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Review Article

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Personalized Medicine: A Future Ahead for Human Health

Sachin C. Narwadiya

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Abstract

Personalized medicine means creatingprecise treatment plans for individuals based on pharmacogenetic and pharmacogenomics data. The practicalities of personalized medicine can be examined by adopting various methods including single nucleotide polymorphism genotyping. In future perspectives, the molecular diagnostics will playkey role in the improvement of personalized medicine, by combination of treatment and diagnosis. In present scenario, there are many examples of personalized medicine, like selecting patients for cancer treatment based on genotype to avoid non-responders or side effects. Self-treatment is economically viable because it reduces drug development costs by shortening the time to drug development. Incorporating pharmacogenomics into clinical trials reduces the likelihood of clinical trial failure and leads to safer, more effective treatments for specific patients. Some of the advantages and challenges of developing personalized medicine are reviewed.The concept of personalized medicine was not new at the time, but it was made possible in the 1990s by advances in DNA sequencing technology, including automation and amplification. The advent of personalized medicine has accelerated the development of health information technology, which involves the electronic processing and storage of patient information. Advances in these areas, especially the use of electronic health records (EHRs) that store patients' medical histories, medications, test results, and demographic information, are important for integrating data from genetic and genomic studies into clinical settings.

Keywords: Cancer; Drug development; Personalized medicine; Tuberculosis.

INTRODUCTION

Early medical practices involved the peoples of Babylon, China, Egypt, and India. The invention of the microscope was a result of enlarged understanding. Before the 19th century, humoral theory (also known as humoral theory) was thought to explain the cause of disease, but it was gradually replaced by the disease theory, which led to a complete treatment that could cure many diseases. Army doctors provided advanced medical and surgical care. Public health measures

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were developed, especially in the 19thcentury, as the rapid growth of cities necessitated sanitation.[2] In the early 20th century, advanced research centres were established, often attached to larger hospitals. In the mid-20th century, new treatments such as antibiotics emerged. These advances, combined with developments in chemistry, genetics, and electricity, led to the emergence of modern medicine. Medicine became more professional in the 20th century, with women entering new professions such as nursing (from the 1870s) and medicine (especially after 1970).[3]

In medical advancement a decade passed always result into incorporation of advance technologies in medicine field. The human genome project during 1990s is one of the key factor towards the personalized medicine. The Human Genome Project (HGP; 1990–2003), had sequenced more than 3 billion pairs of human genomes and made them available to scientists worldwide. Similarly, the global HapMap project (2002–2010) identified genes that predispose people to disease and gave researchers the information they needed to connect the genes to specific diseases and disorders. These advances reflect the effects of treatments over the years, such as drugs that are more effective in some patients and adverse side effects in others. The progress of pharmacogenetics and pharmacogenomics has contributed to improvements in understanding the molecular factors that influence a person's genetic tendency to disease and treatment; studying the genetic reasons behind people's differences in response to drugs; and learning the many variables that affect the effects of drugs.

A person's genetic makeup. about disease and treatment by manipulating the response to drug therapy or using information from pharmacogenetics and pharmacogenomics, researchers have developed more objective and accurate tests to diagnose disease and predict people's pain response to medication. In some cases, researchers have discovered that the development or outcome of certain diseases can be altered by using genetic and other molecular information to guide diagnosis and treatment. [1]

Role in disease prevention, diagnosis, and treatment

Personalized medicine is having many applications which can be helpful in prevention, diagnosis, and treatment. For example, doctors can use family medical history information to assess a patient's risk of disease. In some cases, family history can be used to determine whether a patient should undergo genetic testing. A prediction can be made based on the data, to determine whether the person would specifically benefit from a vaccine. For example, in people with a family history of Lynch syndrome, a common cause of colon cancer, genetic testing can help identify the mutation that causes the disease. Frequent and regular screening for evidence of changes in the colon for people with the mutation can lead to early detection of the disease, which can be lifesaving. Similarly, tests that can detect mutations in multiple genes at once could help diagnose breast, ovarian, and prostate cancers in early stages. A type of treatment that uses drugs to target specific molecules that help cancer grow and spread. The first successful treatment involves the antibody imatinib, designed to treat chronic myeloid leukaemia (CML) patients who carry the BCR-ABL tyrosine kinase, a protein produced by a cytogenetic abnormality in the Philadelphia chromosome. It was observed that the Imatinib effectively reverses the cancer-causing effects by blocking the growth of CML cells with mutated kinases.[1]

Another example of personalized medicine used for treatment is the use of genotyping to identify different enzymes that alter a patient's sensitivity to the anticoagulant warfarin. Information about changes in enzymes that metabolize warfarin can be used to help decide which drug a patient should take to achieve the desired effect.[1]

Challenges and Decisions

Personalized medicine faces major challenges. For example, In the HGP sequence of the human genome, each human genome has approximately three to five million variants. Therefore, disease-modifying or therapeutic responses to genetic modification require careful analysis and translation across multiple disciplines. Furthermore, genomes are geographically and ethnically diverse and are influenced by the environment. Therefore, individual differences found in a population based on race or geography may have a significant impact on disease in other cultures. For example, the structure of electronic medical records impacts their use. Access to and analysis of genomic data in electronic medical records will be limited by the presentation of genomic test results in the context of the analysis tab. There should be no raw data or information about the patient's lifestyle, behaviour, etc. that is critical to the research. Of particular concern is that historically most genomic studies have focused on populations of European descent

and ethnic and racial minorities. This inconsistency in representation may impact the process used to inform drug selection and dosing decisions, leading to poor clinical outcomes and poor outcomes for patients with genetic and lifestyle differences from those in the study population. There are increasing concerns about privacy and security generally associated with the use of electronic health records. For example, flaws in electronic health records can lead to the disclosure of personal and health information as well as medical information. Self-medication is expensive and therefore may not be available to patients without health insurance, and the cost of self-medication may be lower in countries where medical services are less available. Genomics is one of several omics branches of biological science that focus on the structure, function, and heredity of an organism's genome (its entire genetic material). Genetic Proteins

A significant part of genomics is determining the sequence of molecules that make up the deoxyribonucleic acid (DNA) content of the human genome. Genomic DNA sequences are found in one or more sets of chromosomes, in every cell of the body. Chromosomes can also be described as containing the genetic material that is the basic unit of reproduction. Genes are transcripts, which are regions of chromosomes that produce ribonucleic acid (RNA) messages that can be easily translated into protein molecules. Chromosome crossover events are part of recombination. In this process, a region of one chromosome is exchanged for a region of another chromosome, resulting in a unique combination of chromosomes that divide into haploid daughter cells. The chromosomes of each species are unique in number and size and contain the entire genome and all the DNA between them. Although the word "genome" was not used until the 1920s, the existence of genomes has been known since the 19th century, when chromosomes were first discovered as chromosomes that could be seen under a microscope. Genetic maps of chromosomes were drawn in the 20th century after their initial discovery, because most chromosomes are distributed by a process called chiasm, a process that is revealed by testing during the normal recombination and production of cells (gametes). The genes that can be localized by chromosomal exchange are usually those that have been shown to alter phenotype (as viewed by the body's genetics) and are only a small fraction of the total genes in the genome. The discipline of genomics emerged with the advent of technology that could determine the complete nucleotide sequence of the genome (a significant fraction of millions of nucleotide pairs).

Sequencing and bioinformatic analysis of genomes

DNA extraction: The DNA extraction process is necessary to isolate DNA molecules from cells or tissues. The isolation of pure DNA requires several steps, including the use of proteases to remove proteins from the DNA, which are used in subsequent procedures such as cloning or sequencing. Replication and expansion in cells. This allows more DNA to be cloned and extracted from the cells. The DNA is then sequenced and analysed in more detail using bioinformatics techniques. In an attempt to determine the sequence of a genome, genomic DNA is first extracted from a diseased brain sample and then broken into many random pieces. These fragments are cloned into DNA vectors that can carry large amounts of DNA. Since all the DNA needed for synthesis and further testing is several times the total DNA in the bacterial genome, each cloned fragment is copied individually in the brain in living organisms, which proliferate rapidly and form many more clones in it. The cloned DNA is then extracted from the cloned organism and fed into a sequencer. The sequence data is stored in the computer. Once enough sequences have been obtained from many different clones, the computer uses the overlapping sequences to join them together. The result is a sequenced genome that is then stored in a public database. The need for these detailed analyses has given rise to the field of bioinformatics, where computers analyses DNA sequences to find genes using methods based on genetic features, such as nucleotide triplets called start and stop codon stems, DNA segments, or DNA sequences that extend the DNA sequence. Genes are known to be important in size and in regulating neighbouring genes. Once candidate genes are identified, they must be copied to increase functional capacity. These explanations are often based on information about the function of similar genes in other organisms, analysis made possible by the evolutionary conservation of genes, and function due to the genetics of disease. However, there are still some genes whose role remains undetermined after annotation; with further research, these functions are becoming increasingly clear.

CONCLUSION

Doctors know that many patients they treat with drugs will not be effective. Many patients know this, and this may be why some do not take them. The basic idea behind stepwise medicine is that we can be smarter about identifying patients

who will benefit. Long-term expectations are slowly becoming reality, but reforming healthcare, creating regulatory frameworks, and finding business models that support quality care are challenging.[3-4]

In the "14 Grand Challenges of Engineering" established by the National Academy of Engineering (NAE), self-healing medicine is considered important and looks to the future to "completely eliminate concerns about personal health" and thereby meet the challenge of "developing better medicine".[5-6]

In personalized medicine, diagnosis is often used to select appropriate and recommended treatments based on the patient's genetics or molecular or cellular characteristics. Important role (e.g. genetic testing).[7-8] Image analysis, nanoparticle-based theranostics,[9-10] among them.

If the personalized medication adopted on larger scale the Public Health scenario will change to more healthy peoples. Customization is the current need in medication sector for well being and early diagnosis of diseases.

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Review Article

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Hypothyroidism Inceasing Among Women in India

Neha Suthar[1], Sachin C. Narwadiya[2]

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Abstract

Thyroid diseases are prevalent all over the world. The burden of thyroid disease is also high in India. According to various studies on thyroid diseases, about 42 million people in India suffer from thyroid diseases. This review will focus on the prevalence of five thyroid diseases in India: (1) hypothyroidism, (2) hyperthyroidism, (3) goitre and iodine deficiency, (4) Hashimoto's thyroiditis, and (5) thyroid cancer. The present review will also briefly discuss important studies in India that have addressed the use of thyroid hormones, particularly during pregnancy and childhood.[1]

In India due to lack of awareness about healthy diet habits, importance of exercise preferably among girls and women lead to genesis of Hypothyroidism.

Keywords: Hypothyroidism; Hyperthyroidism; Goitre; Iodine deficiency; Hashimoto's thyroiditis; Thyroid cancer.

INTRODUCTION

Thyroid disorders are prevalent in India and the main target in the past was Iodine Deficiency Disorder (IDD). India's international salt iodization service has been in use for over 30 years. However, there are not many studies that have assessed the prevalence of thyroid disease in the post-iodization period. The asymptomatic condition is mild and triiodothyronine levels are slightly elevated.[2]

Hypochondria affects: In India, hypothyroidism has traditionally been classified as an iodine deficiency disorder (IDD). This disease is usually measured by total goiter and urine iodine concentration in schoolaged children. The cost is very low. Adequate iodized salt is consumed.[3]

Cross-sectional studies are needed to fully understand the changes in thyroid disease across the country, especially after iodine supplementation. This study aims to determine the prevalence of hypothyroidism among women in India. Both conditions can have medical, financial and psychological impacts on our lives. Hypothyroidism affects fertility in many ways, causing an ovulatorycycle, luteal phase disorders, high prolactin (PRL) levels and sex hormone imbalances.[4]

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Therefore, normal thyroid function is important for pregnancy, pregnancy, and pregnancy care, even in the first few days after conception. Any woman who is trying to conceive, has a family history of thyroid problems, has irregular menstrual cycles, has had more than two miscarriages, or has not been able to conceive after a year of unprotected intercourse should have a thyroid test.[5]

Thyroid testing should include thyroid autoimmune tests such as T3, T4, thyroid stimulating hormone (TSH), and thyroid peroxidase (TPO) antibodies, thyroglobulin/anti-thyroglobulin antibodies, and thyroid stimulating immunoglobulin (TSI). [6]

Autoimmune thyroid testing may or may not be included in fertility testing because the presence of thyroid antibodies increases the risk of miscarriage in women. It has been found to cause 4% infertility and miscarriage. A mildly elevated TSH level and normal T3 and T4 indicate subclinical hypothyroidism, while a high T3 and low T4 level indicate clinical hypothyroidism. Diagnosis and treatment (including treatment) of subclinical hypothyroidism in pregnancy is important unless there are other independent risk factors.[8]

Many pregnant women with hypothyroidism develop hyperprolactinemia due to failure to ovulate, which results in increased production of thyroid stimulating hormone-releasing hormone (TRH). It is good for fertility and pregnancy.[9]

Thyroid dysfunction is associated with a range of reproductive problems, from sexual dysfunction to irregular menstruation and infertility. Hyperprolactinemia disrupts GnRH pulses, impairs ovarian function and slows growth. Early diagnosis is important, so appropriate treatment is often given to prevent brain damage. Congenital hypothyroidism is common in India, affecting 1 in 2,640 births and 1 in 3,800 births worldwide. In our country, the diagnosis of congenital hypothyroidism is often delayed. This delay may be due to lack of awareness of the disease and lack of facilities or programs to screen and test infants for the disease. 79% had thyroid nodules. The most common causes of hypothyroidism in children are thyroid underdevelopment, hormonal abnormalities and thyroiditis. Some specific issues are not adequately managed.[12]

At the National Advanced Management Workshop on Thyroid Disease held in Chennai, India on June 5, 2014, participants learned that 42 million people in India are affected by thyroid disease.[13]

Hypothyroidism is the most common thyroid disorder in India, affecting one in 10 adults. Despite this unfortunate condition, there are no cases of severe hypothyroidism in the country. The prevalence is higher in the inner cities (like Kolkata, Delhi, Ahmedabad, Bangalore and Hyderabad) than in the coastal cities (like Mumbai, Goa and Chennai) (11.7% vs. 9.5%). Ambrish Mithal, director of health and diabetes at Medanta in Gurgaon, India, said that the overall cause of thyroid-stimulating hormone in India is higher than in Western countries, which could be related to iodine deficiency in India. That's right. The prevalence of hypothyroidism is highest in the 46-54 age group (13.1%), while the 18-35 age group is less affected (7.5%). This disease.[14]

INDIAN SCENARIO

In India, environmental factors such as iodine deficiency can cause hypothyroidism. "Goiter and cyanide affect iodine metabolism," says Mittal. [Pesticide use and endocrine disruptors may be the cause. It affects 5-20% of women and 3-8% of men. The incidence of the disease varies according to genetics, and is more common in white people and in people with high iodine levels. The most common causes of hypothyroidism are autoimmune damage to the thyroid gland and previous thyroid surgery or radioactive iodine therapy. Many drugs, including amiodarone, cytokines, and lithium, often cause hypothyroidism. Symptoms may be atypical and measurement of thyroid-stimulating hormone (TSH) levels should be part of the biochemical investigation in adults without disease.

Findings of elevated TSH levels should be confirmed by repeated testing to identify, assess and differentiate exercise and should be supported by serum thyroxine and thyroid peroxidase antibody levels.

CONCLUSION

Patients with subclinical hypothyroidism should be informed about their disease and other medical conditions. Only a small percentage of patients treated for subclinical hypothyroidism are happy after treatment. Clinical monitoring in adults should include TSH blood tests once or twice a year and minor adjustments in levothyroxine sodium dosage to maintain TSH levels within the normal range. Individual therapy is important for effective management, and many factors such as age, TSH secretion, thyroid autoimmunity, comorbidity burden, and frailty should be taken into account

in the treatment of SHT in the elderly. T4 is the drug of choice for the treatment of hypothyroidism in adults, but the risk of overtreatment, dosage, and patient compliance should be given more consideration, and the thyroid should be monitored regularly. Optimal therapy means administering L-T4 on a case-by-case basis and carefully assessing the risk of overtreatment (e.g., over dosage due to inappropriate initiation of therapy, inappropriate drug changes, etc.). However, the dose of L-T4 should be titrated starting at ±0.3 to 0.4 µg/kg/day and increased by 10 to 15% after 6 to 8 weeks if necessary to a good TSH target of 2.5 to 3.5 mIU/day.[15] Levothyroxine sodium is the most effective treatment for hypothyroidism. If heart disease is suspected, the starting dose should be lower. Addition or withdrawal of tablets can be done at one time because of the long half-life of levothyroxine sodium. Or twice a week. Levothyroxine sodium is only partially absorbed after meals because food, medications, and tablet ingredients can affect absorption. Years of research have shown that combining levothyroxine sodium and liothyronine can improve clinical outcomes, but recent research does not support this theory. Therefore, there is no information on the benefits of liothyronine replacement. If liothyronine is added as an alternative, the liothyronine dose should be kept low to moderate, preferably twice daily. In adults with elevated serum TSH, thyroid hormone therapy is no more effective than placebo. The main risk of levothyroxine sodium therapy is overdose, which can cause side effects such as anxiety, muscle pain, fractures, and atrial fibrillation. Subclinical hypothyroidism (increased serum TSH but using more than one test) is somewhat different from overt hypothyroidism.

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Oxygen Sensing in Biological Systems using Core-Shell Nanoparticles

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Abstract

Core-shell nanoparticles (CSNPs) have emerged as powerful tools for biological oxygen sensing due to their exceptional structural and functional properties. These nanoparticles, designed with a functional core and protective shell, enhance dispersibility, biocompatibility, and cytocompatibility, making them particularly suitable for intracellular and targeted oxygen sensing. Ruthenium and porphyrin complexes, commonly used as fluorescent and phosphorescent probes, are frequently encapsulated within CSNPs to enable precise fluorescence lifetime-based oxygen measurements. Inclusion of these dyes in polymers or shells offers several advantages, such as preventing dye leaching into tissues, mitigating singlet oxygen toxicity, enabling targeted sensing of cells or organelles, and extending probe lifetime. This paper demonstrates the use of fluorescence lifetime measurements in the time-domain approach, leveraging a multi-channel scaler, to evaluate oxygen levels. Additionally, it discusses CSNPs incorporating Ru and porphyrin dyes from three perspectives: (a) preparation methods, (b) spectroscopic characteristics, and (c) biomedical applications. Overall, CSNPs provide a versatile and efficient platform for real-time monitoring of oxygen levels, with significant potential in biomedical and biophysical research.This paper explores the design strategies, mechanisms, and potential of core-shell nanoparticles in advancing the field of biological oxygen sensing.

Keywords: Core-shell nanoparticles; Biomedical applications; Bioactivity; Biocompatibility; Oxygen sensing.

INTRODUCTION

The measurement of oxygen in biological systems is crucial for understanding physiological and pathological processes, including cellular respiration, tissue hypoxia, and tumor microenvironment dynamics[1]. Adenosine triphosphate (ATP), the primary energy currency of cells, is primarily derived through oxidative phosphorylation (OxPhos) in the mitochondria[2-3]. OxPhos relies on oxygen as the terminal electron acceptor in the electron transport chain.[4-5] Consequently, energy metabolism directly

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influences the dynamics of oxygen within and around cells and tissues.[6]

To maintain balanced metabolic activity, tissues and organs have evolved adaptive mechanisms, such as angiogenesis, increased haemoglobin concentration, and accelerated glycolysis, to ensure sustained oxygen delivery.[7] A thorough understanding of these mechanisms and their pathophysiological implications requires precise and localized oxygen sensing.[8]

Traditional methods for sensing oxygen include electrochemical techniques like polarography, electron paramagnetic resonance (EPR), positron emission tomography (PET), magnetic resonance imaging (MRI), and Near-Infrared (NIR) spectroscopy (commonly known as oximetry).[9-10] While these methods have contributed significantly to oxygen studies, many face limitations in resolution, invasiveness, and accuracy. For instance, Clark electrodes, widely used in laboratory settings, are unsuitable for in vivo oxygen measurements because of their large size, oxygen consumption during operation, and inability to probe microscopic or delicate biological domains.[11-12]

Optical techniques have advanced as non-invasive alternatives, employing both endogenous and exogenous probes for oxygen sensing. [13] Endogenous probes, such as NADH and Protoporphyrin IX (PpIX), exhibit limitations, including weak fluorescence signals and cytotoxicity associated with UV-A excitation. [14] Consequently, exogenous probes based on porphyrins, ruthenium (Ru), and iridium (Ir) complexes risen in prominence for their superior sensitivity and adaptability.[15] These complexes offer advantages such as tunable photophysical properties, high photostability, and compatibility with fluorescence lifetime spectroscopy, enabling precise and rapid oxygen measurements.[16]

Core-shell nanoparticles (CSNPs) represent a substantialdevelopment in the field of optical oxygen sensing. By encapsulating fluorescent or phosphorescent dyes like porphyrins, Ru, and Ir complexes, CSNPs provide enhanced stability, dispersibility, and biocompatibility, rendering them suitable for intracellular and localized oxygen measurements.[17] These nanoparticles also mitigate challenges such as dye leaching and singlet oxygen toxicity while allowing extensive chemical modifications to customize their properties for specific applications.[18-19]

This paper explores the use of CSNPs for fluorescence lifetime-based oxygen sensing, focusing on their preparation methods, spectroscopic properties, and applications in biomedical and biophysical studies. With their unique advantages, CSNPs offer a versatile framework for deepening our understanding of oxygen dynamics in biological systems.

Nanoparticles for oxygen sensing

Nanoparticles have revolutionized oxygen sensing by providing advanced platforms that overcome the limitations of conventional methods. Their nanoscale dimensions, large surface area-to-volume ratio, and ability to incorporate functional materials enable precise and localized measurement of oxygen levels in biological and environmental systems.[20] (Kalyani *et al.*, 2021). Nanoparticles can be designed to carry oxygen-sensitive probes, such as fluorescent or phosphorescent dyes, that respond to changes in oxygen concentration through variations in optical properties like intensity, lifetime, or wavelength shifts.[21-22]

Among the various types of nanoparticles used for oxygen sensing, core-shell nanoparticles (CSNPs) are particularly notable. These structures consist of a functional core surrounded by a protective shell, offering enhanced stability, biocompatibility, and tailored performance (Zhao *et al.*, 2020). Commonly used oxygen-responsive dyes include ruthenium (Ru) and porphyrin complexes, which exhibit excellent photophysical properties, including oxygen-dependent fluorescence quenching or lifetime changes.[15,23] Embedding these dyes in nanoparticles prevents issues such as dye leaching, photobleaching, or toxicity, making the sensing system robust and reliable.[24]

Additionally, mesoporous silica nanoparticles, polymeric nanoparticles, and hybrid nanostructures have also been employed for oxygen sensing. These materials provide customizable pore sizes, chemical functionalities, and surface properties, enabling targeted delivery and real-time monitoring of oxygen dynamics in specific cellular or tissue environments. [25-26] (Tang *et al.*, 2010; Wu *et al.*, 2021). The versatility of nanoparticles allows their application in various oxygen-sensing techniques, such as fluorescence lifetime imaging microscopy (FLIM), time-resolved spectroscopy, and multi-channel scaler-based measurements. These methods facilitate non-invasive, high-resolution, and real-time detection of oxygen levels, making nanoparticles indispensable in studying hypoxia, cellular metabolism, and therapeutic responses.[17,27]

Core-shell nanoparticles

CSNPs are a class of nanomaterials composed of a central core material enveloped by an outer shell, both of which can be tailored to enhance the nanoparticle's functionality. The core typically provides the primary material for sensing, drug delivery, or other applications, while the shell serves to protect the core, improve stability, and impart specific functional properties. CSNPs combine the advantages of both core and shell components, making them highly versatile in various fields, particularly in biomedical applications, sensing technologies, and material sciences.

The structure of core-shell nanoparticles (CSNPs) is typically categorized into two main types: Solid Core-Shell Nanoparticles and Core-Shell Nanocomposites. In Solid Core-Shell Nanoparticles, the core is composed of solid materials, such as metals, semiconductors, or organic compounds, and the shell is typically made of polymers, silica, or other biocompatible materials.[28] This configuration is advantageous for creating controlled release systems, where the shell acts as a protective barrier, controlling the release of the core material in response to specific stimuli.[29] The core-shell nanoparticle involves the integration of different materials in the core and shell to take advantage of their distinct properties. For example, a magnetic core might be combined with a polymer shell for drug delivery and magnetic resonance imaging (MRI) applications.[30] The composite nature of these nanoparticles allows for the synergy of multiple functional properties, enhancing their utility in a wide range of applications.[31]

The main advantage of Core-Shell Nanoparticlesis that they have enhanced stability. The shell protects the core material from degradation, oxidation, and other environmental factors, significantly increasing the stability of the nanoparticle under biological conditions. This is especially important for sensitive materials like fluorescent or phosphorescent probes used in oxygen sensing.The outer shell can be engineered to recognize specific biological markers, enabling targeted delivery of drugs, diagnostic agents, or sensors to cells or tissues. This makes CSNPs particularly valuable in medical diagnostics and therapies. The shell can regulate the release of the core material, providing controlled, sustained release over time. This is beneficial for drug delivery applications, where precise timing and dosage are critical. The shell can be functionalized with various ligands, antibodies, or other biomolecules to enhance interaction with specific biological targets. This functionalization also allows for the integration of different imaging, therapeutic, or sensing functionalities into a single nanoparticle

Recent research has focused on advancing the design and functionality of CSNPs to further improve their applications. Some areas of development include:

- **Surface Modification**: Functional groups and targeting moieties are being introduced to the surface of the shell to enhance the nanoparticles' targeting ability and bioavailability.[32]
- **Nanostructuring**: More complex designs, such as multi-layered shells or multi-core structures, are being explored to enhance the nanoparticles' multifunctionality.[33]
- **Biodegradable Materials**: There is increasing interest in the use of biodegradable polymers for the shell material to ensure that nanoparticles degrade safely within the body after use, minimizing long-term toxicity.[34]

Synthesis of Core-shell Nanoparticles

Core-shell nanoparticles (CSNPs) can be synthesized using two primary approaches: the top-down and bottom-up methods. The choice of synthesis technique significantly influences the properties of the nanoparticles, including their size, shape, and functionality, which are crucial for their application in pO_2 sensing. The top-down approach involves microfabrication techniques that deconstruct bulk materials into smaller, desired-sized nanoparticles, typically using physical methods. Conversely, the bottom-up approach builds nanoparticles from molecular building blocks, relying on chemical interactions and properties to form well-defined structures with meticulous control over size and composition.

This section focuses on two widely used protocols for the synthesis of CSNPs, particularly for oxygen sensing: (1) the Stöber method (sol-gel method) and (2) the template-assisted method.

Stöber Method (Sol-Gel Process)

The **Stöber method** is a sol-gel-based wet chemical technique frequently employed for synthesizing silica-based CSNPs. This method involves the hydrolysis and condensation of silicon alkoxide or silicon halide precursors, such as tetraethyl orthosilicate (TEOS), in alcohol or water in the presence of a base catalyst like ammonia.[35] The process leads to the formation of uniform colloidal microspheres, with a controlled core-

shell structure. In this method, the silica precursor (TEOS) undergoes hydrolysis under alkaline conditions, forming silica nuclei, which act as the core material. These silica nuclei are then seeded on the core surface, promoting heterogeneous nucleation.[36]

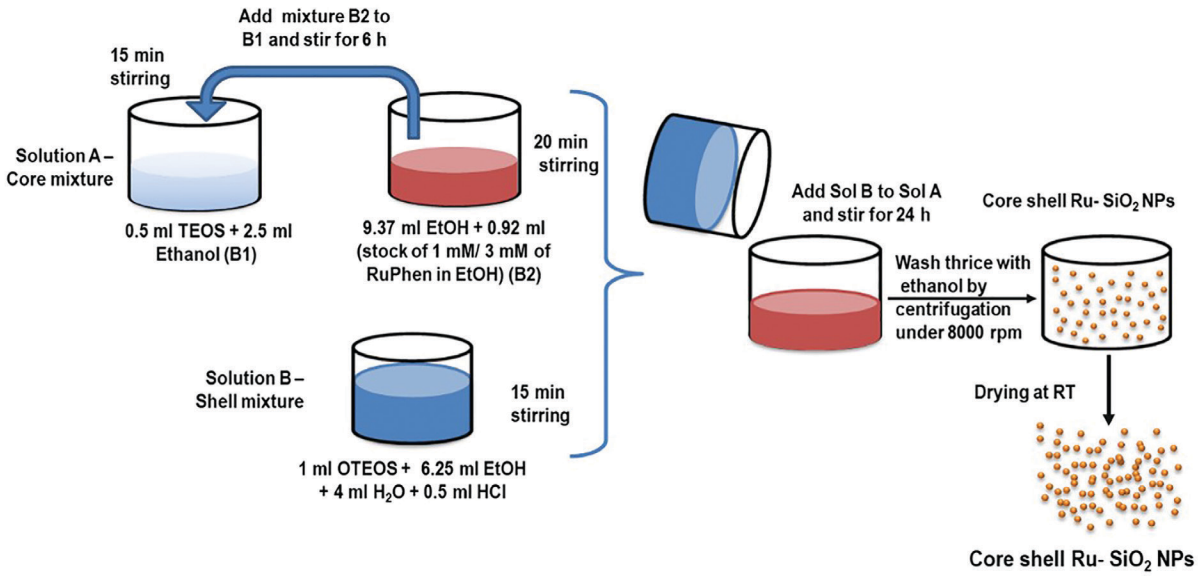

Fig. 1: An illustration of the preparation of Ru-SiO2 core-shell nanoparticles

The growth of the silica shell is regulated through the nucleation and growth phases, which can be precisely adjusted by varying the concentrations of TEOS and alkali catalysts, such as NaOH or NH_2OH. By altering the TEOS concentration or extending the reaction time, the shell thickness can be controlled (Fig. 1). For instance, mesoporous silica shells with pore sizes up to 7 nm can be synthesized using n-octadecyltrimethoxysilane (CTMS) as a surfactant. Additionally, employing block copolymer surfactants like Pluronic P123 facilitates the formation of mesoporous silica shells, enabling controlled porosity suitable for encapsulating fluorescent or phosphorescent dyes used in oxygen sensing.[35] (Stöber *et al.*, 1968).

In the context of CSNPs, the Stöber method is widely employed to create silica shells around cores made of metals, polymers, or other nanoparticles.[3,37] The silica shell protects the core, enhances biocompatibility, and facilitates functionalization with target-specific ligands or fluorescent dyes. For instance:

Ruthenium Complexes: Ruthenium(II) tris(1,10-phenanthroline) ($Ru(dpp)_3^{2+}$) can be encapsulated within the silica shell, ensuring stability and high oxygen permeability.[38]

Porphyrin-Based Dyes: Porphyrin derivatives, such as platinum(II) meso-tetrakis (pentafluorophenyl) porphyrin (PtTFPP), have been incorporated into silica shells for oxygen sensing due to their fluorescence quenching by O_2.[39].

The primary advantage of the Stöber method is that the particle size can be adjusted by varying the concentration of the precursor, solvent, or catalyst[40]. This method produces highly uniform nanoparticles, making it suitable for applications requiring consistency[41]. The silica shells can be modified or functionalized to incorporate fluorescent dyes, magnetic materials, or other biomolecules[42]. The process is easily scalable for large-scale production without significant loss of quality[43].

Template-Assisted Method

Template-assisted synthesis involves three distinct steps: (1) template preparation, (2) template-directed deposition of the shell material, and (3) template removal. The core material, or template, is typically made from rigid materials such as metals, polymers, or metal oxides. The shell material is then deposited uniformly over the core, creating the core-shell structure. The properties of the core material, including its porosity, dictate the final characteristics of the resulting nanoparticles.

There are two main types of template-based methods: **hard template** and **soft template** techniques.

- **Hard Template Method:** In this approach, rigid materials such as polymers, metals, and metal oxides are used as templates for the shell deposition. These templates provide the desired shape and structure, and the porosity of the resulting CSNPs is determined by the characteristics of the hard template. The hard template method is often used for the synthesis of nanoparticles with highly controlled, uniform properties.
- **Soft Template Method:**This approach utilizes surfactants or block copolymers as structure-directing agents (SDAs) to guide the formation of core-shell structures. Unlike the hard template method, the soft template technique does not rely on rigid core materials. Instead, nanoparticles are formed through intermolecular interactions between the SDAs and the molecules, resulting in mesoporous or nanoporous structures. The core of the CSNPs is typically synthesized via sol-gel processes, with the mesoporous structure emerging after the removal of the pore-templating surfactants through low-temperature calcination or washing techniques. This method enables the fabrication of nanoparticles with uniform pores and highly customizable surface properties.[44-45]

The structural precision of the Template-Assisted method enables the synthesis of nanoparticles with precise control over size, shape, and shell thickness. This method applies to a wide range of materials, including silica, metals, polymers, and composites. It facilitates the creation of unique structures, such as hollow, porous, or multilayered nanoparticles.[37,46]

Applications of Core-Shell Nanoparticles for Oxygen and Physiological Parameter Sensing

Monitoring intracellular oxygen is essential for understanding physiological and pathological processes, as oxygen levels are intricately linked to cellular metabolism, signaling, and disease progression. Oxygen sensing can be achieved by evaluating the fluorescence intensity or lifetime of oxygen-sensitive dyes. This section focuses on the applications of core-shell nanoparticles (CSNPs) in detecting oxygen and other physiological parameters, with an emphasis on fluorescence intensity- and lifetime-based measurement techniques of different CSNPs employed for O_2 sensing through various approaches.

A dual-sensor system developed that utilizes doped core-shell nanoparticles (CSNPs) embedded in a sol-gel matrix for simultaneous temperature and oxygen sensing. The sensor incorporates a CdSe quantum dot core, which functions as a temperature sensor, while the silica shell is doped with platinum (II) meso-tetrakis (pentafluorophenyl) porphyrin (PtTFPP) for oxygen sensing. The CSNPs are embedded in a composite xerogel made of n-propyltrimethoxysilane (n-propyl-TriMOS) and 3,3,3-trifluoropropyltrimethoxysilane (TFP-TriMOS), then coated onto an optical fiber. The porous silica shell facilitates the efficient penetration of O_2 molecules, enhancing the quenching effect of PtTFPP and improving the sensor's sensitivity.[46]

Aratiometric core-shell nanoprobedesigned with excellent biocompatibility for intracellular pO_2 sensing. The core incorporated an O_2-sensitive dye, platinum (II) octaethylporphyrin (PtOEP), and two additional fluorophores: coumarin 6 (C_6) as a reference dye and dinaphthoylmethane (DNM) as an energy donor. Upon excitation, C6 provided a stable, O_2-insensitive green fluorescence via intraparticle Förster resonance energy transfer (FRET) from DNM, while PtOEP emitted red phosphorescence, which was quenched by O_2 with a 94% response.[47]

A novel luminescent ratiometricnanosensor designed for pO_2 measurement.[48] The nanosensors featured spatially separated probe and reference dyes within the core and shell, respectively. This configuration ensured a stable reference emission unaffected by environmental factors. The nanosensors exhibited high stability, negligible cytotoxicity, and excellent monodispersity, making them suitable for biological applications.

Anovel, real-time, non-invasive method for O_2 measurement using a custom-built system was studied comprising a custom scalar fluorometer (CSMF), a photomultiplier tube (PMT), and a multi-channel scalar (MCS).[49] CSNPs doped with $Ru(dpp)_3^{2+}$ were prepared using a modified Stöber method and embedded in a TEOS composite xerogel. The system demonstrated improved oxygen diffusivity and sensitivity due to the high surface area and porosity of the silica shell.[49]

Chu *et al.* developed a sensitive optical pO_2 sensor by coating an optical fiber with PtTFPP-entrapped CSNPs embedded in a composite xerogel of n-octyltriethoxysilane (Octyl-triEOS) and tetraethylorthosilane (TEOS). These sensors demonstrated good sensitivity, making them suitable for real-time oxygen monitoring.[50]

The synthesized CSNPs with a hydrophobic core embedded with O_2-sensitive PtTFPP dye and

a biocompatible silica shellwas demonstrated.[51] These nanoparticles exhibited enhanced O_2-sensing performance due to their improved photophysical properties. The biocompatible shell reduced cytotoxicity and minimized chemical interferences, making the nanoparticles ideal for intracellular measurements.

The use of dual lifetime referencing with core-shell nanoparticles (CSNPs) for the simultaneous detection of pO_2 and pH was demonstrated by Ehgartner *et al*.[52] These nanoparticles featured the O_2-sensitive dye Pt(II) meso-tetra(4-fluorophenyl) tetrabenzoporphyrin (PtTPTBPF) in the polystyrene core, while a pH-sensitive BF_2-chelated tetraarylazadipyrromethene (aza-BODIPY) dye was incorporated into the polyvinylpyrrolidone shell. This system enabled reliable, multi-parameter sensing, making it suitable for applications in biological environments.

Xue *et al.* reported the use of poly(ether sulfone) (PES) or polysulfone (PSU) fibers with a polycaprolactone (PCL) shell designed for cell attachment.[53] Oxygen-sensitive dyes, such as PtTFPP or PdTFPP, were incorporated into the fiber core via electrospinning. The PdTFPP-based fibers demonstrated improved sensitivity, attributed to the extended lifetime of the porphyrin dye, enhancing the detection of oxygen levels.

CONCLUSION AND FUTURE WORK

Core-shell nanoparticles (CSNPs) represent a transformative advancement in the field of biological oxygen sensing, owing to their unique structural attributes and functional versatility. By incorporating oxygen-sensitive dyes such as ruthenium and porphyrin complexes into the core or shell, these nanoparticles enable highly precise and efficient fluorescence lifetime-based pO_2 measurements. The protective shell not only enhances the stability and biocompatibility of the dyes but also minimizes issues such as dye leaching, cytotoxicity, and interference from environmental factors. This makes CSNPs an excellent choice for intracellular and targeted oxygen sensing applications.

The combination of robust synthesis techniques, such as the Stöber method and template-assisted approaches, with state-of-the-art spectroscopic systems offers a reliable platform for real-time, non-invasive oxygen monitoring. The ability to fine-tune the properties of CSNPs, including their fluorescence characteristics and surface functionalities, further enhances their adaptability to diverse biomedical and biophysical research needs.

As demonstrated in this study, CSNPs have immense potential in advancing our understanding of physiological and pathological processes associated with oxygen dynamics. The integration of these nanoparticles with advanced imaging and sensing technologies paves the way for groundbreaking applications in cellular biology, disease diagnosis, and therapeutic monitoring. Moving forward, continued innovation in nanoparticle design and dye incorporation strategies will be critical to unlocking the full potential of CSNPs in oxygen sensing and beyond.

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Conflicts of interest: None to declare

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Review Article

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Technology Playing Crucial Role in Early Diagnosis of Tuberculosis

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Abstract

Tuberculosis is a deadly disease that has hovered humanity for numerous decades. It's caused by *Mycobacterium tuberculosis*. Tuberculosis(TB) exploration and invention are critical to achieving global TB targets that will help reduce TB prevalence and TB- related deaths. The WHO End Tuberculosis Strategy, espoused in 2014, envisages a 17 periodic decline in global TB prevalence between 2025 and 2035, compared to a reference line of 2 annually in 2015 and 20 in 2016. It's conceded that achieving the unknown decline from 2025, it'll bear significant technological advances, similar as the development of new TB vaccines that can be used both ahead and after infection by 2025." Progress in exploration and invention" is the third pillar of the final TB law.

Keywords: Diagnosis; Tuberculosis; Technology; Xpert MTB/ RIF.

INTRODUCTION

A crucial step in tuberculosis(TB) care is rapid-fire and accurate TB testing. In recent times, specific and sensitive rapid-fire molecular tests have revolutionized the opinion of TB, which was preliminarily grounded on microscopy and culture. TB positive is defined as "bacteriologically verified" TB by side inflow urine lipoarabinomannan (LF-getaway) testing or foam smear microscopy. Microbiological testing for TB is important because it allows people to make a correct opinion and start the stylish treatment as early as possible. Those diagnosed with TB without bacteriological results are classified as "diagnosed with TB." Viral testing is needed to descry primary and secondary antibodies to pneumonia.[3]

An aggregate of 6.4 million people was recently diagnosed and reported with tuberculosis worldwide in 2021; the proportion of bacteriological conditions worldwide has increased in recent times, from 59 in 2020 to 63 in 2021. The largest share is in Europe and the Americas, with other regions not yet rising to a similar position.

In a political protestation held at the First United Nations(UN) High- Level Meeting on Tuberculosis(TB) on 26 September 2018, Member States committed to four new global targets. One target is to diagnose and treat 40 million TB cases

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in the 5 times from 2018 to 2022. The target breaks down to roughly 7 million people per time in 2018.[4]

The World Health Organization(WHO) provides an estimate of the global prevalence of isoniazid resistance in 2019, there were 1.4 million cases of isoniazid- resistant tuberculosis, of which 1.1 million were susceptible to rifampin.

1. numerous are not diagnosed with anti-TB medicines and do not admit applicable treatment. The DST) highlights the important part of laboratories in the rapid-fire and accurate discovery of TB and vaccination after 2015.
2. Of the 7 million new and returning cases reported in 2018, 5.9 million had TB. Among these, 55 were verified bacteriological conditions, a slight drop from 56 in 2017 and 58 in 2013. Abnormalities or reported histology.[1]

World Health Organization's Recommendations 1 original tests for estimation of TB with medicine-resistance detection.

In grown-ups with signs and symptoms of pulmonary TB

- Xpert MTB/ RIF should be used as individual test for TB and RR discovery in foam rather than smear microscopy/ culture and pDST.
- And without a previous history of TB (≤ 5 times) or with a remote history of TB Tx (> 5 times since end of Tx), Xpert Ultra should be used as individual test for TB and RR discovery in foam, to replace smear microscopy/ culture and pDST.
- And with a previous history of TB and an end of Tx within the last 5 times, Xpert Ultra may be used as individual test for TB and for RR discovery in foam, to replace smear microscopy/ culture and pDST.
- And Xpert Ultra trace positive result on the original test, repeated testing with Xpert Ultra may not be used.[1]

In children with signs and symptoms of pulmonary TB

Xpert MTB/ RIF or Xpert Ultra should be used as individual test for TB and RR in foam, GA, NPA and coprolite rather than smear microscopy/ culture and pDST.

- In settings with pretest probability below 5 and an Xpert negative result on the original test, repeated testing with Xpert MTB/ RIF or Xpert Ultra in foam, gastric fluid, nasopharyngeal aspirate or coprolite samples may not be used.
- In settings with pretest probability 5 or further and an Xpert negative result on the original test, repeated testing with Xpert MTB/ RIF or Xpert Ultra(for aggregate of two tests) in foam, gastric fluid, nasopharyngeal aspirate and coprolite samples may be used.[1]

Nucleic acid testing (NAT)

Nucleic acid testing (NAT) is a system used to hit upon nucleic acid sequences. Generally, NAT is used to discover and pick out precise pathogens or pathogens (together with disease- causing contagions or bacteria in the blood, apkins, or urine). NATs differ from other assessments in that they stumble on inheritable cloth(RNA or DNA) in preference to antibodies or both(it generally takes time for antibodies or antibodies to start to feel in the blood. Because inheritable cloth is generally low in quantum, numerous NATs correspond of way to round the inheritable material(as an illustration, making further than one clones)- a kind of NAT called a nucleic acid modification test(NAAT).[5] The inheritable cloth is amplified using the polymerase chain reaction (PCR) system, a popular system that calls for thermal cycling. still, a many strategies, which include the circle- intermediated isothermal modification(Beacon) system, do now not cycle but operate isothermally. Modification ways can come across amplicons incontinently the operation of fluorescent widgets, in which different strategies bear visual analysing. In general, four generation companies and 4 products are proposed Phenotypic Examinations Smear microscopy of acid-speedy bacilli(AFB) is the simple and maximum astronomically to be had individual approach for the prognostic of pulmonary TB(PTB).[6] Despite its benefits like cost effectiveness, ease of use, and operation in resource- confined settings, the important disadvantage of smear microscopy consists of its drop perceptivity (50 – 60) which has dropped its use in recent times. Another trouble of those molecular exams is the lack of differentiation among silent mutations from the mutations that bog down drug efficacy, resulting in an expanded fee of fake resistance results. Eleven in such times, whole genome sequencing (WGS) gives a complete analysis of the complete MTB genome with a 96%.[7]

New skin tests: The WHO recommends three new antigen-primarily based pores and skin tests for TB contamination: Cy-Tb, C-TST, and Diaskintest. These exams carry out better than tuberculin pores and skin tests, specifically in phrases of specificity.[8]

Xpert MTB/RIF and Truenat: These cartridge-based totally nucleic acid amplification exams (NAAT) are the WHO's recommended preliminary diagnostic tests for suspected pulmonary TB. They can come across TB DNA and commonplace mutations associated with rifampicin resistance in approximately hours. Molecular beacons: These oligonucleotides emit light when a chemical reaction takes place. A new test makes use of molecular beacons to unexpectedly discover mutations associated with drug resistance.[9]

Computer-aided detection (CAD): This technology uses virtual chest radiography for TB screening.

Aerosol-capture technology: These technologies hit upon TB disorder.

Other latest improvements in TB research and innovation:

Other latest improvements in TB research and innovation include: Culture-unfastened, focused-sequencing solutions to test for drug resistance immediately from sputum specimens Broth micro dilution methods for drug-susceptibility checking out (DST) New IGRAs to test for TB contamination Technologies advocated by way of World Health Organization: Molecular detection of TB ailment and/or drug resistance Xpert MTB/RIF, MTB/RIF Ultra and MTB/XDR, Cepheid, USA GenoType® MTBDRplus, Hain Lifescience/Bruker, Germany Genoscholar® NTM+MDRTB II; Nipro, Japan GenoType® MTBDRsl, Hain Lifescience/Bruker, Germany TB LAMP, Eiken, Japan Truenat MTB, MTB Plus and MTB-RIF Dx assays, Molbio Diagnostics, India FluoroType MTB and MTBDR assays Hain Lifescience, Germany Abbott RealTime MTB and MTB RIF/INH on m2000sp and m2000rt structures, Abbott, USA BD Max MDR-TB, Becton Dickinson, USA Roche cobas® MTB and MTB-RIF/INH on Cobas 6800/880 systems, Roche Diagnostics, Switzerland Genoscholar PZA TB II, Nipro, Japan Interferon gamma release assays (IGRAs) for TB contamination detection T-SPOT. TB, Oxford Immunotec, UK QuantiFERON-TB Gold Plus (QFT-Plus), Qiagen, USA Wantai TB-IGRA, Wantai, China Mycobacterium tuberculosis antigen-primarily based pores and skin assessments Diaskintest, JSC Generium, Russian Federation Cy-Tb pores and skin check, Serum Institute of India, India C-TST, Anhui Zhifei Longcom Biopharmaceutical Co. Ltd, China Culture-based technologies Commercial liquid way of life, DST structures and fast speciation Microscopy Light and mild-emitting diode microscopy (analysis and remedy monitoring) Biomarker primarily based assays Determine TB-LAM Ag, Abbott, USA Computer-aided detection (CAD) for digital chest radiography CAD4TB v6, Delft Imaging, Netherlands Lunit INSIGHT CXR (TB set of rules v4.9.Zero), Lunit, Republic of Korea qXR v2, qure. Ai, India.[9]

CONCLUSION

Since past 5-6 decades the diagnosis of Tuberculosis shifted to more on genomic side. The ease of using the techniques, rapid results, less quantity of chemicals and more accurate results makes genomic based assays more useful over traditional assays. The correct and timely diagnosis is always helpful for treatment and cure of diseases. The World Health Organization authorized many new techniques in past decades for accurate diagnosis of Tuberculosis.

The study revealed the use of genomic and nanotechnology has potential for more accurate and rapid diagnosis in coming future for stop tuberculosis strategy.

Conflict of Intestate: No conflict of interests

Funding: Not required

Ethics Declaration: Not applicable

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