



“Advancements And Innovations In Novel Drug Delivery Systems (NDDS): A Comprehensive Review”

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Abstract: The field of drug delivery has witnessed transformative advancements through the emergence of Novel Drug Delivery Systems (NDDS), which aim to optimize therapeutic efficacy, minimize side effects, and enhance patient compliance. This comprehensive review explores the latest innovations in NDDS, focusing on key technologies such as nanoparticles, liposomes, dendrimers, and transdermal systems. It highlights their applications in targeted drug delivery, controlled release mechanisms, and overcoming challenges associated with conventional methods, such as poor bioavailability and systemic toxicity. Furthermore, the article discusses the integration of nanotechnology, polymer science, and biotechnology in advancing NDDS, along with their implications in treating chronic diseases, cancer, and neurological disorders. Emphasis is also placed on regulatory challenges and future directions to ensure the successful translation of these innovations into clinical practice. This review underscores NDDS as a pivotal aspect of modern pharmacology, promising to redefine therapeutic strategies and improve global healthcare outcomes.

Index Terms – Novel Drug Delivery System (NDDS), Drug Delivery System (DDS), Nanoparticles (NPs).

I. INTRODUCTION

A Novel Drug Delivery System (NDDS) refers to the development of new pharmaceutical formulations that offer improved characteristics, such as reduced particle size, enhanced permeability, and targeted delivery to specific sites. These systems can significantly improve the efficacy of biotherapeutic agents, offering advantages over conventional dosage forms. Various design strategies exist for NDDS, and they have demonstrated effective clinical applications in treating a range of conditions. [1] The way a drug is delivered plays a crucial role in its effectiveness. Many drugs work best within a specific concentration range and exceeding or falling below this range can either cause toxicity or fail to provide any therapeutic benefit. However, the slow progress in treating severe diseases has highlighted the need for a more multidisciplinary approach to deliver treatments directly to tissue targets. This has led to the development of new methods for

controlling the pharmacokinetics, pharmacodynamics, toxicity, immunogenicity, and overall effectiveness of drugs. These approaches, known as drug delivery systems (DDS), combine expertise from fields like polymer science, pharmaceuticals, bioconjugate chemistry, and molecular biology. Current drug delivery and targeting systems aim to reduce degradation, minimize side effects, and improve drug bioavailability, ensuring that more of the drug reaches the desired site. The concept of controlled and novel drug delivery, once considered a distant possibility, is now a reality thanks to significant research and advancements made in the past decade and a half. [2] Traditional drug formulations often face issues like low bioavailability, instability, the first-pass effect, plasma fluctuations, and rapid drug release. Novel Drug Delivery Systems (NDDS) help address these challenges, improving performance, patient compliance, and shelf life. Nanoparticles, with sizes between 10 and 100 nm, are gaining attention for their environmental impact and potential in drug delivery. They can encapsulate or adsorb active agents and improve the pharmacodynamics and pharmacokinetics of drugs, enhancing targeted delivery to tissues. Nanoparticles also increase drug stability and retention at the target site, benefiting from solubilization and enzyme action. [3]

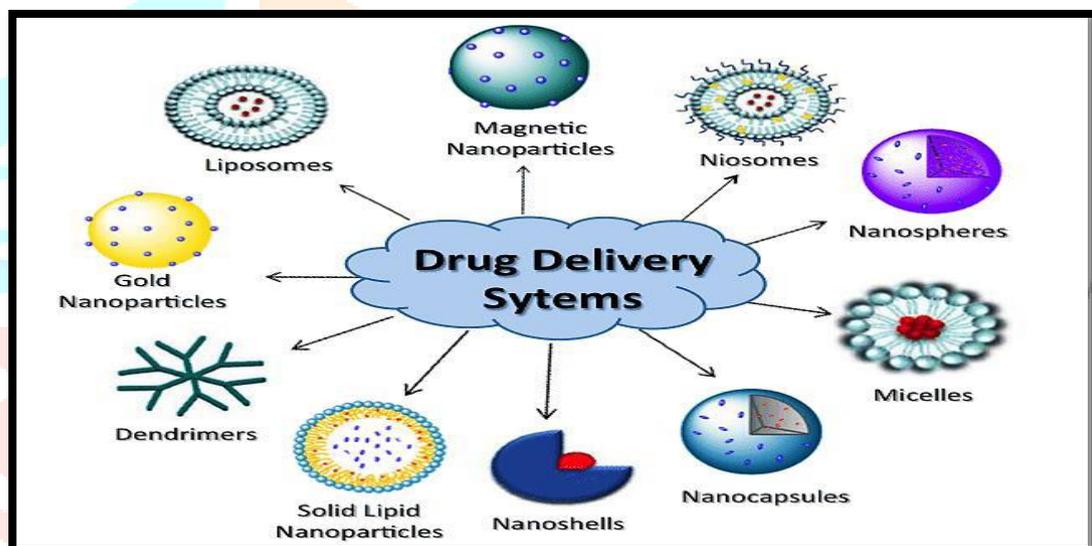


Figure No. 01: The several advance drug carrier in the novel drug delivery system (NDDS)

II. OBJECTIVE

The primary objective of Novel Drug Delivery Systems is to achieve site-specific drug action with an optimized rate and dosage regimen. This involves designing drug delivery nanoparticles with precise control over their particle size, surface characteristics, and release mechanisms for active pharmaceutical agents. The goal is to ensure that the medication delivers the desired therapeutic effect at the targeted site while minimizing side effects and avoiding adverse interactions with other tissues or organs. Novel Drug Delivery Systems aims to enhance the therapeutic index by improving the efficacy and safety profile of medications, resulting in a more effective and localized pharmacological response. [4]

Characteristic	Description	Example	Application
Controlled release	Drug is released at a predetermined rate over an extended period of time.	Transdermal patches, Implants, Oral extended-release tablets	Chronic diseases (e.g., hypertension, diabetes), Pain management, Vaccines
Targeted delivery	Drug is directed to a specific site in the body, reducing side effects and increasing efficacy	Liposomes, Nanoparticles, Antibody-drug conjugates	Cancer therapy, Gene therapy, Infectious diseases
Mucosal delivery	Drug is absorbed through the mucosal membranes of the nose, mouth, or lungs	Nasal sprays, Inhalers, Buccal patches	Allergies, Asthma, Pain relief
Transdermal delivery	Drug is absorbed through the skin.	Patches, Gels, Creams	Pain relief, Hormone replacement therapy, Smoking cessation
Implantable delivery	Drug is released from a device implanted in the body.	Biodegradable implants, Pumps	Cancer therapy, Chronic pain management, Contraception
Responsive delivery	Drug release is triggered by a specific stimulus, such as changes in pH, temperature, or enzymes	Glucose-responsive insulin delivery systems, Tumor-activated drug delivery systems	Diabetes, Cancer therapy

Table No. 01: The list of characteristics, description, example and their application of novel drug delivery system

TYPES OF NOVEL DRUG DELIVERY SYSTEM (NDDS)

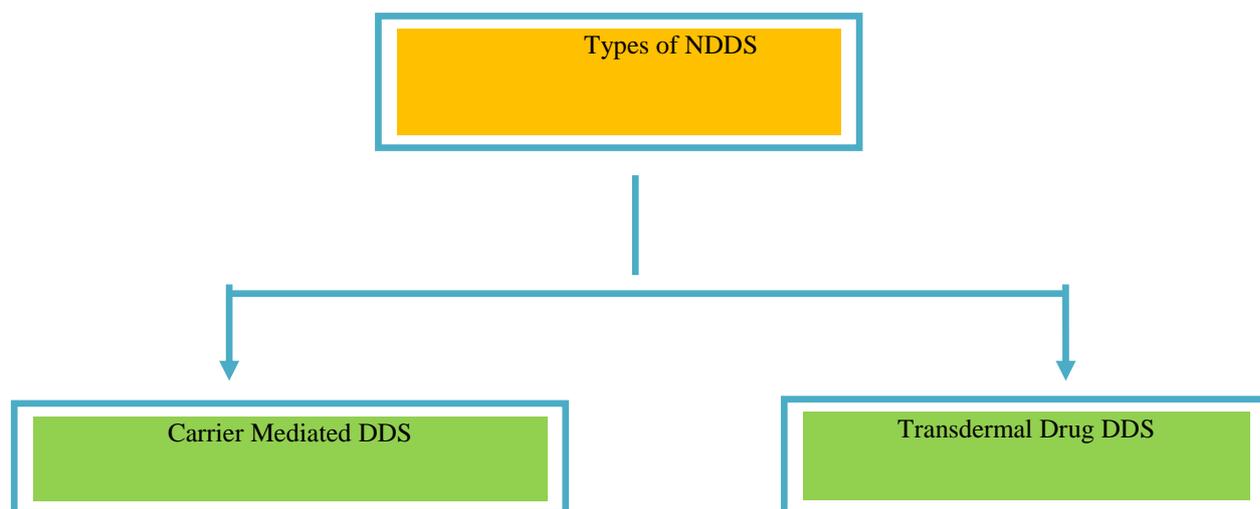


Figure No. 02: The major types of NDDS as carrier mediated and Transdermal DDS

➤ The benefits of these modern systems include :

1. improved drug efficacy
2. precise site-specific delivery
3. reduced toxicity and side effects
4. greater convenience
5. potential for treating previously untreatable conditions prophylactic applications and enhanced patient compliance.[5]

❖ Carrier Based Drug Delivery System

1. Nanoparticles
2. Microsphere
3. Liposomes
4. Niosomes
5. Monoclonal Antibodies
6. Resealed Erythrocytes as Drug carriers
7. Polymer Micelle
8. Hydrogel

1. NANOPARTICLES

Nanoparticles (NPs) are tiny particles, measuring between 1 to 100 nanometers that are transforming medicine and technology due to their unique properties. Their small size gives them a high surface area relative to their volume, enabling them to engage with biological systems on a cellular and molecular scale.

Composition:

The composition of nanoparticles can vary based on their intended application. Materials such as gold, silver, silica, polymers, and lipids are commonly used, each providing distinct properties that can be customized for specific purposes.

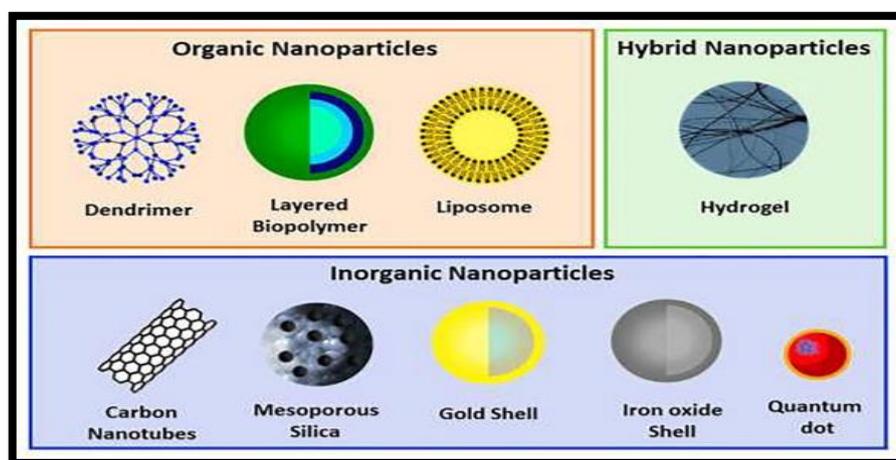


Figure No. 03: The schematic classification of Nanoparticles (NPs)

- Metallic Nanoparticles:** Made from metals like gold and silver, often used in diagnostics and therapeutics.
- Polymeric Nanoparticles:** Composed of biocompatible polymers, suitable for drug delivery and imaging.
- Lipid Nanoparticles:** Liposomes and solid lipid nanoparticles used for drug delivery and gene therapy.
- Ceramic Nanoparticles:** Inorganic materials with applications in catalysis, electronics, and biomaterials.

Nanoparticles are commonly used in drug delivery systems because they can encapsulate drugs, protect them from degradation, and provide controlled release. The enhanced permeability and retention (EPR) effect enables nanoparticles to accumulate specifically in tumor tissues. Given their unique properties, nanoparticles continue to be a major focus of research, offering a wide range of potential applications in various fields. [6]

2. MICROSPHERE

Microspheres are small spherical particles, typically ranging from 1 to 50 μm in size, used in drug delivery systems to target specific sites and maintain the desired drug concentration without causing side effects. Microencapsulation helps prolong drug effects, improving patient compliance while reducing adverse reactions and ensuring a steady plasma concentration. Various plant-based active ingredients, like rutin and quercetin, have been developed into microspheres. Additionally, immune and magnetic microspheres, which incorporate antibodies or antigens for immune function, have gained attention in recent years. [7]

3. LIPOSOME

Liposomes are spherical vesicles with a lipid bilayer, widely used as carriers in cosmetics and pharmaceuticals to enhance drug delivery. They improve antibiotic efficacy by increasing pharmacokinetics, reducing toxicity, and enhancing interaction with bacteria. Liposomal formulations, such as those containing fluoroquinolones and aminoglycosides, lower MIC values for Gram-positive and Gram-negative bacteria. Cationic liposomes and proteoliposomes show promise in targeting bacterial biofilms, with some lipids also acting as anti-infective agents. By altering drug absorption, metabolism, and half-life, liposomes enhance therapeutic outcomes, and research on new formulations continues. [8]

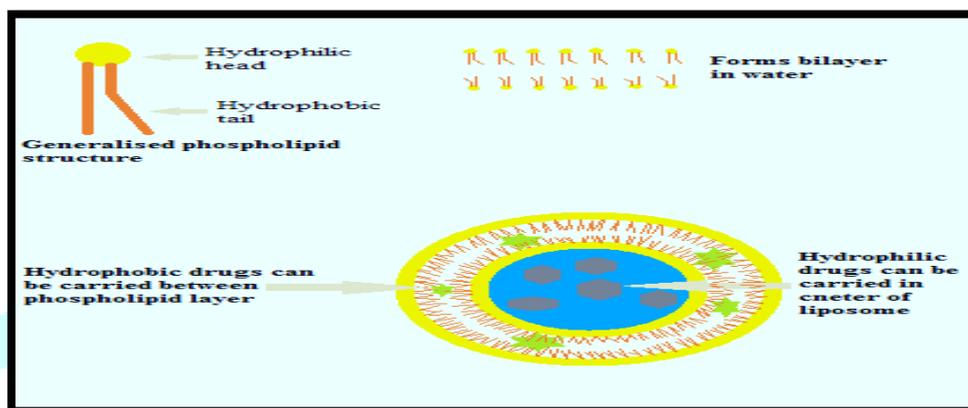


Figure No. 04: Structure of bilayer liposomes

4. NIOSOME

Niosomes are nonionic surfactant-based vesicles, structurally similar to liposomes but more stable due to their composition, often including cholesterol and other excipients. They have enhanced penetration capabilities compared to emulsions and offer several advantages over liposomes. Niosomes are microscopic, with particle sizes typically ranging from 10 to 100 nm. [9]

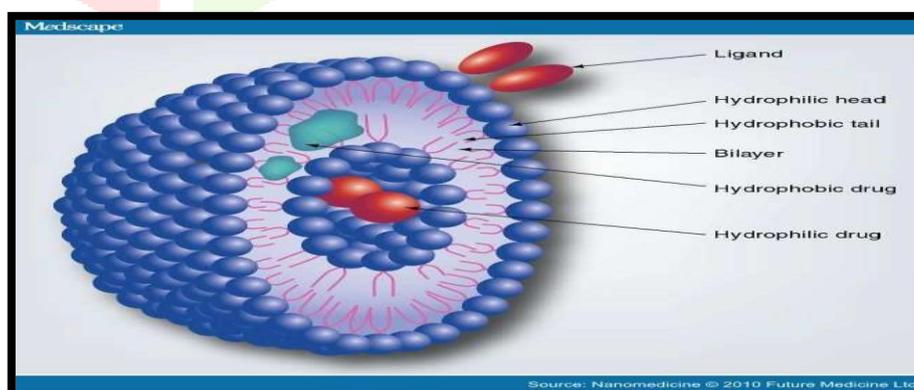


Figure No. 05: Structure of Niosomes

5. MONOCLONAL ANTIBODIES

Monoclonal antibodies are uniform antibodies targeting specific antigens, often used to deliver cytotoxic drugs to cancer cells while sparing normal cells. They are also explored as sensitive probes for targeting cells or organs and for delivering enzymes or drugs. These antibodies are valuable in diagnosing and treating conditions like multiple sclerosis, heart diseases, leukemias, and malaria.

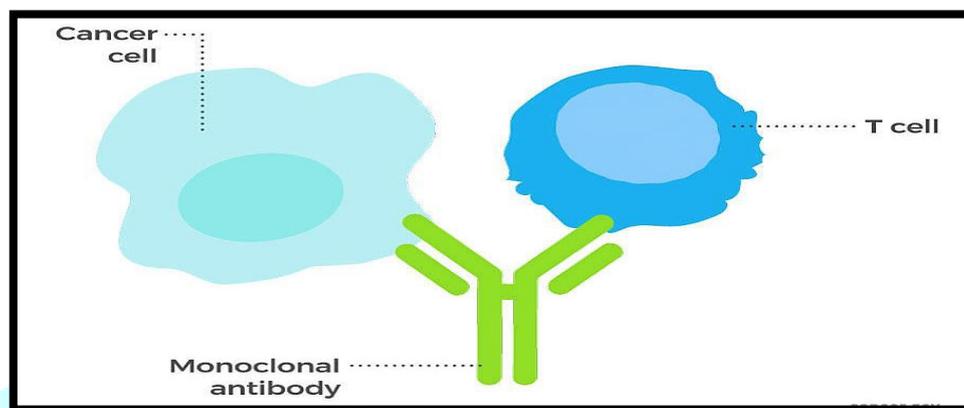


Figure No. 06: Monoclonal Antibodies

6. RELEASED ERYTHROCYTES AS DRUG CARRIER

Red blood cells (RBCs), or erythrocytes, are explored as drug delivery systems called "resealed erythrocytes," created by isolating and loading drugs into cells before resealing them. These carriers can hold various active compounds and act as slow-release depots, targeting the reticuloendothelial system, reducing drug degradation, maintaining steady drug levels, and minimizing side effects. [10]

7. POLYMER MICELLES

Polymer micelles, formed by amphiphilic block copolymers, are stable, nanosized carriers ideal for hydrophobic drug delivery. Their hydrophilic shell prevents premature clearance, allowing extended circulation and targeted delivery. They are used in antifungal therapy, cancer treatment, and traditional medicine, effectively delivering drugs like paclitaxel and curcumin. With clinical trials ongoing, micelles are promising tools for improving drug solubility, targeting, and therapeutic outcomes.

8. HYDROGEL

Hydrogels, water-swallowable polymer networks, are valued for their biocompatibility and low toxicity in drug delivery. They enhance tumor therapy with near-infrared activation for intracellular drug release and support wound healing by aiding fibroblast migration and angiogenesis. Hydrogels also deliver immune adjuvants, sustain drug release in veterinary vaccines, and combat resistant bacteria like MRSA. While challenges like rapid disintegration in oral delivery exist, hydrogels hold promise for controlled, site-specific drug delivery, with ongoing research aimed at improving in vivo performance. [11]

❖ **Transdermal Drug Delivery Systems:**

1. Sonophoresis
 - a. Mucoadhesive delivery systems
 - b. Supramolecular delivery systems
 - c. Variable release delivery systems
2. Osmotic pump
3. Microencapsulation

2. TRANSDERMAL DRUG DELIVERY SYSTEM:

Over the past decade, controlled release technology has gained attention due to the limitations of conventional drug delivery methods, which often cause fluctuating drug levels and toxicity. Transdermal drug delivery systems (TDDS) have emerged as a solution, using the skin for systemic treatment through controlled drug release. Inspired by medicated plasters from China and Japan, TDDS bypasses gastrointestinal absorption issues, ensures consistent drug levels, reduces side effects, and allows rapid cessation of therapy when needed. [12]

❖ **Advantages:** The transdermal route of drug delivery is an attractive option due to its convenience and safety. Key advantages of using this method to achieve systemic effects include:

- ✓ Drugs bypass hepatic and presystemic metabolism, avoiding first-pass metabolism and improving bioavailability.
- ✓ It eliminates the risks and drawbacks associated with IV therapy.
- ✓ It allows for self-administration.
- ✓ It helps minimize undesirable side effects.
- ✓ Drug level fluctuations are avoided.
- ✓ Plasma concentrations of potent drugs are maintained.
- ✓ Therapy can be stopped at any time.
- ✓ The drug can be delivered more precisely to a specific site.
- ✓ It improves patient compliance and ease of administration.
- ✓ It enhances therapeutic efficacy. [13]

2.1 SONOPHORESIS

Ultrasound in the range of 20 to 100 kHz can increase skin permeability for transdermal drug delivery by causing cavitation, which creates areas of high permeability. Drugs can be applied either after a brief ultrasound session or alongside it. Adjustable parameters, such as frequency, intensity, and application time, allow for a controlled and reversible skin breach. Devices like SonoPrep use low-frequency ultrasound (55 kHz) to enhance permeability quickly, facilitating faster local anesthetic absorption. Additionally, research has explored the use of small ultrasound transducers to improve insulin delivery through the skin. [14]

a) Mucoadhesive Drug Delivery Systems

A study on bioadhesive liposomes for controlled levonorgestrel delivery found that the mesophase proliposomal system mainly consisted of unilamellar and some multilamellar vesicles. The drug release followed zero-order kinetics, with alcohol improving transdermal flux more than oils. In vivo results showed a delay in reaching therapeutic levels, indicating the need for a loading dose. The proliposomal system outperformed a PEG-based ointment. A liposomal reservoir for benzocaine was also developed for controlled, localized delivery via topical application, offering sustained release over 24 hours, in contrast to the rapid release from plain ointment. In vivo studies showed a longer duration of action with the liposomal formulation. [15]

b) Supramolecular Drug Delivery Systems

A supramolecular system is formed by two or more molecular entities bound together by non-covalent interactions. Macrocyclic compound structures have become important models for exploring natural self-assembly and molecular recognition, and for creating new nanomaterials applicable in electronics, biomedicine, and pharmaceuticals

c) Osmotically Controlled Drug Delivery Systems:

Osmotic drug delivery systems use osmotic pressure to control the release of drugs, making them well-known and extensively researched. Alza pioneered the development of these systems and holds numerous patents on osmotic technology, offering products based on this method. These systems are used for both oral administration (gastrointestinal therapeutic systems, GITS) and parenteral administration (implantable pumps).

2.2 CLASSIFICATION OF OSMOTIC DRUG DELIVERY SYSTEM: Many forms of osmotic pumps are reported in the literature but, in general they can be divided in oral and implantable.

- a. **Single chamber osmotic pump:** Elementary osmotic pump
- b. **Multi chamber osmotic pump:** Push pull osmotic pump, Osmotic pump with non expanding second chamber
- c. **Specific types:** Controlled porosity osmotic pump, Osmotic bursting osmotic pump, Liquid OROS, Delayed Delivery Osmotic device, Telescopic capsule, Oros ct (colon targeting), Sandwiched oral therapeutic system, Osmotic pump for insoluble drugs, Monolithic osmotic system and OSMAT 40 .[11]

2.3 MICROENCAPSULATION

Microencapsulation involves enclosing solids, liquids, or gases in microscopic particles with a thin polymer coating. It originated in the 1930s for use in business machines and later evolved in the 1950s with the development of reproduction paper containing dye-filled gelatin capsules. This led to the creation of microencapsulated materials, including drugs, to enhance therapeutic efficacy by delivering controlled doses to target tissues with minimal toxicity and side effects. Microspheres, made from biodegradable proteins or synthetic polymers, are one such method for sustained drug delivery. Bioencapsulation, a subset of microencapsulation, focuses on trapping biologically active substances to improve performance and shelf life. [16]

❖ APPLICATIONS OF NOVEL DRUG DELIVERY SYSTEMS

Sustained and controlled- drug delivery

Novel Drug Delivery Systems (NDDS) improve the pharmacokinetics and pharmacodynamics of drugs, offering more effective antibiotic delivery for H. Pylori treatment and reducing the need for frequent administration through sustained-release implants. NDDS technologies, such as microparticle systems, are used to create sustained-release formulations for short-acting peptides like leuprorelin acetate and triptoreline, treating conditions like prostate cancer and endometriosis. Other peptides, including L-158809 for hypertension and salmon calcitonin for hypercalcemia, are also formulated as sustained-release micro particles. [17]

CONCLUSION

The conclusion of the review emphasizes that advancements in Novel Drug Delivery Systems (NDDS) are transforming the way medicines are developed and delivered. These innovations focus on improving how effectively drugs work, reducing side effects, and making treatments more convenient for patients. NDDS offers promising solutions to longstanding challenges in healthcare, helping to create safer and more personalized therapies for better patient outcomes.

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