not exactly new, in the movie “Fantastic Voyage (1966)” a submarine called Proteus with its crew gets miniaturized and enters the body of a scientist to save him from a blood clot. This might have been the inspiration behind Jerome Schentag’s invention. Jerome Schentag from the University of Buffalo [2] invented the “smart pill” which can be used to load the medication off at a site deemed suitable for the cause. It is particularly helpful in digestive system disorders like Crohn's disease.

However, The first company to get FDA approval on “digital pills” was Proteus Digital Health in 2017. A coincidence in the name do you think?
This is different from Jerome Schentag’s smart pill, which is not used to monitor the medication and does not give any further information about it.

The first digital pill

A Silicon Valley company, Proteus Digital Health (Proteus) developed the technology named “Ingestible Event Marker” (IEM), which helps patients monitor the intake of their prescribed pills, supporting those who don't remember or have simply forgotten if they have taken a pill.
Proteus partnered up with a pharmaceutical company “Otsuka Pharmaceutical Co., Ltd” (Otsuka), using the former's IEM technology and the latter's drug, they created Abilify MyCite®, which is a combination of IEM and the drug aripiprazole.
Abilify MyCite® does not work alone, it works along with a smartphone app developed by Proteus called MyCite® app, a wearable sensor - MyCite® Patch, and a portal for healthcare providers to track the ingestion of prescribed pills. [3]

But why Digital Pills?

Let's go through some statistics:

- Medication errors to occur at home are estimated to be around 2%-33% (Patient Safety Network, 2018)
- Older patients are more likely to be affected by medical errors during medical care because they tend to take more medications than younger adults (Paul & Perkins, 2021).
- As many as 18 million people aged 12 or older may misuse prescription psychotherapeutic drugs every year (NSDUH Data Review, 2015).
- Two million Americans misused prescription pain relievers in 2017 (National Institute on Drug Abuse, 2017). [4]

Digital pills were developed to track the intake and dosage of medications, in other words, to enhance adherence and monitoring.
Adherence to medications has always been a problem in healthcare. Almost half of the non-adherence is intentional, while the other half is because the patient is unaware of or the medication regimen is too complex, and that's where digital pills play their important role.

Non-adherence to antipsychotics has also been a problem, maybe due to negativity, patient unawareness, and stigma. A solution to this problem of non-adherence towards antipsychotic drugs was brought to attention by Abilify MyCite®, which contains the drug aripiprazole, which is used to treat patients with schizophrenia.

So, non-adherence, in other words, is an incorrect intake of medications, and it can cause rehospitalization, worsening conditions, and decreased quality of life. In psychiatric patients, it can cause relapse, suicidal tendencies, and ineffective outcomes.

In cases like these, digital pills can aid a patient in adhering to the preferred medication regimen safely and effectively. It accurately supplies reports to the healthcare provider about the dosage, frequency, missed doses, etc.

It can also be utilized to monitor the use of analgesic drugs. As a result, the inappropriate use of painkillers and extra paperwork with prescriptions can be taken under control.

Another digital health company “Celero Systems” has developed a digital pill that can measure heart rate, breathing patterns, and other vitals. Interestingly, it can detect even cardiac arrhythmias as well as opioid overdose.1000s of people die of opioid overdose in the United States- and most of them die alone. The pill can measure the number of breaths per minute, and if it goes below the limit, it will automatically call out for help, and an antidote can be administered immediately if present. [5]

If it is so good, then what is the problem?

Digital pills were developed to increase medication adherence, but along with this comes a set of problems, such as patient privacy concerns.

Imagine being monitored all the time by a big tech company while you are at home. The thought of all your vitals, medication information, and data all being monitored by someone else other than your healthcare provider, a complete stranger, seems eerie, doesn't it? Increased monitoring may cause the patient to feel a lack of privacy and the constant idea that ‘’I am under watch’’.

The patients may feel that they have lost control of their personal health data as it can be accessed and used by someone else, and they may feel powerless. It's like your social media account or email not being protected by a password, and anyone is welcome to go through it. How would you feel?

The patients are not the only ones feeling watched but also their doctors; it affects both patient and doctor autonomy. The doctors may feel the added pressure of the work they are doing. Additionally, with digital pills the user may feel too confident in the system as well, and hospital visitations may be reduced, which can decrease the quality of patient-doctor relationships.

Another aspect is the cost; digital pills do not come cheap. Abilify MyCite® 2 mg is around $1,799 for a supply of 30 tablets with sensors, whereas the generic aripiprazole drug costs less than $20 per month. Due to this, health insurers, healthcare workers, and patients may not ideally choose this option.

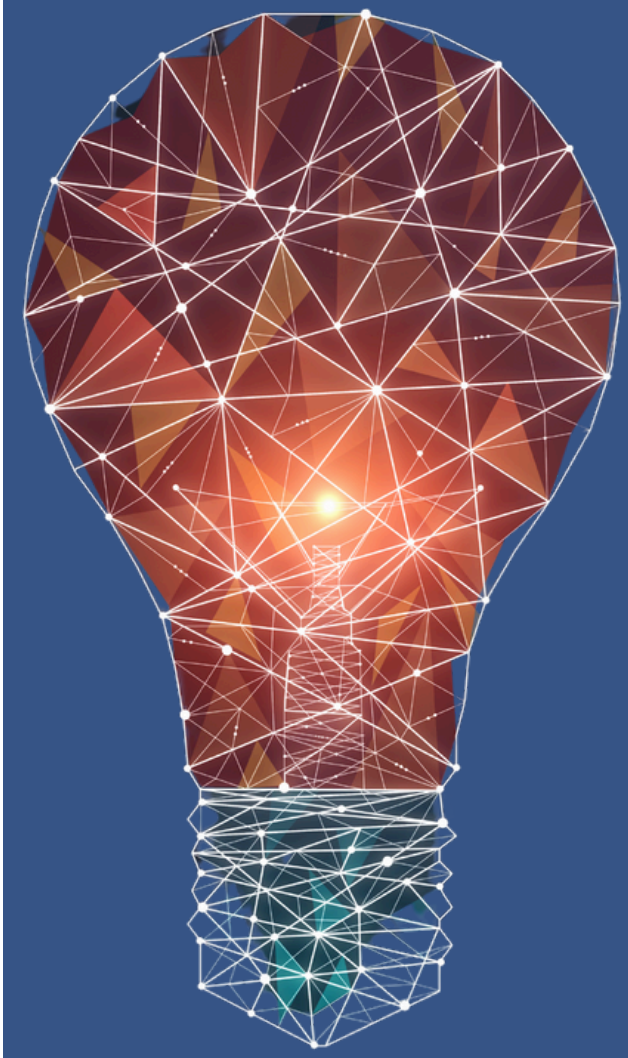
Moreover, taking the example of Abilify MyCite®, which was developed for patients with schizophrenia, it somewhat defeats the purpose as they already suffer from paranoia, and using digital pills with tracking devices makes things worse for them.

The downfall of Proteus

Proteus pioneered in the sector of digital healthcare, but the company filed for bankruptcy. It is definitely not due to their technology, which is considered to be exemplary in the field, but because of many factors, including the ones we have discussed above. They have also failed in product marketing, management, and integration into the current healthcare system. Even though it led to a not-so-happy ending, it should be clear that Proteus paved the way for other companies to develop and explore digital pills that are more compatible for use and also account for the setbacks and drawbacks of Proteus.

Conclusion

Yes, digital pills do come with a lot of problems with patient autonomy, costs, overall effectiveness, etc. However, the technology is promising and has the potential to revolutionize healthcare with advancements in technology like A. We might be able to see it sooner. Resources state that the digital pills market was valued at USD 3.64 billion in 2021 and is expected to reach USD 6.91 billion by 2029, registering a CAGR (Compound annual growth rate) of 8.35 % during the forecast period of 2022 to 2029 [6], which looks promising. In conclusion, the future of digital pills holds a lot of potential in the future of the healthcare sector, even though it might seem a little blurry now.



Artificial Intelligence in Oncology

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Computers that mimic human intellect are the subject of the dynamic field of artificial intelligence (AI). As a branch of AI, machine learning applies statistical and mathematical techniques to improve computer performance. Another subgroup, deep learning (DL), uses multilayered artificial neural networks and has produced notable improvements across several fields. [1,2]

The phrase "deep learning" refers to a collection of methods that, especially in domains like speech recognition and image classification, have significantly surpassed conventional machine learning algorithms. These developments have completely changed industries, including biomedicine, where DL methods have shown exceptional accuracy in diagnosing diseases by analysing radiological or pathological pictures; in many cases, these algorithms have even surpassed the performance of clinical professionals in diagnosing diseases. [3,4]

DL has been particularly effective at identifying conditions such as retinopathy from fundus photos, demonstrating its potential for use in medical imaging analysis. DL is already expanding into drug development in response to growing expectations, to expedite and improve the process of finding viable medicinal molecules. [5,6,7]

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Since DL's revolutionary triumph in the ILSVRC (ImageNet Large Scale Visual Recognition Challenge) in 2012, image analysis has seen a substantial transformation. Early identification of cancer is vital for saving lives. Researchers and doctors are now much more interested in using AI, especially Convolutional Neural Networks (CNN), for applications in clinical radiology and pathology. The benefit is that it can automate feature extraction, which removes the requirement for feature creation by hand. [2,8,9]

One prominent use is in the categorization of dermoscopy images, where AI has shown outstanding area under the curve (AUC) values and precision in labelling skin lesions, including melanoma, that is on par with skilled dermatologists. Like medical specialists, AI has demonstrated promise in reading mammograms for breast cancer screening, achieving accuracy comparable to that of the field. Deep neural networks have also proved successful in detecting abnormalities in computed tomography images, such as colonic polyps or enlarged lymph nodes, expanding the potential uses of AI in radiology. [10]

DL in pathological diagnosis is now possible thanks to the widespread use of whole-slide imaging in industrialised countries, which has aided in the collection of digital pathology images. For example, many algorithms have been developed to detect breast mitosis, identify malignant regions in specimens from prostatectomy, and automatically assign Gleason scores. To identify tumour-infiltrating lymphocytes (TIL), which have been found to have predictive significance across a variety of cancer types, DL methods have also been used. [11]

DL algorithms can also predict gene mutations and transcriptome profiles, among other molecular features of tumours, using pathology data. These developments highlight how adaptable DL is for cancer diagnosis, frequently matching or even exceeding the ability of highly skilled medical professionals. [12]

There are still issues, nevertheless, mainly with standardising histopathology methods to take institutional differences in staining chemicals and protocols into consideration. To standardise image quality and address disparities in feature segmentation, automated tools, and methods, such as CNN-based tools and Generative Adversarial Networks (GANs), are being developed. [13]

The incorporation of DL into histopathological analysis has great potential to improve the precision and effectiveness of cancer diagnosis, which will ultimately lead to better treatment choices. To fully utilise AI in this discipline, more investigation and standardisation work are necessary. [13,14]

Compared to natural picture collections, medical image analysis has a hurdle because of the limited availability of training data, often less than one million images. Researchers use techniques like data augmentation, which expands the size of a dataset by manipulating images, and transfer learning, which repurposes features from models developed on substantial picture datasets like ImageNet, to overcome this. These methods have demonstrated efficacy in diagnosing diabetic retinopathy and melanoma detection. [14]

Progress depends on sharing image data, and as AI becomes more popular in oncology research, more medical image datasets should become available, allowing for the creation of increasingly sophisticated algorithms. [14]

A wealth of genomic information from cancer patients has been made available by the decreasing cost of genome sequencing, which frequently reveals hundreds to tens of thousands of mutations per tumour sample. In genomic medicine, connecting these mutations to specific clinical consequences is still difficult. Clinical interpretation requires the synthesis of enormous volumes of data because it primarily relies on information from scientific and medical literature. Databases such as COSMIC provide a summary of these correlations, but manual curation is not feasible given the approximately 200,000 new articles on cancer published in 2019 alone. Thus, AI has become more and more necessary. [15]

Sequences are converted into binary tables and filtered using convolution before AI is applied to genetic data. Because DL can multitask and integrate many forms of data, it is helpful in the field of cancer genomics. Combining several data sources allows for the analysis of large-scale "omics" data and the identification of genes related to medication susceptibility. DeepVariant and ExPecto are two examples of algorithms that make variant calling easier and connect genetic mutations to disease prediction, respectively. [16]

AI plays an increasingly important role in interpretation as clinical cancer genetic data mounts. Additionally, new biological discoveries can be revealed by machine learning, such as the regulatory function of Fbxw7 in the metabolism of cancer cells. Furthermore, AI predicts RNA splicing accurately, providing possible targets for therapy. A deeper understanding of cancer biology and the prediction of splicing patterns are possible with further breakthroughs in AI. [17]

In the field of medicine, accurate disease diagnosis and the creation of the best treatments are critical to achieving better patient outcomes. Expert pathologists' histological examination and assessment of molecular markers' expression at the protein or mRNA level, such as the PAM50 classification for breast cancer subtypes, are currently considered the gold standards in oncology. Nonetheless, significant variability still exists within these subtypes, highlighting the necessity for a more thorough characterization of illness subtypes to forecast future behaviour and treatment response. [18]

The molecular Prognostic Score (mPS), a measure designed to accurately predict the prognosis of patients with breast cancer, is a recent innovation. Using meta-analysis to combine data from around 6000 breast cancer patients, 184 genes related to prognosis were found, allowing for precise prognosis prediction independent of biological knowledge. Even for individuals with oestrogen receptor-negative breast cancer, this scoring system, which combines a random forest classifier with a neural network, performed better than previous techniques in predicting overall survival, offering important information for treatment choices, and preventing overtreatment. [19]

A digital pathology test that uses samples from the ECOG 2197 clinical trial to predict recurrence risk in breast cancer patients is one attempt to predict recurrence risk from pathological images. Significant hazard ratios for patient stratification are made possible by this AI-driven method. [20]

Precision medicine has benefited greatly from AI, with global contests encouraging the development of new algorithms to handle challenging medical problems. The transformative potential of AI in cancer research and diagnosis is shown by the FDA's recent clearance of clinical medical devices based on DL, including the cloud based Arterys imaging platform and the digital pathology solution PAIGE.AI. Proscia, PathAI, PAIGE.AI, and other startups that use DL algorithms are advancing the field of cancer diagnosis, prognosis, and detection through innovation. [21]

Healthcare digitalization is redefining clinical procedures by moving towards patient-centred, evidence-based medicine, which is being fuelled by advances in AI. Healthcare practitioners and researchers need to develop strong statistical and computational abilities to fully utilise AI in cancer research and therapy; several medical schools have already started offering AI coursework. Nonetheless, issues like the requirement for extensively annotated datasets and the opaque nature of DL models' decision-making process need to be resolved. Notwithstanding these challenges, the growing applications of AI in cancer research point to an impending oncology revolution.

Integrating Artificial Intelligence into Emergency Medicine: Opportunities and Challenges

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Artificial intelligence (AI) is a digital computer software that can learn, reason and execute cognitive functions, including decision-making, and problem-solving through a complex of algorithms and neural networks. In other words, it mimics the human brain. However, the phrase “augmented intelligence” is preferred over “artificial intelligence” by the American Medical Association to emphasize that the role of such technology is to aid and enhance physician skills and not replace them [1]. With that said, in recent years, particularly, post-COVID-19, the push and interest of integrating AI in emergency medicine has risen and is expected to continue. Nevertheless, whilst AI integration promises workflow efficiency enhancements in this field, it also presents significant challenges and ethical considerations that require closer inspection.

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In emergency medicine, overcrowding can result from systemic issues, patient-related factors, and resource constraints. Common causes of overcrowding in the emergency departments are increased patient volume, low staff-to-patient ratio, unnecessary visits, limited bed availability, and boarding of admitted patients. Unfortunately, overcrowding increases the burden on staff. A few examples of such consequences are exhaustive waiting times, exhausted staff, walkouts, increased risk of complications and prolonged hospital stay, decreased patient satisfaction and increased risk of burnout, and medical errors [2]. Consequently, it is not surprising that there is an increased interest in finding ways to improve the efficiency of emergency medicine workflows.

AI offers many potential opportunities in emergency medicine. Firstly, AI algorithms can be used to "data-mine" the electronic medical record database to enable the diagnosis of complicated medical conditions. This means that AI algorithms would be able to analyze vast amounts of medical data, identifying subtle patterns and trends that might be missed by human physicians, and by doing so it can lead to an earlier and more accurate diagnosis, particularly, those that are time-sensitive emergencies like a neutropenic fever [3]. Additionally, AI can help reduce the indirect bias caused by humans during decision-making by providing objective recommendations based on data, a crucial factor in fast-paced emergency departments.

Moreover, the integration of AI technology in emergency medicine can optimize the workflow, resulting in increased efficiency and improved patient outcomes. For instance, autocompletion and vocal AI assistance, can potentially reduce the time spent documenting patient notes, freeing up valuable time for emergency physicians. This allows them to focus on patient interaction and care [4]. AI-powered tools can also assist with emergency department management, including optimizing staff hours, resource allocation, and patient satisfaction by analyzing patient volume and acuity levels. This allows hospitals to distribute resources more effectively, ensuring that critical care is delivered to those who need it the most as well as preventing burnout of healthcare staff.

Despite its potential benefits, challenges remain in the widespread adoption of AI in emergency medicine. A significant concern is the lack of transparency in AI algorithms [5]. Firstly, complex AI recommendations without clear explanations or user-friendly interfaces for clinicians can lead to delays in patient care as doctors grapple to understand the reasoning behind an AI's recommendations, potentially hindering trust and acceptance. Secondly, reward hacking, where programmers optimize AI for specific outcomes rather than patient well-being, can result in unintended patient consequences. To mitigate these issues, clinicians require proper training and education on AI tools to minimise errors stemming from a lack of technological fluency. Additionally, AI algorithms must be designed to account for factors like race, genetics, and gender to avoid biased predictions due to an aggregation bias (focusing on a specific population group) or representation bias (limited data diversity) [6,7]. Moreover, over-reliance on AI and automation bias, the tendency to trust computer-generated results over human judgment, can lead to hesitancy in overriding AI recommendations, potentially compromising patient care [6,8]. Finally, the cost of developing and implementing AI systems in healthcare can also be a significant barrier.

Integrating AI into healthcare creates a complex web of responsibility. Legal frameworks in most countries struggle to assign clear blame when AI-related decisions cause harm. Hospitals have to take responsibility for the choices made by AI systems they use. A possible solution is a "collective responsibility" model where all involved parties (developers, deployers, etc.) share accountability, incentivizing responsible behaviour. Alternatively, some propose a compensation plan funded by stakeholders, regardless of fault [4]. For medical professionals, potential liability depends on factors like the AI's accuracy, adherence to the standard of care, and the practitioner's actions. Traditional malpractice laws may need to adapt to this new paradigm. Uncertainties remain regarding malpractice insurance coverage for AI use and how to defend medical professionals in AI-related lawsuits. These are pressing issues requiring solutions from the legal community.

To ensure the responsible integration of AI in emergency medicine and maximize its benefits, several recommendations are crucial. Firstly, regulations and legislation safeguarding patient confidentiality and privacy are essential. Clinicians must also exercise caution and leverage their expertise to interpret AI-generated information and recommendations. Additionally, healthcare institutions should develop policies promoting best practices for AI use. Finally, regular external audits are vital to monitor the impact of AI technologies and ensure they do not harm patients or specific groups [3].

In conclusion, adopting AI in emergency medicine necessitates meticulous attention to ethical, legal, and technical challenges to optimize its advantages. While AI can streamline cognitive processes, improve patient communication, and drive progress in care, its dependence on vast datasets raises concerns about patient confidentiality. Integrating AI into healthcare demands a shift in entrenched practices while ensuring the trustworthiness and precision of AI guidance. Ultimately, addressing existing gaps and uncertainties through further research is essential for the successful integration and utilization of AI in emergency medicine.

The Future of Healthcare: Personalized Medicine

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Thanks to advances in medical technology, the field of medicine is rapidly improving with each passing day. One of the most promising developments is the rise of personalized medicine, also known as precision medicine. This approach tailors medical treatment to an individual's unique characteristics, allowing for more effective and efficient healthcare. This exciting new era in medicine is leading us towards a brighter and healthier future. However, what exactly is personalized medicine, and how is it used in the medical field? What distinguishes personalized medicine from traditional medicine?

Traditional medicine typically follows a "one size fits all" approach that is based on population averages. Even if two people exhibit the same signs and symptoms of a particular disease, they might still receive an identical medical treatment, despite their many differences [1,2]. This is because traditional medicine fails to account for the fact that each person's genetic makeup is slightly different from everyone else's. As a result, traditional medicine often falls short of its intended goal [3].

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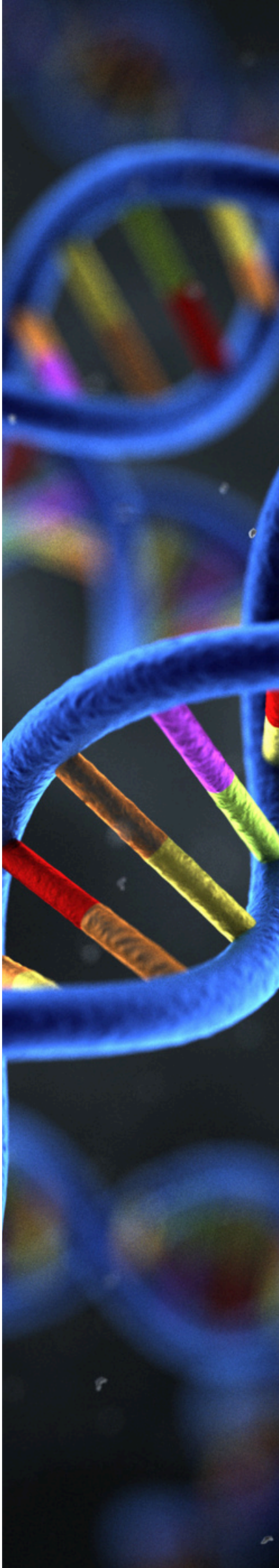
The doctor-patient relationship is crucial for proper diagnosis and treatment in both traditional and modern practice. However, recent advancements in biomedical research have enabled doctors to go beyond the observable signs and symptoms. Personalized medicine combines a wide range of individual data such as the lifestyle of a patient, their clinical history, genetics, and other important information. Consequently, creating more effective treatments and reducing side effects, improving patient outcomes [3,4].

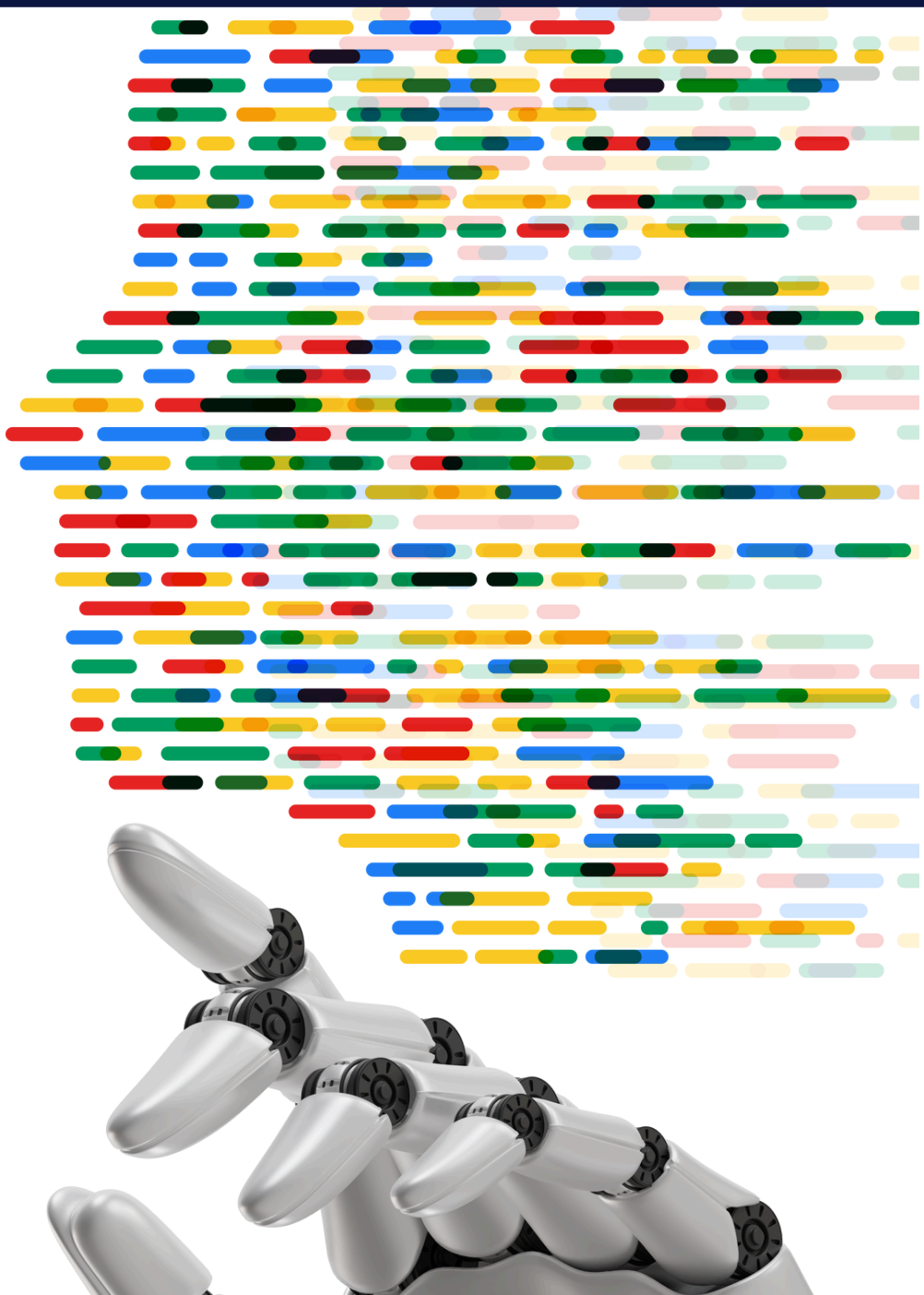
To clarify how personalized medicine uses individual data, we can delve into genomics. Genomics is the study of an organism's entire genome, including organisation, function, and variations. Thanks to advancements in genomics, doctors can now utilise key technologies like genome sequencing and gene editing to analyse a person's genome and predict their susceptibility to diseases, including cancer [5]. This enables them to choose the most effective medications and customise suitable treatment plans, thus optimising patient outcomes. For instance, patients with HER-2 (human epidermal growth factor receptor-2) breast cancer can benefit from targeted therapies by receivingdrugs that are specifically designed to block HER-2 signals. This prevents HER-2 from promoting cancer cell growth and helps in controlling the cancer [6].

We can also integrate data science and artificial intelligence (AI) into personalized medicine. It’s like having a smart and quick assistant that can help you make decisions for each patient. AI models can predict how a disease progresses and the potential reactions of a patient by doing their data analysis that includes their genomic data and medical history etc. AI can also help with drug discoveries and their developments, for example, through patient stratification. By dividing patients into specific groups, AI can calculate the efficiency of a drug according to the similarities or differences of certain patient groups or individuals.[6,7].



However, as much as personalized medicine has many benefits it also has drawbacks, such as data privacy. Since it includes an individual's genetic and clinical data, it must be heavily protected against personal data theft. Also, personalized medicine can create a gap between people who can have access to treatments and people who can not due to the heavy cost of it. This can create challenges for equitable access to personalized medication [8, 9].

In conclusion, although personalized medicine is still in need of continued research, collaboration, and policy support to realise its full benefits, it is an indisputable fact that personalized medicine has an incredible role to play both now and in the future.



Data Usage in Healthcare: Electronic Health Records

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Recent global events, such as the COVID-19 pandemic, have stressed the urgent need for digital transformation in healthcare. However, despite the increasing adoption of digital technologies, the healthcare sector still faces challenges, such as when it comes to Electronic Health Records (EHRs).

Navigating the Digital Landscape

The digital revolution in healthcare represents a fundamental shift in how this field is delivered and managed [1]. Therefore, centralising EHR is a key part of this change, as they act like databases that store information regarding the patient's health, helping healthcare providers to have a holistic view. Thus, this helps them communicate better, coordinate care more effectively and make evidence-based decisions [2]. Ultimately, the centralisation of EHRs not only streamlines healthcare processes but also lays the foundation for collaborative and data-driven approaches that hold the potential to revolutionise patient care.

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Harnessing the Power of Health Data

The proliferation of health data, from wearable devices and medical imaging to genomic information, offers unparalleled opportunities for discoveries [3]. Data Lakes, which are centralised places where data is stored, integrate multiple data sources, enabling a comprehensive analysis. Through advanced analysis methods, healthcare organisations can identify patterns, predict outcomes and personalize treatment plans [4].

Transforming Healthcare Delivery

Centralised EHR systems play a crucial role in driving significant changes in healthcare delivery, fostering the transition to patient-centered approaches [5]. Moreover, by using data analytics and predictive modeling, healthcare providers can group patients based on their needs, identify high-risk individuals and tailor interventions accordingly. Prioritising patients' needs at the centre of care, allows healthcare organisations to enhance engagement, improve adherence to treatment plans and promote better communication between patients and providers [6].

Addressing Challenges and Seizing Opportunities

While the centralisation of EHRs holds great promise, it also presents challenges that must be addressed to maximize its potential. Concerns regarding data privacy and security, interoperability issues and the establishment of robust data governance frameworks are among key factors to consider. Thus, regulatory frameworks, such as the General Data Protection Regulation (GDPR), serve as a foundation for safeguarding patient privacy, while facilitating responsible data sharing for research and public health endeavors [8].

Furthermore, investments in data infrastructure, interoperability standards, and digital literacy are crucial for overcoming barriers to adoption and ensuring equitable access to digital healthcare solutions. By fostering collaboration among various stakeholders and cultivating a culture of innovation, healthcare organizations can navigate the complexities associated with data-driven transformation and establish a healthcare system that is more resilient, responsive and centered around the needs of patients [9].

Finally, integration of digital health education into medical curricula could also change the paradigm in healthcare, by, for instance, fostering digital literacy and data fluency in future medical doctors.

Conclusion

In conclusion, centralizing EHRs is vital for streamlining healthcare processes and improving patient care. While challenges like data privacy and interoperability persist, investments in infrastructure and digital literacy are key to maximizing the benefits of digital transformation in healthcare.

Will artificial intelligence replace surgeons? Exploring the future of healthcare

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The year is 2100. You enter the operating room only to find the artificial intelligence robot which is about to operate on you. There is no human surgeon, only the latest technological advancement with peak surgical abilities. This scenario would be considered science fiction ten years ago though today it would not impress many. Such a scenario, although it might appear to be getting closer and closer to its incarnation, should not be a concern as there are emerging limitations from a technical and ethical point of view that prevent it.

Initially, to understand the possibilities and the constraints of artificial intelligence in surgery, it would be useful to define the five levels of autonomy a surgical robot can reach [1]. Level zero implies zero autonomy for the robot/program while level one uses artificial intelligence to facilitate the surgeon but still relies on human control. At levels 2 and 3 surgeon and robot interact complementary while at levels 4 and 5 we approach full autonomy of the robot surgeon. The restrictions in the autonomy of surgical imaging, the lack of required precision in the management of tissue when placing a suture and the complexity of the tasks are some of the challenges that do not seem to be able to be overcome soon making the complete automation of surgery almost impossible from a technical point of view [2].

Artificial intelligence of crucial utility for surgery is already being used without threatening the human surgeon. "Sturgeon", a recent achievement since past October, is a tool that, using algorithms, recognizes with great accuracy (approximately 90%) and speed the subtype of a cancerous tumor in the brain and indicates to the surgeon the aggressiveness with which to remove the neoplasm [3]. Of equal importance is the "STAR: Soft Tissue Autonomous Robot" which, after the necessary approval of a specialized surgeon, designs and implements a strategic plan for suturing two segments of the small intestine together [4]. The above applications make good use of partial autonomy and benefit the surgeon.

However, beyond the technical limitations, there are ethical issues that affect both the patient and the surgeon and put the nail in the coffin to the complete automation of surgery. With automation, the surgeon loses their occupation, while if they manage to keep a collaborative job with the artificial intelligence robot, the difficulty of the service they offer will be reduced, with a parallel reduction in their salary. Equally important is the social inequality that would be caused by the access to technology exclusively by financially robust, dividing patients between those who can be admitted to certain hospitals and those who cannot. Now imagine that the surgery you just underwent by a surgical robot has some complication. Who takes responsibility in this case? Who is legally and morally responsible?

Concluding, artificial intelligence is not coming to replace the surgeon but to facilitate his demanding social service. The patient is not a set of symptoms, not a piece of flesh that remains motionless during surgery. They are a person in a very mentally vulnerable position in need to place their vulnerability to another human being, in need to share their pain with another human being, in need to feel that their human life depends on a human.

Human Receives Transplant of Genetically Edited Pig Kidney: Advancing Kidney Transplantation Through Genetic Innovation

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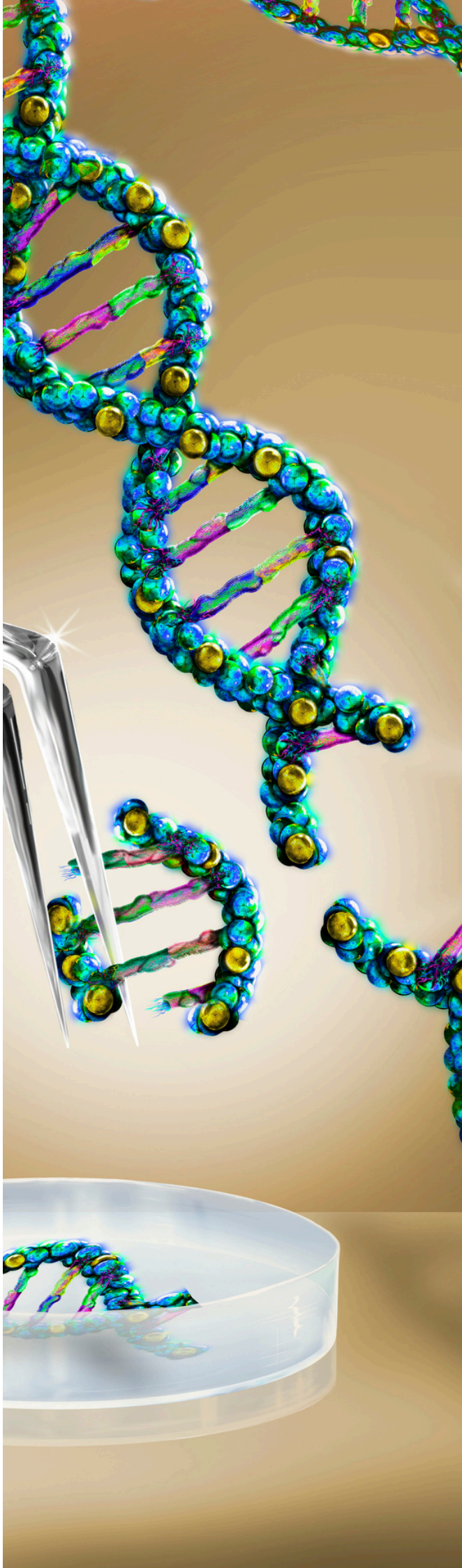
On March 16, 62 years-old Richard Slayman, a resident of Weymouth, Massachusetts, underwent a ground-breaking four-hour surgery to get a genetically modified pig kidney. This extraordinary procedure is a significant milestone in the field of medicine which illuminates the potential of using xenotransplantation to address the severe organ shortage, and represents hope for millions of people suffering from end-stage renal failure.

Slayman's medical history reveals a challenging journey marked by the pervasive impacts of chronic kidney disease, propelled by underlying conditions such as type 2 diabetes and high blood pressure. Despite a prior human kidney transplant in 2018, Slayman faced the grim reality of kidney failure once again after five years, necessitating a return to dialysis and regular hospital visits. However, his plight took a transformative turn with the advent of xenotransplantation, a cutting-edge approach that holds promise in revolutionizing organ transplantation.

However, the journey towards xenotransplantation is not devoid of challenges. Safely transplanting organs from animals into humans necessitates meticulous planning and execution to minimize immune rejection, prevent infections, and mitigate other potential complications. As Joren Madsen, the Paul S. Russell/Warner-Lambert Professor of Surgery at Harvard Medical School and director of the Mass General Brigham Transplant Center, aptly notes, the barrier to pig xenotransplantation is formidable, requiring relentless perseverance and scientific ingenuity to surmount.

The result of decades' worth of work by thousands of doctors and scientists is essential to Slayman's surgery's success. The modified kidney, generously provided by eGenesis, a leading xenotransplantation therapy company co-founded by Harvard Medical School geneticist George Church and former HMS postdoctoral fellow Luhan Yang, underwent rigorous testing and refinement to ensure safety and efficacy. Leading the transplant team, an HMS professor of surgery and director of Mass General's Legorreta Center for Clinical Transplant Tolerance, Tatsuo Kawai utilized genetic modification techniques for enhancing the pig kidney's immunological compatibility with the human body. CRISPR-Cas9 technology was used for precise gene editing to reduce the risk of infection by eliminating the pig genes that trigger immune responses, incorporating human genes to enhance compatibility, and rendering viral components inactive. Moreover, Slayman received specialized monoclonal antibody drugs aimed at suppressing immune reactions against pig tissue, underscoring the multifaceted approach adopted by the medical team to maximize transplant success.



Despite the remarkable success achieved in Slayman's case, the long-term viability of xenotransplantation remains a subject of ongoing inquiry. The Mass General team acknowledges that more thorough investigation and ongoing assessment are required to determine the longevity and effectiveness of pig kidney transplantation. Slayman's eventual independence from dialysis will determine the success of the procedure, highlighting the revolutionary potential of xenotransplantation in improving patients' quality of life and extending their life expectancy.

The significance of Slayman's surgery extends beyond the realm of medical innovation, touching upon broader societal implications, including healthcare equity and accessibility. Winfred Williams, HMS associate professor of medicine at Mass General and Slayman’s nephrologist, draws attention to the differences in access to kidney transplants that patients from ethnic minorities face and stresses how xenotransplantation may be able to help with this widespread problem. Slayman's brave choice to participate in the experimental surgery highlights the need for inclusive healthcare solutions. Slayman's journey epitomizes resilience, hope, and the relentless pursuit of medical progress, offering a glimpse into a future where life-saving treatments are within reach for all.

Digital Twin in Healthcare – How they apply space science in today's medicine

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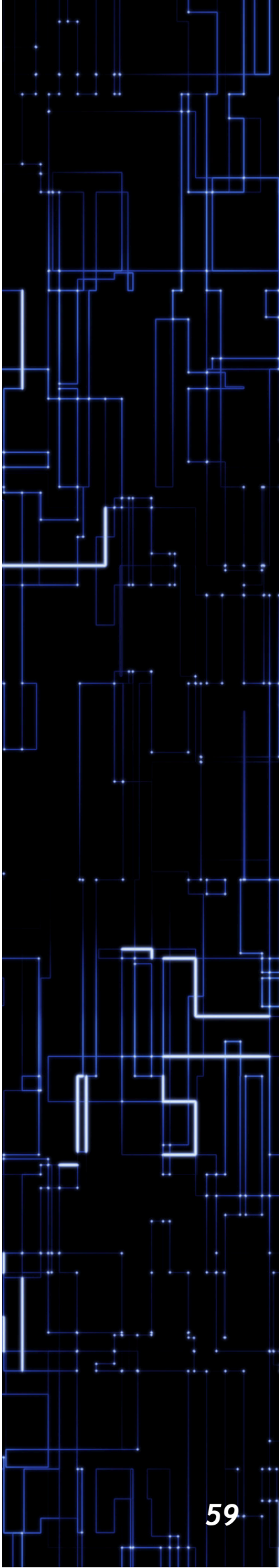
The idea of Digital Twin (DT) first came to life in the 1960s, when NASA made simulators to mimic the spatial environment before sending their spacecraft on a mission. Since then, the idea has been used in a wide range of domains, from Military application to Manufacturing, Urbanization, and Agriculture. Currently, more DT prototypes are finding practical uses in the medical field due to the simultaneous development of technologies that make possible fast data collection, storage, and analysis [1].

A DT is defined by E. VanDerHorn et al. as "a virtual representation of a physical system (and its associated environment and processes) that is updated through the exchange of information between the physical and virtual systems" [2]. To put it simply, a DT is a virtual copy ("in silico") of an original physical system ("in vivo"). This replica requires a lot of data collection about the original system that needs to be processed with the help of Machine Learning (ML), Deep Learning (DL), Big data, and Artificial Intelligence (AI) to create a simulation, named the "in silico" system. The DT is then used to analyze the data, make predictions, and give prognostics about the life course of its "in vivo" twin. Later, with more collected data, the DT will use the same processes to improve the model's precision of deduction. As time passes, a DT should accurately represent the current state of the physical system and be able to make real-time predictions [3].

REFERENCES

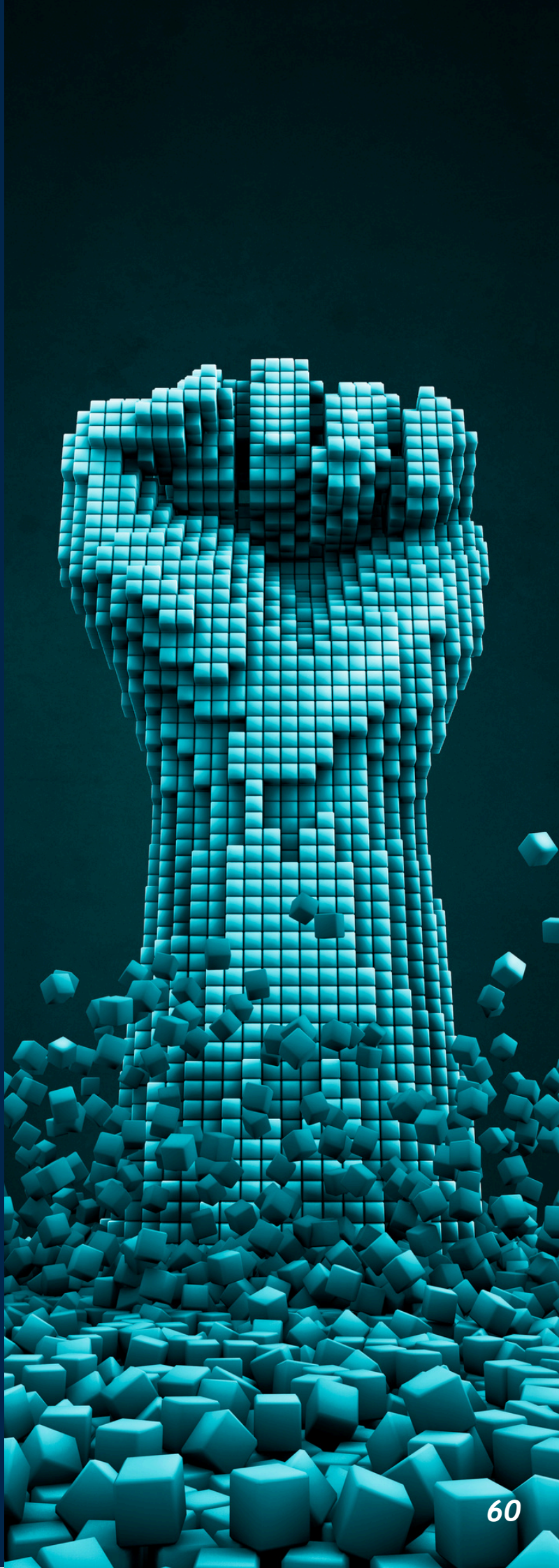
Watching the newest trends in the medical field, digital twins have proven to be useful tools to understand and simulate biological processes. In treatment research, with the help of databases that provide the biological system functions and drug specifications, it can analyze and simulate new drug effects, its interactions with other drugs, and the possible adverse effects. With this tool at our fingertips, we may reduce trials of treatment testing and avoid animal experimentation. From a patient-oriented perspective, digital twins could optimize treatment strategies and deliver personalized care through just predictions based on the simulations made on the virtual replica [3].

People with diabetes could also benefit from DT-like models applied in insulin pumps. In the past decade, insulin pumps have developed enormously with the purpose of mimicking the activity of a real pancreatic function in accordance with glucose levels, predicted catabolic activity, and additional hormones secreted by the body [5]. One insulin pump consists of a few cybernetic modules. It comes with a continuous glucose monitoring sensor that will allow for subcutaneous glucose readings. First, a denoising module is added, which will consider that the glucose levels measured subcutaneously are contaminated with glucose from the extracellular space and use a signal-to-noise ratio to reduce the measurement of noise based on data previously collected from patients. Then the enhancement module will provide real-time data from external influences (such as physical exercise, heart rate, and caloric intake) to connect homeostasis parameters to the loop of glucose-insulin equilibrium, providing more accurate secretion following the patient's activity. Lastly, it adjoins the prediction module that analyses the variables and can predict future glucose levels with the purpose of functioning as an artificial pancreas system [3].



Other honorable mentions of digital twins have also made their way into the medical world. Liver DT is used to understand regenerative mechanisms after drug-induced damage [6]. DT for Multiple sclerosis patients to better predict its evolution and strategize management plans to individual patient's needs [7]. But also in oncology research, using single-cell DT to better discern cancer phenotypes [3].

To conclude my analysis, I see in digital twins a transformative technology that has the potential to revolutionize various aspects of healthcare, including personalized medicine, diagnosis, treatment planning, and medical research. With continued research, development, and collaboration, digital twins are poised to play a certain role in shaping the future of healthcare delivery and providing patients with the best outcome treatment.



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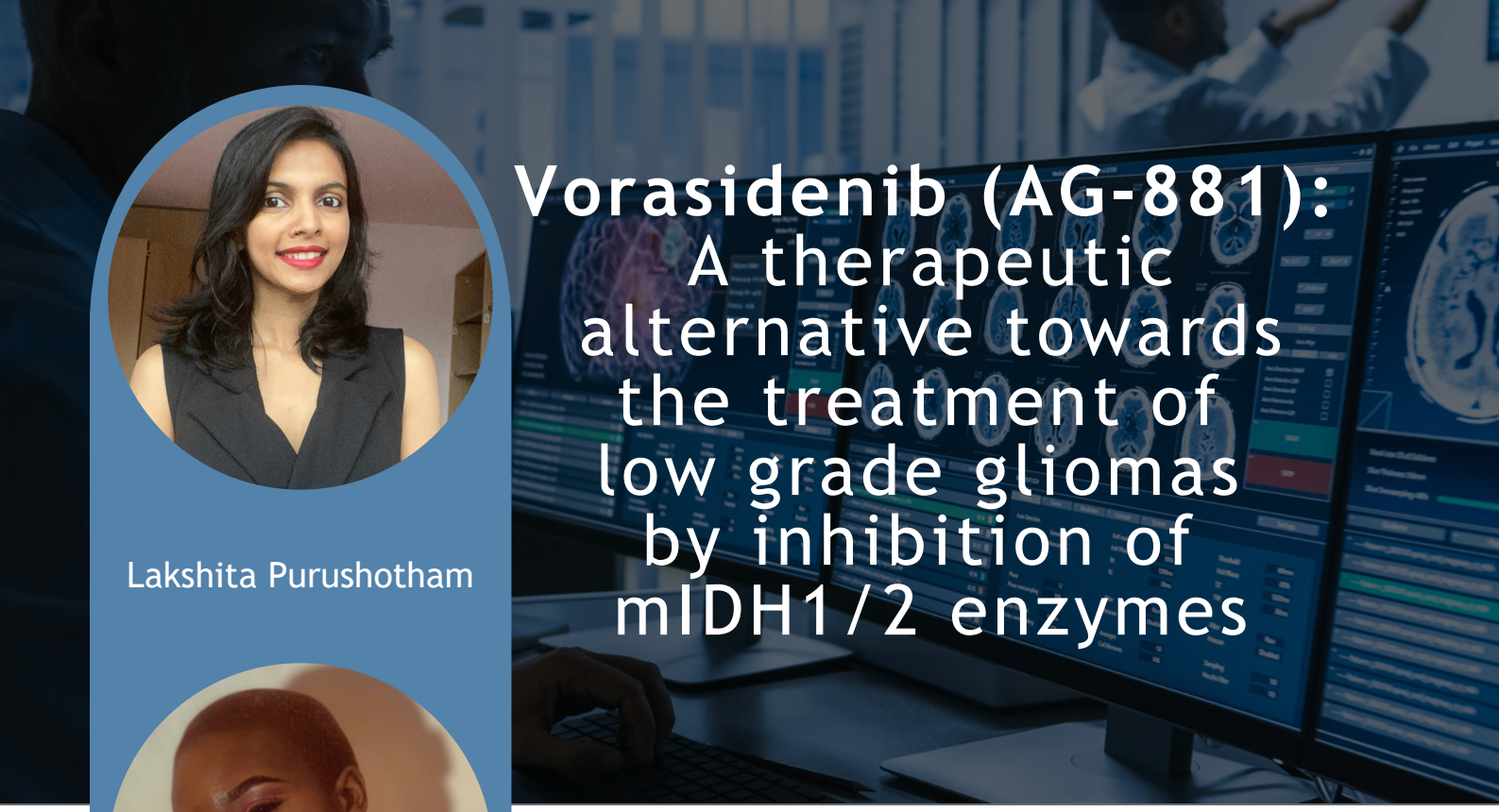

Vorasidenib (AG-881): A therapeutic alternative towards the treatment of low grade gliomas by inhibition of mIDH1/2 enzymes

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Introduction :

Low grade gliomas are a type of malignant tumor that starts in the glial cells of the brain. In most cases, low grade gliomas harbor mutations in the genes encoding isocitrate dehydrogenase 1 or 2 (IDH1/IDH2). Targeting mIDH1/2 is one of the major strategies for the treatment of glioma. Vorasidenib (AG-881), an oral, brain-penetrant dual inhibitor of mIDH1/2 enzymes has been an emerging therapeutic alternative towards the treatment of low grade glioma.

Methodology :

A literature search was performed using 'Google scholar', 'Pubmed' and 'Cochrane library' databases . A total of 12 articles were reviewed.

Results :

Study Characteristics

- We found 3 studies that met the inclusion criteria.
- All evaluated vorasidenib in relation to low-grade gliomas (LLG).
- Out of 3 studies, 2 were phase I trials and 1 was a phase III trial.

Table 1. Characteristics of included studies

Author, Year	Phase	Condition	Arm (n)	Outcome measure
Mellinghoff IK *et al.* 2023	III	LGG	Vorasidenib, *n*=168; placebo, *n*=163	Progression-free survival
Mellinghoff IK *et al.* 2023	I	LGG	Vorasidenib, *n*=24; Ivosidenib, *n*=25.	2-HG concentration
Mellinghoff IK *et al.* 2021	I	LGG	Nonenhancing glioma, *n*=22; Enhancing glioma, *n*=30; Non-glioma, *n*=41.	Maximum tolerated dose

Abbreviations: LGG, low-grade glioma

An exploratory evaluation of tumor volumes in patients with non enhancing glioma demonstrated sustained tumor shrinkage in multiple individuals. This positive response was further supported by the protocol-defined objective response rate, showing an 18% response rate among patients with non enhancing glioma.

Median progression-free survival (PFS) ranged from 24.0 to 36.8 months for more than 60% of patients with non-enhancing glioma and 3.6 months for patients with enhancing glioma.

In vivo studies using orthotopic glioma models revealed the effectiveness of ivosidenib (IVO) and vorasidenib (VOR) in reducing 2-hydroxyglutarate (2-HG) levels. IVO achieved an 85% reduction, while VOR impressively achieved a 98% reduction.

Additionally, VOR showed better brain-to-plasma ratio than IVO, indicating improved brain penetration potential, which could be advantageous for targeting brain tumors.

Hence, vorasidenib is more consistent than other IDH1/2 inhibitors i.e. ivosidenib.

Safety profile :

One important aspect of the evaluation was the safety profile of vorasidenib (VOR). The drug was well-tolerated in the study, with an increased alanine aminotransferase level of grade 3 or higher occurring in only 9.6% of patients who received vorasidenib. This is in contrast to patients who received placebo, in whom no such elevation was observed.

Discussion :

Ivosidenib, an allosteric competitive inhibitor of mIDH1, has been a FDA approved inhibitor in treatment of gliomas. It has shown moderate blood-brain barrier penetration. While vorasidenib is a dual inhibitor of IDH1/2, Ivosidenib is only mIDH1 inhibitor.
Vorasidenib has also shown efficacy in other diseases with IDH mutations, such as acute myeloid leukemia (AML) and cholangiocarcinoma

Conclusion :

The ongoing studies involving vorasidenib (AG-881) have shown encouraging results in inhibiting mIDH1 and mIDH2, respectively. The sustained tumor shrinkage and prolonged progression-free survival in patients with nonenhancing glioma highlight the potential of mIDH1/2 inhibitors as a therapeutic strategy. By addressing the limitations of current inhibitors and potentially overcoming dose-dependent toxicity and blood-brain barrier penetration issues, these findings provide hope for improving treatment outcomes for glioma patients.Moving forward, further research and development efforts are warranted to capitalize on these findings and bring novel mIDH1/2 inhibitors to the forefront of glioma treatment.

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