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**Next-Gen Therapeutics:
Bioengineering at the
Molecular Scale**

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Article 1:

Next-Gen Therapeutics: RNA Medicines and Molecular Biosensors Are Re-writing How We Treat and Track Disease

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From the COVID-19 mRNA vaccines to app-connected glucose monitors, the last few years have made something clear: biology is becoming programmable. Two fast-moving fronts-RNA therapeutics and molecular biosensors-illustrate how engineering at the molecular scale is reshaping both treatment and real-time care. This article tours each area with current, concrete examples and the science that powers them.

1) RNA therapeutics: treating disease by writing messages

What they are. RNA medicines use short, designed nucleic acids to modulate gene expression in human cells. Messenger RNA (mRNA) delivers protein “blueprints,” while small interfering RNA (siRNA) and antisense oligonucleotides (ASOs) silence or edit messages by recruiting RNase H or the RNA-induced silencing complex (RISC). The therapeutic logic is elegant: if a disease is driven by too much of protein X, instruct cells to make less; if you need more of protein Y, transiently supply the instructions to make it. Clinically, this has moved from promise to practice. The first FDA-approved siRNA, patisiran (Onpattro) for hereditary transthyretin amyloidosis (hATTR), arrived in 2018, proving RNA interference can work in humans (Coelho et al., 2023).

Approvals you should know. Since patisiran, the RNA toolbox has widened. Vutrisiran (Amvuttra), another siRNA against transthyretin, gained approval in 2022, offering subcutaneous dosing and durable knockdown (Yu et al., 2024). In cardiovascular disease, inclisiran (Leqvio) uses siRNA to reduce hepatic PCSK9 production, lowering LDL-cholesterol with just two maintenance injections per year (Novartis, 2021). ASOs are advancing too: nusinersen (Spinraza) was the first disease-modifying therapy for spinal muscular atrophy by correcting SMN2 splicing, approved in 2016 (U.S. FDA, 2016). More recently, eplontersen (Wainua), a ligand-conjugated ASO that depletes transthyretin mRNA, was approved in 2023 for hATTR polyneuropathy (Coelho et al., 2023; U.S. FDA, 2023).

Why delivery tech is the real star. RNA is fragile and polyanionic; getting it into the right cells matters as much as the sequence itself. Two engineering breakthroughs dominate:

- **Lipid nanoparticles (LNPs)** encapsulate and ferry mRNA into cells, using pH-responsive ionizable lipids to promote endosomal escape. LNPs enabled the first mRNA vaccines and remain the most mature platform for systemic delivery (Hou et al., 2021; Jung et al., 2022).
- **GalNAc (N-acetylgalactosamine) conjugation** tethers siRNA/ASOs to a sugar that binds the asialoglycoprotein receptor on hepatocytes, creating highly efficient liver-specific uptake after a simple subcutaneous shot—precisely why many early RNA drugs target liver-made proteins (Yu et al., 2024; Zhang et al., 2024).

What's newest at the frontier. Personalized cancer vaccines based on individualized neoantigen mRNA are moving through late-stage testing. In a randomized phase 2b study in resected high-risk melanoma, Moderna's mRNA-4157/V940 plus pembrolizumab improved three-year outcomes compared with pembrolizumab alone, catalyzing phase 3 trials (Weber et al., 2024). Meanwhile, delivery science is racing ahead: organ-selective LNPs and improved ionizable lipids aim to reach tissues beyond the liver—lungs, spleen, and even bone—broadening the disease map for RNA therapies (Yu et al., 2024; Jung et al., 2022). So what? RNA therapeutics compress the drug-development cycle. Once delivery and safety are established, swapping a sequence lets you retarget a new gene quickly. For genetic diseases, metabolic disorders, and oncology, that speed and modularity are game-changers.

2) Molecular biosensors: from snapshots to continuous, personalized care

What they are. Molecular biosensors transduce biochemical events (like glucose, lactate, troponin, cytokines, or tumor DNA) into readable electrical or optical signals. The shift from lab-based assays to on-body, continuous sensing means therapy can be titrated to physiology in real time.

The flagship case-diabetes. Continuous glucose monitoring (CGM) has transformed diabetes care by streaming interstitial glucose every few minutes, enabling closed-loop insulin delivery (the “artificial pancreas”). Next-gen devices such as the Dexcom G7 and FreeStyle Libre 3 are smaller, more accurate, and integrate with automated insulin delivery systems (Dexcom, 2022). Randomized trials show hybrid closed-loop systems improve time-in-range and hemoglobin A1C across age groups, including very young children and pregnant women (Wadwa et al., 2023; Ware et al., 2022). Reflecting this, the American Diabetes Association Standards of Care 2024/2025 recommend early CGM use and broader adoption, even for many with type 2 diabetes (American Diabetes Association [ADA], 2024a; ADA, 2024b; ADA, 2024c).

Beyond glucose—what's next? Engineers are translating lab immunoassays into wearable or near-patient biosensors for high-value biomarkers:

- Cardiac troponin I (cTnI) for early heart-attack detection: rapid, ultrasensitive electrochemical and optical sensors are approaching real-time monitoring (Shrivastav et al., 2024).
- Sweat analytics (electrolytes, lactate, hormones, and even drugs): flexible, skin-interfaced sensors and microfluidics enable non-invasive, continuous sampling. While validation versus blood remains critical, recent reviews highlight rapid progress in sensor design (Min et al., 2023).

Consumer products like athlete-focused hydration patches hint at near-term adoption, even as the evidentiary bar for medical decision-making remains high.

Why sensors matter for therapy. Continuous data closes the loop: therapy can adapt to you, not averages.

- In diabetes, coupling CGM with adaptive algorithms dynamically tunes insulin (Wadwa et al., 2023).

- In cardiology, miniaturized troponin sensors could accelerate triage and enable home monitoring after high-risk procedures (Shrivastav et al., 2024).
- In inflammation or oncology, future wearables might track cytokines or tumor markers to time dosing “windows” or flag relapse earlier than imaging.

Engineering levers. Progress hinges on four areas: (1) biorecognition (antibodies, aptamers, molecularly imprinted polymers), (2) transduction (electrochemical impedance, field-effect, fluorescence, SERS), (3) materials (nanoporous gold, graphene, hydrogels), and (4) systems integration (skin-safe adhesives, antifouling coatings, low-power radios). The most impactful advances combine all four—such as sweat microfluidics paired with antifouling nanofilms and ratiometric optical readouts for drift-resistant, on-body quantitation (Min et al., 2023).

The convergence: “sense-and-respond” medicine

Put these threads together and you get a compelling future: RNA drugs provide programmable interventions; biosensors stream personal biology; and algorithms coordinate the two.

- **Highly targeted cardio-metabolic care.** An LDL-lowering siRNA such as inclisiran can keep PCSK9 suppressed for months with two doses a year, while home lipid testing and cardiac sensors could personalize secondary prevention (Novartis, 2021).
- **Oncology, individualized and dynamic.** Neoantigen mRNA vaccines train immunity to a patient’s tumor mutations; biosensors could track responses and help time booster doses or add-on therapies (Weber et al., 2024).
- **Rare diseases at scale.** GalNAc-conjugated oligos already simplify dosing. As organ-selective LNPs mature, RNA medicines may move beyond the liver, while sensors verify target engagement and safety remotely (Yu et al., 2024).

Challenges worth watching

1. **Delivery beyond the liver.** GalNAc cracked hepatocyte targeting; the next leap is safe, efficient delivery to heart, lung, or CNS (Yu et al., 2024).
2. **Immunogenicity and durability.** Modified nucleotides and ionizable lipids reduce immune activation but repeat dosing and long-term safety remain under study (Hou et al., 2021; Jung et al., 2022).
3. **Sensor calibration and validation.** For non-glucose analytes, sweat/blood correlation, drift, and fouling remain hurdles; head-to-head trials will determine which readouts become standard of care (Min et al., 2023).
4. **Equity and access.** CGM coverage has broadened, but costs, training, and data connectivity still create disparities (ADA, 2024b).

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Article 2:

Personalized CRISPR base-editing therapy - A breakthrough in Gene Therapy



Dr. Shalaka Patil (Assistant Professor, DoBT)

2025 marked a major scientific milestone as the world's first CRISPR-therapy on a patient, offering a precision cure for an ultra-rare genetic disorder, was performed in February 2025 ([Musunuru et al., 2025](#)). Children's Hospital of Philadelphia and Penn Medicine administered a novel, personalized CRISPR base-editing therapy to a six-month-old infant named KJ, born with severe carbamoyl phosphate synthetase 1 (CPS1) deficiency, an extremely rare urea-cycle disorder ([Sepp-Lorenzino, 2025](#)). KJ had elevated ammonia levels, threatening his brain and liver. Before this treatment, his survival strategy included harsh protein restriction and the use of nitrogen-scavenger drugs. These approaches barely managed the symptoms, but not the root cause. Today, early data suggest that CRISPR base-editing therapy not only reversed the metabolic dysfunction but also allowed KJ to tolerate more protein and reduce medication, a promising sign that his underlying condition is improving.

From Genome “Misspelling” to Precision Medicine

Urea-cycle disorders, such as CPS1 deficiency, are characterized by incompetency in converting toxic ammonia into urea for elimination - a process requiring precise enzyme function in liver cells ([Diez-Fernandez & Häberle, 2017](#)). Lack of this conversion during protein catabolism results in the accumulation of ammonia, which quickly reaches neurotoxic levels.

KJ inherited two rare mutations in the CPS1 gene, one of which had previously been documented in other patients. Instead of waiting months or years for a traditional liver transplant, researchers in the USA decided to correct the specific DNA base error using CRISPR-based adenine base editors (ABEs) ([Eghbalsaied et al., 2024](#)). Unlike standard CRISPR-Cas9, which cuts DNA, base editors chemically convert one nucleotide to another - ideal for single-base misspellings like those seen in KJ (Figure 1C) ([Anzalone, Koblan, & Liu, 2020](#)). This technology uses adenine deaminase, fused with a Cas9 protein, to facilitate the conversion of adenosine to inosine (A to I). These converted bases are then recognized by cellular DNA repair mechanisms, leading to the desired base change (A to G).

Building a Bespoke Therapy in Just Six Months

After KJ was born (August 2024), the doctors at the Hospital of the University of Pennsylvania (Penn) noticed something was wrong. Though the baby seemed healthy at birth, he had become unusually

lethargic in just two days ([Musunuru et al., 2025](#)). He did not eat and struggled to maintain body temperature. The doctor checked KJ's blood ammonia level, a marker for some metabolic diseases, and found that it was extremely high. KJ was diagnosed with CPS1 deficiency, a rare urea cycle disorder. It's a genetic condition caused by a deficiency in carbamoyl phosphate synthetase 1 and leads to a toxic buildup of ammonia in the body (hyperammonemia) ([Diez-Fernandez & Häberle, 2017](#)). Left unchecked, the toxic accumulation can be fatal. KJ was placed on dialysis to filter the ammonia out of his blood and stabilize his condition while clinicians considered long-term treatment. At the time, the only lifesaving treatment for CPS1 deficiency was a liver transplant, which is rare and often better suited to children who are older and in better health ([Häberle et al., 2012](#)).

In 2023, Dr. Rebecca Ahrens-Nicklas, a pediatric geneticist, CHOP's Metabolic Disease Program, and Dr. Kiran Musunuru, a cardiologist, geneticist and gene editor at Penn. initiated a collaborative framework supported by the Somatic Cell Genome Editing Consortium of National Institute of Health (NIH) USA to develop "n-of-1" (single subject) therapies comprising custom treatments tailored to a single patient's mutation ("CRISPR Gene Editing Outpaces Gene Therapy: The Groundbreaking Case of KJ Muldoon - DNA Science," n.d.). The plan was to scale this approach for individual rare-disease patients. Once KJ's precise genetic mutation was confirmed, teams from CHOP, Penn Medicine, UC Berkeley's Innovative Genomics Institute (IGI), and company partners (Danaher/Aldevron, Integrated DNA Technologies, Acuitas Therapeutics) came together to develop the n-of-1 pipeline as follows, from corrective mutation to dosing:

1. Design: Develop guide RNA (gRNA) and optimize an Adenine Base Editor (ABE) to precisely target KJ's CPS1 mutation. This was developed using the genome sequencing data of KJ and his father.
2. Preclinical Safety/Efficacy: Use of cell culture models to confirm editing efficiency and to perform off-target analysis of ABE using CHANGE-seq-BE in a few weeks.
3. Manufacturing: Producing clinical-grade ABE packaged in lipid nanoparticles (LNPs) for liver-specific delivery.
4. FDA Engagement: Submit data and secure emergency IND-fast-track approval from the FDA (Food and Drug Administration) at NIH USA in just one week.
5. Clinical Dosing: The first low-dose infusion was done on February 25, 2025, followed by two escalated doses in March 2025 and April 2025.

This was an exceptionally rapid strategy to invent and administer a precise therapy, which was made possible by integrative scientific efforts and a pre-existing logistics framework ([Musunuru et al., 2025](#))

Preliminary findings and perspectives

By April 2025, following three gene-editing infusions, no serious adverse events have been reported for KJ. He began tolerating more dietary protein. KJ's medication has also been reduced significantly, including the use of ammonia-lowering drugs. He recovered from a viral illness (like a rhinovirus) without dangerous ammonia spikes, indicating an improvement in immune resilience ([Ledford, 2025; Musunuru et al., 2025](#)). He has also started sitting upright, which is an important developmental milestone for babies. KJ has been discharged home after a seven-month critical period. These outcomes reflect proof-of-concept for utilizing personalized CRISPR-base editing therapy to treat genetic diseases ([Musunuru et al., 2025](#)). KJ's story marks the first successful clinical case with in vivo, personalized CRISPR base-editing therapy, offering a powerful proof-of-concept for treating fatal, ultra-rare genetic diseases ([Sepp-Lorenzino, 2025](#)).

Although early observations show promising outcomes for KJ, there are some outstanding questions - Will one-time base editing provide a lasting cure or attenuated phenotype? Will off-target events or immune reactions emerge over time? Will improved ammonia control translate into sustained neurological development? Therefore, long-term monitoring of KJ's physiological conditions, growth milestones, liver biopsy, and genomic follow-up remains essential to assess the durability and safety of this treatment. Moreover, expanding this strategy to other urea-cycle disorders or metabolic diseases will depend on the quick identification of the base-editable mutations and the availability of pre-existing infrastructure. Academics and industry experts recognize this as a blueprint for future personalized gene therapies. If it turns out to be reproducible and financially sustainable, it can revolutionize treatments for ~7,000 known rare genetic diseases.

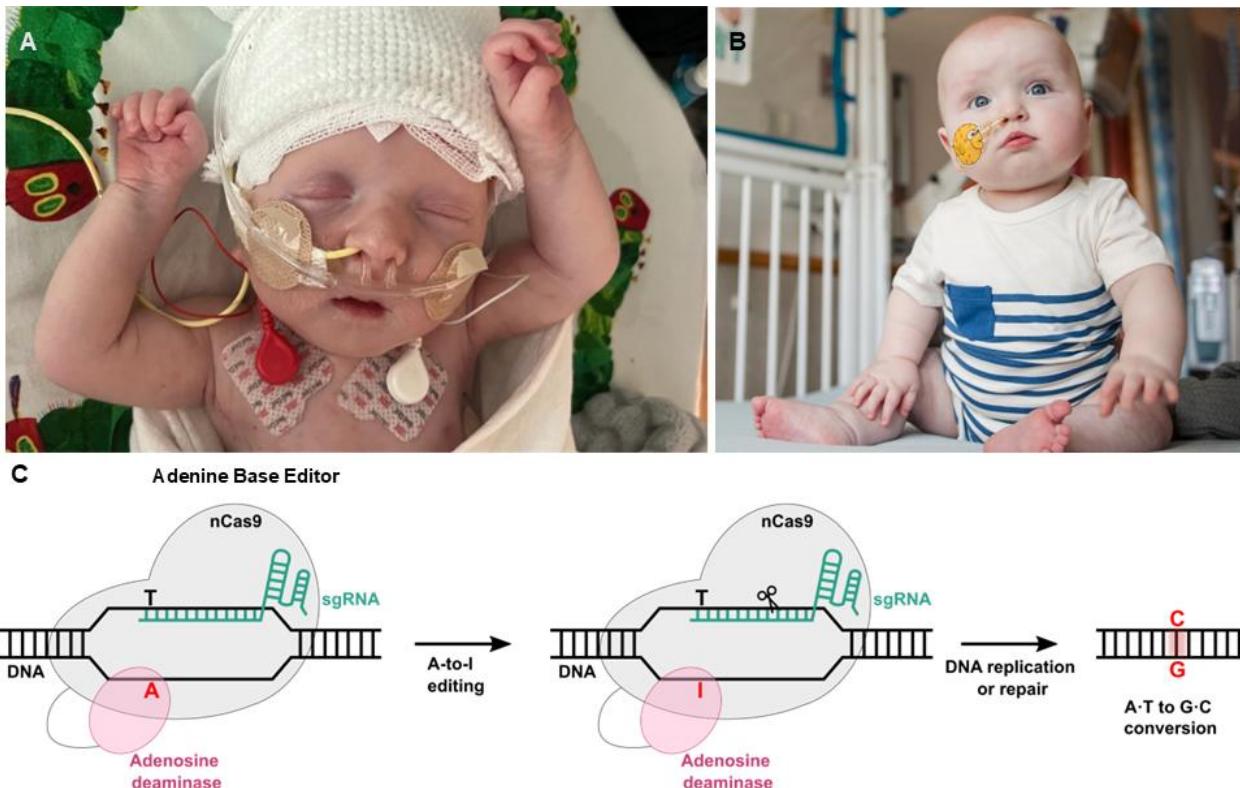


Figure 1: **A.** KJ was two days old when his hyperammonemia was detected **B.** KJ after three infusions of precision medicine **C.** CRISPR-Adenine Base Editor for the correction of single-nucleotide mutations

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Article 3:

Reinventing Medicine: Molecular-Scale Bioengineering Ushers in a New Therapeutic Era

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Introduction:

Across the cutting-edge labs of biotech hubs, a revolution is unfolding: therapeutic strategies are now being engineered at the molecular level, ushering in a new wave of precision medicine. From programmable nucleic acids to designer proteins and synthetic biomaterials, molecular-scale bioengineering promises more effective, personalized, and durable treatments than ever before.

The Frontier: Precision at the Atomic Level

Traditional small-molecule drugs and biologics like monoclonal antibodies have long underpinned modern medicine. Yet these treatments often act broadly, climbing into side effects or losing effectiveness over time. Enter molecular-scale bioengineering, where researchers choreograph interactions between individual molecules of RNA, proteins, lipids, and sugar scaffolds to achieve unparalleled control.

As Dr. Maya Lin, a synthetic biologist at the forefront of this field, puts it: “We’re no longer just discovering natural biology—we’re redesigning it. At the molecular level, we can specify how a therapeutic interacts with, when, where, and how long.” [[Qi, L. S., Larson, M. H., et.al \(2013\)](#)]

Synthetic RNA Therapeutics: Beyond mRNA Vaccines

The explosive success of mRNA vaccines launched RNA therapies into the spotlight. But now, tailored nucleic acid molecules—aptamers, siRNAs, and guide RNAs—are being engineered to function with surgical precision:

Aptamers are single-stranded nucleic acids folded into complex structures that can bind specific proteins like tiny antibodies, without requiring an immune response. When folded just so, an aptamer can disable a disease-causing enzyme with nanomolar affinity.

siRNAs (small interfering RNAs) can flag mutant proteins for destruction. Next-gen chemical modifications can now make them last longer and enter cells more efficiently.

CRISPR guide RNAs, paired with precision-engineered Cas proteins, can be programmed to repair or disable genes in situ. Companies like Beam Therapeutics are developing base editors to correct single-letter mutations, with no double-strand breaks, enhancing safety.

These RNA molecules aren't just powerful, they can be modular, delivered together in lipid nanoparticles, and designed to shut down disease processes only in specific tissues. [Kwon, Y. J., James, et.al \(2017\)](#)

Designer Proteins: Engineering Nature's Workhorses

Proteins accomplish most of the cell's heavy lifting, and molecular bioengineers are now customizing them:

De novo enzymes are being built to catalyze novel reactions, like converting metabolic waste to therapeutic compounds. The computational tools behind Rosetta and AlphaFold2 allow us to design entirely new protein folds and active sites not found in nature.

REINVENTING MEDICINE

MOLECULAR-SCALE BIOENGINEERING USHERS IN A NEW THERAPEUTIC ERA



Bispecific and multispecific antibodies leverage precise linkers that bring immune cells into proximity with cancer cells, only where needed.

Protein-based logic circuits: Designer proteins can act as logic gates, sensing multiple molecular cues (e.g., the presence of two tumor markers) before triggering a therapeutic response like toxin release or cell death. [[Anzalone, A. V., Koblan, L. W., et.al \(2020\)](#)]

Such proteins are engineered not just to bind or cut, but to compute, sense, and respond in real time within living systems.

Nanodevices and Biomaterial Scaffolds

Parallel to RNA and protein therapies, molecular engineering of materials is delivering breakthroughs:

DNA origami nanorobots fold strands of DNA into hollow cages loaded with drugs. They remain inert until they encounter the right molecular “lock”—say, a tumor-specific antigen—then open to release payloads precisely where needed.

Lipidoid nanoparticles can be tuned in charge, size, and hydrophobicity so that they circulate safely and home in on the liver, lungs, bone marrow, or tumors. By chemically tailoring each lipid tail, scientists control biodistribution with molecular specificity.

Self-assembling peptide hydrogels act as 3D scaffolds for tissue repair, created from designer peptides that respond to environmental cues like pH or enzymes. These can support cell growth or locally deliver growth factors with spatiotemporal precision. [[Mullard, A. \(2021\)](#)]

Key Applications: From Rare Disease to Cancer

1. Genetic Disorders

One of the most promising areas is the treatment of rare genetic diseases. Conditions caused by a single gene mutation—like Duchenne muscular dystrophy or spinal muscular atrophy—are targets for molecular editing. Base editors can correct pathogenic single-nucleotide variants in muscle cells, restoring protein function with minimal off-target activity.

2. Cancer Therapeutics

Engineered protein–RNA drug combinations can recruit T cells only where cancer antigens are present. Molecular logic gates guard against “on-target, off-tumor” toxicity. Some therapies use multiplexed guide RNAs to edit tumor suppressor pathways directly in malignant cells.

3. Autoimmune Conditions

Designer cytokine mimetics with modified receptor-binding surfaces can dampen overactive immune responses. Nanoscale delivery vehicles loaded with tolerogenic peptides are being trialed in multiple sclerosis and lupus to re-educate immune cells.

4. Antimicrobial Strategies

With antibiotic resistance on the rise, molecular approaches are gaining ground: custom nucleic acid sequences that disable resistance genes, or protein nanobodies that puncture bacterial membranes. There's also growing work on phage-derived enzymes targeting resistant strains. [[Evans, K. E., et.al \(2020\)](#)]

Challenges and Safety Considerations

Engineering at this scale comes with inherent challenges:

Off-target activity remains a pressing concern, particularly for genome editing tools. Detection and mitigation strategies are critical.

Immunogenicity of engineered molecules must be minimized—unintended immune reactions could neutralize the therapy or cause inflammation.

Manufacturing complexity: Molecular therapeutics often require highly controlled environments (GMP-grade enzymatic reactions, ultra-pure lipids, aseptic nanofabrication).

Delivery limitations: Penetrating solid tissues or the blood–brain barrier is still a bottleneck. Molecular surface tags and localized delivery methods are actively being developed.

The Road Ahead

Despite these hurdles, the pace of progress is breathtaking:

Improved algorithms mean protein structures and interactions can be predicted and designed in silico with increasing confidence.

New chemical modifications for RNA backbones create molecules with weeks-long half-lives and reduced immune detection.

Platforms now allow multiplexed edits—either simultaneous base-editing of several sites or combinatorial protein–RNA therapies tailored to each patient’s genetics. [\[Das, R., et.al \(2008\)\]](#).

The result: a future where “one-size-fits-all” therapies give way to bespoke molecular solutions—a treatment designed the way you design a smartphone app. This convergence of computational bioengineering, synthetic chemistry, and clinical science is revolutionizing what’s possible.

Conclusion

Molecular-scale bioengineering is not a futuristic dream—it’s already delivering transformative therapies. In the next decade, expect to see a wave of ultra-precise, programmable medicines built molecule by molecule. For patients, that means higher efficacy, fewer side effects, and personalized treatments for diseases once deemed untreatable. For science and medicine, it marks a new chapter: mastering life’s machinery to heal from its smallest parts. The revolution has begun—and it’s happening at the molecular scale.

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Article 4:

Nano-Bio Conjugates: Smart Therapeutics for Targeted Drug Delivery

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Introduction

Nano bioconjugates, modern treatment technologies, combine the targeting potential of biomolecules with the functional properties of nanomaterials. Targeted, site-specific medicine delivery made possible by these increases treatment efficacy and reduces systemic toxicity (Ghosh et al. , 2008; Torchilin, 2011). While stimuli-responsive properties enable controlled drug release (Lee et al., 2017), when functionalized with ligands like antibodies or aptamers, these conjugates may actively identify sick cells. Because they are used in gene editing, cancer treatment, and infectious diseases, they are a vital step forward in individualized medicine (Santos-Carballal et al., 2021).

Structural Components of Nano-Bio Conjugates

Nano-bio conjugates are multifunctional entities made up of separate but interrelated parts, each essential for achieving targeted, controlled, and efficient therapeutic delivery. A typical architecture consists of stimuli-responsive linkers, targeting ligands, a therapeutic payload, and a nanocarrier core.

- Nanocarriers like liposomes, gold nanoparticles (AuNPs), and polymeric nanoparticles (such as PLGA) are used as delivery vehicles because of their biocompatibility, adjustable size, and surface characteristics (Ghosh et al., 2008; Torchilin, 2011).
- Therapeutic payloads can be surface-bound or encapsulated substances, such as proteins, drugs, or genetic materials like siRNA or CRISPR components (Bagalkot et al., 2006).

- By attaching to specific receptors on sick cells, targeting ligands like antibodies, peptides, or aptamers facilitate active targeting and increase drug accumulation at the site of action (Lee et al., 2017).
- The medication is released in response to internal (pH, enzymes) or external (temperature, magnetic) stimuli, allowing for controlled and site-specific administration (Torchilin, 2011).

Bioconjugation Strategies

The creation of stable and functional nano-bio conjugates depends heavily on bioconjugation. One of the most popular methods is

- Durable connections between biomolecules and nanocarriers are formed by covalent linkages like thiol and amide bonds, guaranteeing sustained stability in biological settings.
- Click chemistry enables precise and effective conjugation without changing biomolecule function through highly specific, bio-orthogonal reactions like azide–alkyne cycloaddition.
- Reversible electrostatic and affinity-based interactions, such as biotin-streptavidin or antibody-antigen binding, are beneficial for systems that respond to stimuli.

Proper ligand orientation guarantees target recognition, whereas stable binding reduces off-target effects or early release (Bagalkot et al., 2006).

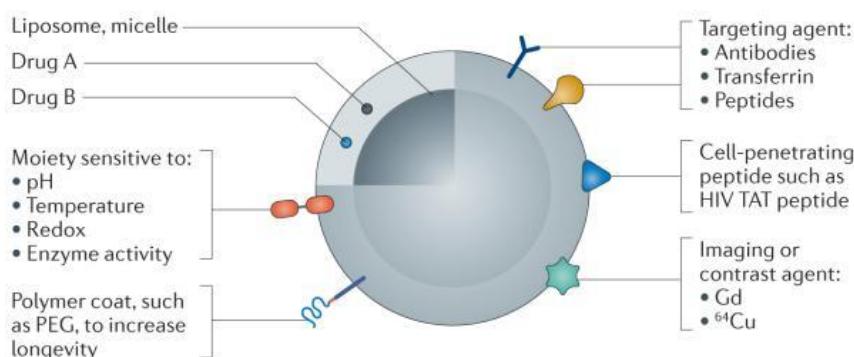


Figure 1. Schematic of a nano-bio conjugate showing nanocarrier core, targeting ligand, therapeutic payload, and stimuli-responsive linker. Adapted from Torchilin (2011)

Therapeutic Applications

Nano-bio conjugates have a wide range of uses in contemporary medicine because of their accuracy and ability to deliver treatments in a controlled manner.

1. Cancer Treatment: Conjugates that include targeting ligands (such as anti-HER2) transport medications, such as doxorubicin, straight to tumor cells. This process minimizes adverse effects and enhances effectiveness (Bagalkot et al., 2006).
2. Infectious Diseases: The use of nanoparticles along with antibiotics or peptides improves the ability to fight germs, particularly those that are resistant to treatment (Galdiero et al., 2011).
3. Gene therapy utilizing siRNA, mRNA, and CRISPR-Cas9, conveyed through nano-bio systems, enhances the absorption by cells and safeguards genetic material throughout the delivery process (Santos-Carballal et al., 2021).

Advantages of Nano-Bio Conjugates

Nano-bio conjugates provide numerous benefits compared to traditional drug delivery systems:

1. Targeted Delivery: Biomolecule ligands direct the conjugate to particular cells, improving treatment accuracy and minimizing unintended effects.
2. Controlled Release: Linkers that respond to specific stimuli guarantee that the drug is released solely at the intended location, thus enhancing both its effectiveness and safety.
3. Decreased Toxicity: By reducing contact with healthy tissues, nano-bio systems lessen overall side effects.
4. Multifunctionality: Conjugates can be created for simultaneous therapy and diagnostics (theragnostic), allowing for real-time monitoring of treatment.
5. Improved Bioavailability: Nanocarriers enhance the solubility and stability of drugs, resulting in extended circulation time and therapeutic effects.

Challenges and Limitations

Although nano-bio conjugates have significant potential for therapeutic use, various challenges hinder their application in clinical settings:

- Toxicity and Immune Response: Certain nanoparticles have the ability to trigger immune reactions or cause oxidative harm (Santos-Carballal et al., 2021).
- Concerns About Stability: Insecure connections can cause early release or breaking down of the drug.

- Scaling Up and Reproducibility: Producing accurate and consistent conjugates in large quantities is still a challenging task.
- Restricted Tissue Penetration: Larger systems may struggle to traverse barriers such as the blood-brain barrier efficiently.

Future Perspectives

Nano-bio conjugates are anticipated to be vital in the future development of precision medicine. Improvements in AI-driven design, eco-friendly materials, and versatile Nano-carriers will enhance targeting, safety, and effectiveness in therapy. Combining technologies such as CRISPR, RNA therapies, and the ranostics will broaden their application in clinical settings. To guarantee safe translation, it is important to focus on standardized regulations and conduct long-term toxicity studies (Santos-Carballal et al., 2021).

Conclusion

Nano-bio conjugates provide an effective method for accurate and controlled drug delivery by merging nanotechnology with biological targeting. Their achievements in treating cancer, genetic disorders, and infectious diseases underscore their promise. Although issues such as toxicity and scalability still exist, continuous research and innovation are creating opportunities for their wider application in future personalized medicine.

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From Crisis to Cure: Therapeutics Through Next-Gen Opioid Receptor Design

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Molecular Basis of the Opioid Epidemic

The widespread abuse of synthetic and prescription opioids, including Fentanyl, Oxycodone, Tramadol and many more has led to the global opioid pandemic, which is now a serious public health concern. The lack of quick, affordable, and accessible detection methods remains a barrier to early diagnosis and intervention. Addressing this challenge necessitates the development of innovative diagnostic tools for effective monitoring of opioid exposure. ([Lambert, 2023](#)) To support the development of such diagnostics and therapeutics, it is essential to first understand the molecular basis of opioid action and receptor engagement.

Once we've identified potential drug targets by modelling, the next phase of creating safer painkillers involves grasping how these targets function within the body and how we might engineer them to perform optimally. One such group of targets are the opioid receptors, which have a key role in how our nervous system perceives pain. They are part of the extensive family of G-protein-coupled receptors (GPCRs) and consist of the mu (MOR), delta (DOR), and kappa (KOR) subtypes. ([Sanchez-Reyes et al., 2023](#))

Old-school opioid medicines such as morphine or fentanyl are excellent at alleviating pain, but they have an expensive price tag , side effects such as respiratory depression, constipation, tolerance, and dependence. These issues are not simply issues with the drugs themselves they're closely linked with how the opioid receptors communicate within our cells. ([Ma et al., 2025](#))

Two Paths of Receptor Signalling

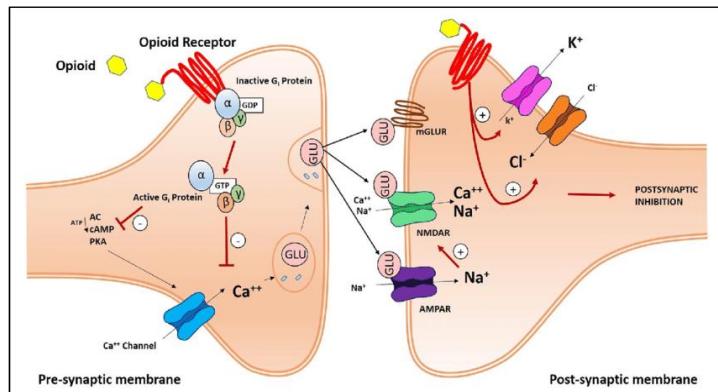
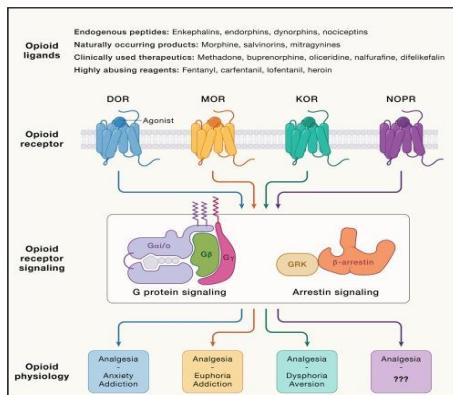


Fig 1: Pharmacological Basis of Opioid Receptor Signaling and Its Impact on Synaptic Physiology (DOI: [10.1016/j.cell.2023.10.029](https://doi.org/10.1016/j.cell.2023.10.029), <https://doi.org/10.13140/RG.2.2.30945.58727>)

When an opioid is bound to its receptor, it initiates a cascade of events inside the cell. The receptor alters its shape and binds to proteins named as G-proteins, which initiate the first signalling process. In the pathway of G-protein, the receptor activates the Gi/o proteins, which block adenylyl cyclase a standard enzyme for enhancing cell activity by increasing the concentration of cyclic AMP (cAMP), with cAMP levels lowered, the cell is less excitable, which will numb the pain signals. ([Zhuang, Y., Wang, L., Yu, F., et al., 2023.](#))

Meanwhile, components of the G-protein complex (the G $\beta\gamma$ subunits) modulate ion channels. They activate potassium channels, making neurons less probable to fire, and inactivate calcium channels, limiting the release of pain-associated neurotransmitters such as glutamate and substance P. The outcome is decreased signal transmission along pain pathways, wherein opioids exert their defining analgesic effects. ([Sanchez-Reyes et al., 2023](#))

But there is a second, more complicated pathway: the β -arrestin pathway. After the receptor is activated by a drug, enzymes like GRKs (G-protein receptor kinases) phosphorylate it, which provides a docking site for β -arrestin proteins, specifically β -arrestin-2, and they bind to the receptor. With the β -arrestins attached, they prevent additional G-protein interaction and escort the receptor into the interior of the cell (a process known as internalization), temporarily silencing it. ([Bean et al., 2022](#))

The issue is that β -arrestins also initiate their own signaling cascade, which stimulates molecules such as ERK1/2, JNK, and Akt signals that have been associated with undesirable side effects of tolerance, constipation, and even inhibited breathing. Scientists have since delved into the idea of a so-called biased agonism, where a drug is engineered to prefer G-protein signaling but not β -arrestin recruitment. ([Ma et al., 2025](#))

Safer Molecules: Biased Agonists and Engineered Receptors

Based on this information, scientists have begun developing drugs that specifically bias the response of the receptor. An example of such a drug is oliceridine (TRV130), which is biased toward G-protein signaling but reduces β -arrestin activation. ([Ma et al., 2025](#)) Oliceridine, compared to morphine, has demonstrated fewer side effects in clinical trials. A second drug, PZM21, designed based on careful structural research, demonstrated excellent pain killing in animal models with significantly less risk of respiratory depression. ([Lambert, 2023](#))

In addition to designing novel molecules, we can engineer the receptors themselves. By modifying the amino acids on the receptor that regulate phosphorylation or arrestin binding, researchers have created mutant MORs that still activate G-proteins but are resistant to arrestin binding. Such receptor bioengineering can lead ultimately to gene therapy strategies in which only safe, altered receptors are expressed in the appropriate brain regions. ([Bean et al., 2022](#))

There is even more space for innovation. Researchers have constructed chimeric receptors, combining fragments from different GPCRs to dictate how they respond. Others are employing optogenetics and chemogenetics to generate receptors that respond only to light or man-made chemicals, allowing researchers millisecond command over pain signalling in the lab and someday, possibly, in patients. ([Zhang et al., 2017](#))

How do opioids affect the brain and body?

When a person takes an opioid, it enters the brain rapidly due to its lipophilic properties, meaning it loves fat. The drug then binds to the MORs within the important regions such as the periaqueductal gray, thalamus, and dorsal horn of the spinal cord—all central locations for pain processing. ([Lambert, 2023](#))

The instant the drug binds, G-protein signaling is initiated. Neurons are less likely to fire, pain signals are shut off, and the brain's descending inhibitory pain pathways are reinforced. This creates opioids' potent pain-relieving effect.

But cumulative use accumulates β -arrestin signaling. The receptors become internalized, and G-protein signaling wanes, making the body less sensitive to the drug. This is tolerance. Eventually, increasingly larger doses are required, and the risk of side effects, including overdose, increases dramatically. ([Sanchez-Reyes et al., 2023](#))

In peripheral tissues such as inflamed joints or sites of injury, opioids also decrease pain locally by soothing hyperactive pain-sensing neurons. But these tissues tend to have fewer receptors, lower risk of side effects but less drug effect.

A New Generation of Pain Therapies

Table 1: Tools Advancing Our Understanding of Opioid Receptor

Technology	Role in Opioid Research	Reference
Cryo-EM	High-res receptor-ligand structure visualization	Zhuang et al., Cell, 2023
cAMP assay (G-protein)	Quantifies receptor activation	Lipinski et al., J Mol Model, 2019
BRET/FRET biosensors	Measures β -arrestin recruitment	Mahinthichaichan et al., Nat Commun, 2020
Molecular Docking	Predicts aptamer/drug binding affinity	Our current study
Synthetic Biology	Future direction for localized gene-based analgesics	Conceptual (proposed therapeutic framework)

With the help of technology like cryo-electron microscopy, scientists can now see opioid receptors nearly as well as atoms. This has opened up the door to more precise drug design and better understanding of how every chemical tweak of a receptor or ligand changes the cell's response. Designed receptors can be tested in living cells like HEK293 or CHO cells to measure G-protein signal (through cAMP assays) and β -arrestin activity (with BRET/FRET biosensors). This allows scientists to screen drug candidates rapidly and select the optimal signalling characteristics prior to animal or human trials commencing.

The future might instead be in multi-target drugs that simultaneously target both opioid and non-opioid systems, or cell-targeted gene therapies with safer, engineered receptors delivered only where pain is to

be alleviated. Integrating synthetic biology, molecular pharmacology, and systems neuroscience might enable us to rethink pain treatment entirely.

In conclusion

Opioid receptor engineering represents a bold new step in the quest for safer pain management. We can alter the way opioids interact with the body to preserve their unmatched analgesic effects while reducing the risks that have fuelled the global opioid crisis, rather than outright prohibiting them. If we can learn to modulate these powerful biological switches, we may finally strike the right balance between relief and responsibility.

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TARGETED HEALING: THE SCIENCE OF CAR T -CELL THERAPY



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Abstract

Immunotherapy was a promising new treatment for advanced malignancies ten years ago. It is the basis of cancer treatment today. CAR T-cell treatments are a type of immunotherapy that has received significant attention. Although not everyone benefits from CAR T-cell therapy, some patients with advanced cancer have been completely cured of their disease, often for extended periods. CAR T-cell therapies are unique because they are derived from a patient's T cells, which are the body's primary defenders against sick and contaminated cells. This distinguishes them from other immunotherapies and cancer treatments.

Introduction

Chimeric antigen receptor T cells (CAR-T cells) are a revolutionary advancement in immunotherapy. These genetically modified T cells express artificial receptors that enable them to target and attack cancer cells with precision, offering new hope in the fight against cancer. This groundbreaking modification empowers the body not only to locate but also to eliminate cancer cells by precisely identifying specific tumor antigens. Unlike natural T cells, which require human major histocompatibility complex (MHC) molecules to recognize their targets, CAR-T cells can directly detect antigens on cancer cells. As a result, they can target a wider variety of cancer cell types. When CAR-T cells bind to their specific antigens, they become activated and function as "living drugs," actively targeting and attacking tumors. Since 2017, the Food and Drug Administration (FDA) has authorized six CAR-T cell therapies for blood cancers. (Y.-J. Chen et al., 2023)

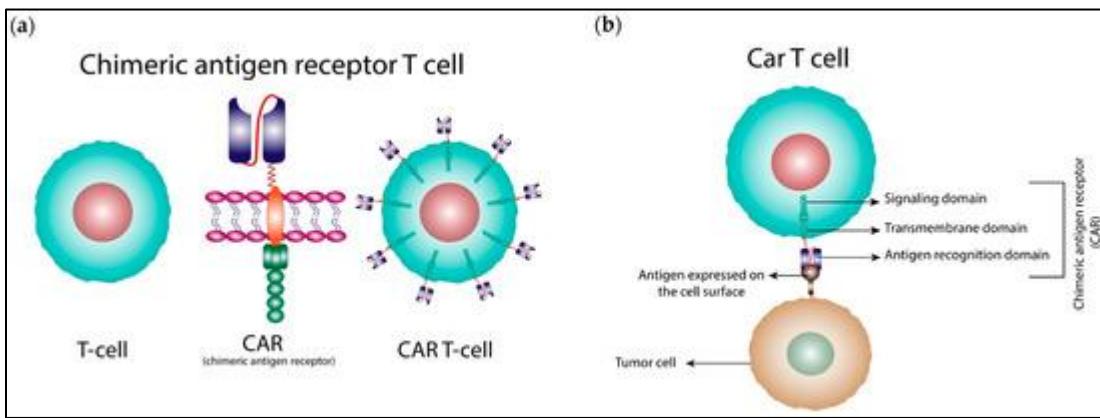


Figure 1. (a) The T cell, CAR, and CAR-T cell. (b) The structure of CAR-T cells and their mechanism for recognizing tumor cells.

Reference: <https://cdn.ncbi.nlm.nih.gov/pmc/blobs/733d/9913679/35c401a06689/cancers-15-00663-g001.jpg>

Structure, production, and development

Chimeric Antigen Receptors (CARs) are fascinating molecules composed of three essential components: the ectodomain, the transmembrane domain, and the endodomain. The ectodomain includes the spacer region, antigen recognition domain, and the signal peptide. The function of the signal peptide is to direct the developing protein into the endoplasmic reticulum. The hydrophobic alpha helix that spans the membrane defines the transmembrane domain, which is the closest part of the endodomain to the membrane. This transmembrane domain influences the stability of the receptor. The endodomain's most significant component is CD3 ζ , which features three immunoreceptor tyrosine-based activation motifs (ITAMs) (Zhang et al., 2017).

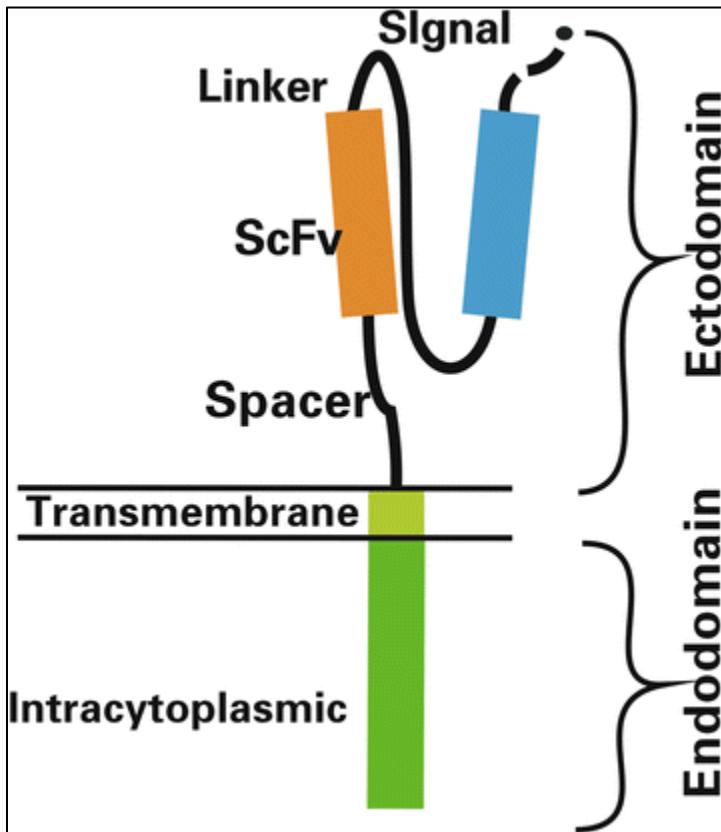


Figure 2. The chimeric antigen receptor (CAR) consists of an ectodomain, a transmembrane domain, and an endodomain.

Reference: <https://link.springer.com/article/10.1186/s40364-017-0102-y/figures/1>

First, leukapheresis is performed to extract leukocytes from the body of either the donor or the patient. Next, the leukocytes undergo a process of enrichment and washing to separate the T cells. Certain antibody bead conjugates or markers are then used to identify the T cell subsets based on their CD4/CD8 composition. The T cells must be cultured to activate them. This process requires the use of autologous antigen-presenting cells (APCs) from donors or patients, alongside beads coated with anti-CD3/anti-CD28 monoclonal antibodies or anti-CD3 antibodies. These components, combined with growth factors such as IL-2 and feeder cells, are essential for promoting robust T cell proliferation. Furthermore, the culture conditions are meticulously optimized to effectively polarize T cells toward a specific phenotype.

Viral vectors effectively reverse transcribe RNA into DNA and integrate it into the patient's genome to encode chimeric antigen receptors (CARs). During the activation process, the viral vector is artfully eliminated from the culture through a combination of dilution and medium exchange, ensuring a pristine environment for optimal results. Lentiviral vectors are used more frequently in clinical studies than gammaretroviral vectors due to their safer profile regarding integration sites. Other methods include mRNA transfection and the Sleeping Beauty transposon system.

CAR-T cells are expertly crafted using three cutting-edge bioreactor systems: CliniMACS Prodigy, G-Rex, and WAVE Bioreactor. Each of these innovative technologies plays a vital role in enhancing the

efficiency and effectiveness of CAR-T cell production, paving the way for revolutionary advancements in personalized cancer therapies. (Zhang et al., 2017)

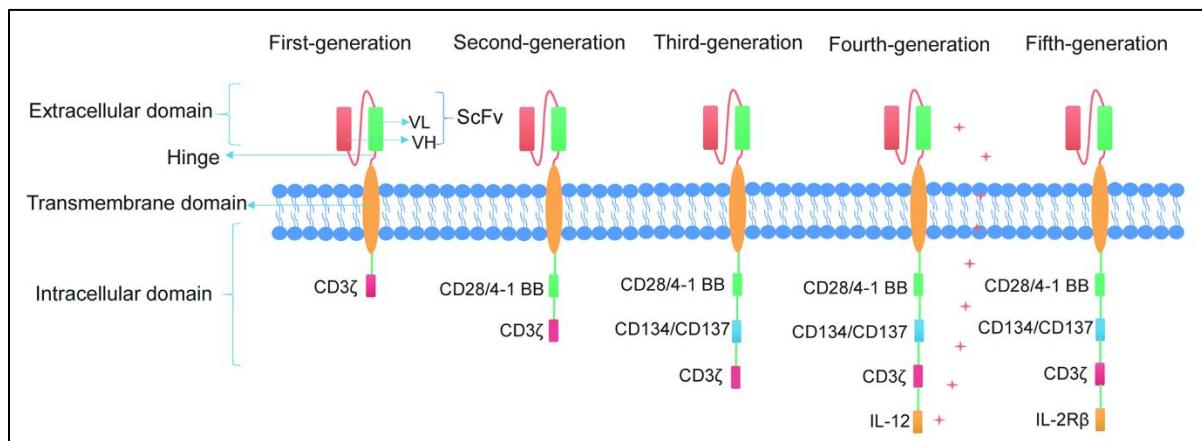


Figure 3. Development of CARs- Five generations

Reference: <https://cancerci.biomedcentral.com/articles/10.1186/s12935-024-03315-3/figures/1>

Advantages

Chimeric antigen receptor (CAR)-T cell therapy is the leading cancer treatment due to its longer-lasting remission, fewer side effects, and enhanced quality of life. In the past decade, significant research has been conducted on the creation and delivery of CAR-T cells. This advancement has facilitated the expansion of CAR therapy, resulting in favorable outcomes for patients with leukemias, lymphomas, and multiple myeloma. CAR-T cell therapy offers the advantage of a shorter treatment duration. Most patients experience a swift recovery with CAR-T cell therapy, unlike stem cell transplants, which require intensive chemotherapy. Additionally, CAR-T cells can recognize specific antigens without needing the target cells to process these antigens or rely on the Major Histocompatibility Complex (MHC). This capability allows CAR-T cells to effectively eliminate tumor cells, in contrast to tumor-infiltrating lymphocytes (TILs) and T cell receptors (TCRs), which depend on MHC for antigen recognition (Rohit Reddy et al., 2021).

Limitations

The success of CAR-T cell therapy relies on selecting the right target antigens, which should be stable, specific, and broadly covered. At present, one of the biggest hurdles in tackling solid tumors lies in the scarcity of effective tumor-specific antigens (TSAs) and the diverse nature of antigens themselves. This variability makes it a complex battle against these formidable opponents (T. Chen et al., 2024). Tumor antigen escape and a variety of resistance mechanisms pose significant challenges to the effectiveness of CAR-T cell therapy in treating solid tumors, particularly lung cancer. The tumor microenvironment's immunosuppressive effect on CAR-T cells in lung cancer reduces their effectiveness. CAR-T cell exhaustion is a state where these remarkable engineered immune cells lose their effectiveness, undermining the impact of CAR-T therapy. This challenge drives the quest for innovative solutions to

fully harness the potential of this groundbreaking treatment. CAR-T cell therapy has severe toxicities that pose challenges, including cytokine release syndrome (CRS), neurologic toxicity, tumor lysis syndrome (TLS), on-target off-tumor effects, anaphylaxis, and hematologic issues. (Kandra et al., 2022).

Conclusion

CAR T-cell therapy is a major advancement in cancer treatment, transforming the way we utilize the immune system to fight the disease. Recent improvements have increased its safety and effectiveness, leading to broader clinical use.

Researchers are exploring new strategies to reduce the risk of tumor recurrence and manage toxicity in CD19-expressing disorders treated with CAR T-cells. This therapy holds significant promise for the future, as ongoing research into tumor biology and treatment protocols is expected to enhance its impact, offering hope to many worldwide.

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Article 7:



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CRISPR-Cas9 Mediated Gene Editing: A Molecular Therapeutic for Neurodegeneration

Abstract

Neurodegenerative diseases, including Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis (ALS), pose profound clinical challenges due to progressive neuronal loss and limited therapeutic options. Recent advances in genome editing, especially the CRISPR/Cas9 system, have transformed our approach to targeting genetic and molecular drivers of these conditions, offering hope for durable and personalised therapies. This article reviews the molecular mechanisms underlying CRISPR/Cas9 technology and highlights its therapeutic applications, demonstrated efficacy, current limitations, and future prospects in treating neurodegeneration, drawing upon published primary research.

Introduction

Neurodegenerative disorders are marked by the gradual loss of structure or function of neurones and include some of the most debilitating chronic conditions affecting millions worldwide. Their complex aetiologies, often involving genetic mutations and protein misfolding, have hindered the development of effective treatments. The emergence of CRISPR/Cas9 genome-editing technology, distinguished by its specificity, efficiency, and versatility, has generated excitement as a molecular tool to combat these diseases at their genetic roots. ([Nojadeh et al., 2023](#)) ([Aslam et al., 2024](#))

Molecular Mechanism of CRISPR/Cas9

The CRISPR (clustered regularly interspaced short palindromic repeats)/Cas9 system was adapted from a bacterial immune defence and functions by inducing site-specific double-stranded breaks in DNA, enabling efficient gene modification. CRISPR/Cas9 employs a guide RNA (gRNA) to direct the Cas9 nuclease to a complementary DNA sequence, instigating breaks that can then be repaired by either the error-prone non-homologous end joining (NHEJ) pathway (typically resulting in gene disruption) or the more precise homology-directed repair (HDR) pathway, permitting targeted sequence correction or insertion. ([Shin & Lee, 2017](#)) The simplicity and programmability of the gRNA set this system apart from previous gene-editing tools such as zinc finger nucleases and TALENs, allowing for nearly limitless applications in mammalian cells, including neurones and glia. ([Shin & Lee, 2017](#)) ([Khan et al., 2025](#))

CRISPR/Cas9 in Huntington's Disease

Huntington's disease (HD) is an autosomal dominant, monogenic neurodegenerative disorder induced by expanded CAG repeats within the huntingtin (HTT) gene, producing a mutant protein prone to aggregation and cytotoxicity. Because the genetic basis is clear and localised, HD has emerged as a prime candidate for genome-editing therapies. Research using Cas9 delivered via adeno-associated virus (AAV) to the striatum of HD mouse models has resulted in targeted disruption of mutant HTT and substantial reduction of neuronal inclusions, improved motor function, and increased lifespan. Remarkably, Cas9 not only mitigated protein aggregation but also demonstrated therapeutic effects without apparent off-target toxicity in these animal studies. While permanent gene inactivation does not restore lost neurones, combining CRISPR with cell replacement strategies could enhance efficacy in the future ([Ekman et al., 2019](#)) ([Nojadeh et al., 2023](#)).

CRISPR/Cas9 for ALS and Other Proteinopathies

ALS (amyotrophic lateral sclerosis) is characterised by the degeneration of upper and lower motor neurones, often caused by mutations in genes such as SOD1, FUS, and C9orf72. The CRISPR/Cas9 platform has been harnessed to excise pathogenic expanded hexanucleotide repeats (HREs) in the C9orf72 gene, leading to reduced toxic RNA foci and dipeptide repeat proteins in patient-derived neurones and ALS mouse models ([Nojadeh et al., 2023](#)). Similar strategies have corrected SOD1 mutations in iPSCs and animal models, reverting the disease phenotype and prolonging neuronal function. Such studies illustrate how CRISPR can effectively target multiple genetic causes underlying neurodegeneration, directly addressing the roots of protein misfolding and aggregation ([Aslam et al., 2024](#)).

Alzheimer's and Parkinson's Disease Applications

For Alzheimer's disease (AD), which features accumulation of misfolded amyloid-beta and tau proteins, CRISPR/Cas9 offers a means to precisely modify disease-associated genes. Successful editing of pathological mutations in APP, PSEN1, and PSEN2 genes in human neurones has reversed amyloidogenic phenotypes and improved synaptic function in cellular and mouse models. In Parkinson's disease (PD), Cas9/gRNAs can be delivered directly to the substantia nigra, targeting genes such as SNCA (alpha-synuclein), Parkin, and PINK1. Editing these genes in animal brains not only helps elucidate disease mechanisms but also offers the potential for therapeutic gene correction in affected neurones ([Yang et al., 2016](#)).

Current Limitations and Technical Challenges

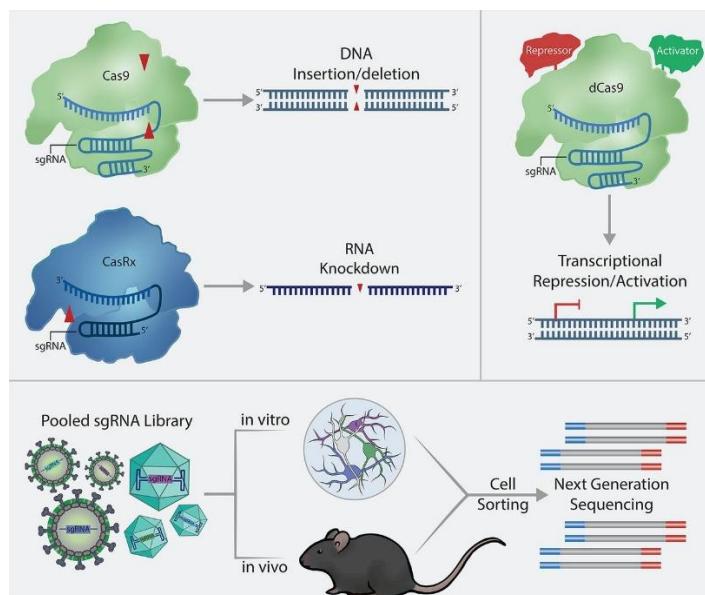
Despite its promise, several hurdles must be surmounted before CRISPR/Cas9 can become a mainstream neurotherapeutic. Efficient and targeted delivery systems—such as AAV vectors, lipid nanoparticles, or nanocarriers—are under development to overcome challenges presented by the blood-brain barrier and tissue specificity. Off-target DNA cleavage remains a concern, and rigorous screening and next-generation Cas variants are being designed to improve specificity. Moreover, ethical considerations surrounding germline editing and potential immune responses to Cas9 proteins are subjects of active debate and research. Long-term studies are needed to ensure durable efficacy and safety in human patients.

Innovations and Future Prospects

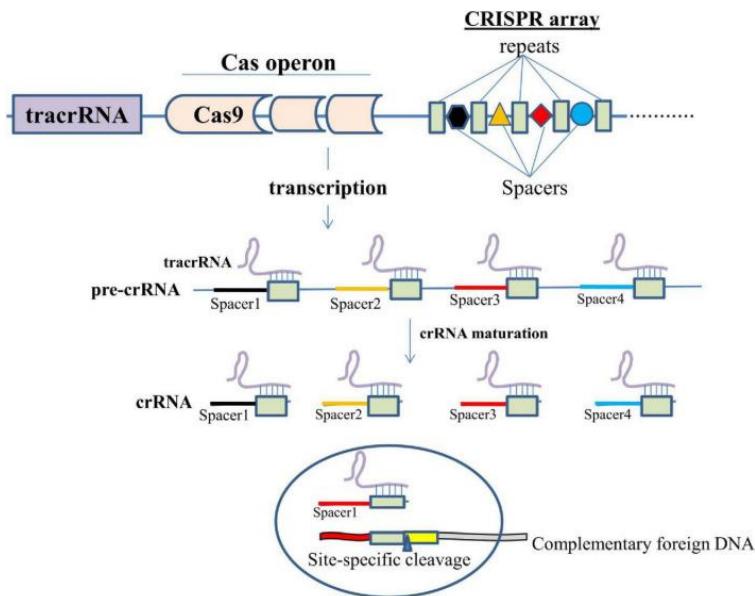
Ongoing advances in CRISPR/Cas9 technology are addressing present limitations by refining base editors and prime editing, capable of precise single-nucleotide corrections without double-stranded breaks. Researchers anticipate movement from preclinical to human trials as delivery systems improve and risks are minimised. The ability to combine CRISPR with stem cell replacement, somatic gene therapy, and disease modelling heralds a future in which neurodegenerative diseases can be not just studied but fundamentally altered or potentially cured at the genetic level ([Zhang et al., 2024](#)).

Conclusion

The body of research on CRISPR/Cas9-mediated gene editing underscores its groundbreaking potential to transform our approach to neurodegenerative disorders. By enabling the precise correction, disruption, or silencing of pathogenic genes, CRISPR/Cas9 targets molecular events at the heart of these diseases, not merely alleviating symptoms but offering disease-modifying and potentially curative options. Overcoming delivery, specificity, and ethical challenges will be critical in translating these advances into real-world clinical success.



([Sandoval et al., 2020](#))



Diagrammatic representation of the mechanism of action of CRISPR/Cas9 ([Khan et al., 2025b](#))

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Article 8:

Artificial Womb Technology: Next Generation Therapeutics at Molecular Scale



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Abstract

This report provides a comprehensive overview of the transformative potential at the intersection of molecular bioengineering and artificial womb technology (AWT). It highlights how advancements in CRISPR-based gene editing, sophisticated biosensors, synthetic biology, and advanced computational modelling are not merely enhancing but fundamentally enabling the development and precise control of artificial womb systems. The analysis underscores a profound synergistic relationship: the artificial womb serves as an unprecedentedly controlled environment for advanced molecular interventions, while molecular bioengineering provides the precision tools required for mimicking, monitoring, and regulating the complex biological processes essential for healthy foetal development *ex vivo*.

Introduction

The earliest medicines were mostly serendipitous discoveries from nature. Then, in the late 20th century, we entered a new era of targeted therapeutics based on proteins or small molecules. Although modern medicine has vastly improved human health, small-molecule drug discovery takes an enormous amount of time and money. Broad scientists have also catalysed a major paradigm shift in therapeutic development by pioneering breakthrough gene-editing technologies, such as CRISPR-Cas9 and base editing, that strike at the root causes of diseases. These revolutions promise to both dramatically accelerate the speed at which medicines are created and open new therapeutic avenues for difficult-to-treat diseases. The next generation of therapeutics is a new wave of treatment that goes beyond traditional pharmaceutical and biological treatments. These advanced therapies often involve novel technologies and approaches, including gene editing, cell therapies, nucleic acid therapy, and advanced drug delivery systems. They are designed to address the diseases with great precision and effectiveness, often targeting the underlying cause of illness at the genetic or cellular level. [Romanis, E. C. \(2019\)](#)

Methodologies and approach

Molecular-scale bioengineering focuses on the manipulation of molecules such as proteins and nucleic acids to engineer biological systems for therapeutic purposes.

Gene Editing and Gene Therapy: Technologies like CRISPR-Cas9 are central in molecular bioengineering, as they allow precise gene editing to correct genetic defects, holding immense promise in developing therapies for genetic disorders.

Protein Engineering: Manipulation of proteins for various applications, including therapeutic antibodies, enzymes, and vaccines. For example, monoclonal antibody drugs like Rituximab or Herceptin are engineered to target specific cancer cells. ([Zafar et al., 2021](#))

Synthetic Biology: Designing new biological systems using standard molecular tools to create organisms with specific engineered capabilities. This includes the creation of synthetic life or reprogramming cells to perform specific functions. ([Zou, Y., et al. 2024](#))

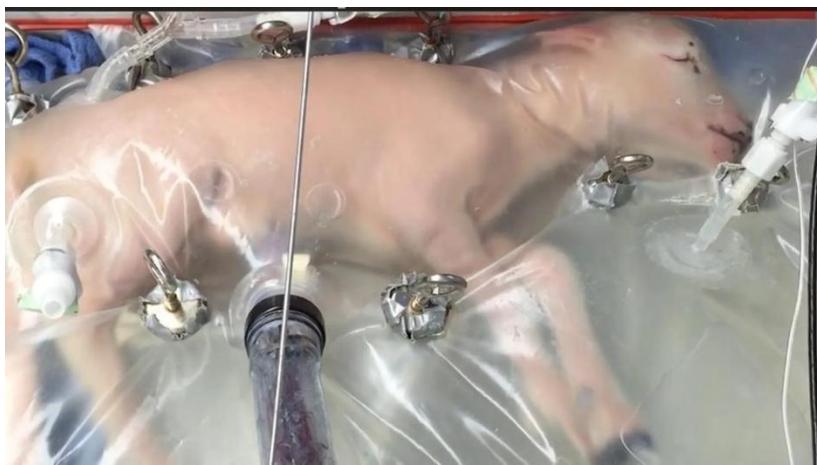
Nanomedicine: At the molecular level, when bioengineering overlaps with nanotechnology to create nanoparticles, it can deliver drugs more precisely, monitor biological systems, and assist in tissue regeneration. ([Swingle, K. A., et al. 2022](#))

An artificial womb, also known as an ectogenesis system, mimics the conditions of the human uterus, supporting the growth and development of a foetus outside of the mother's body. This technology is still in early stages but has made significant changes:

Animal Models: Recent progress has been made with animal models, particularly with preterm lambs. Researchers have been able to simulate the conditions of the uterus using bioreactors that control oxygen levels, nutrients, and waste removal. These artificial wombs are used to support and study foetal development in a controlled environment. ([Banstola & Reynolds, 2022](#))

Premature Birth Intervention: One of the primary goals of artificial womb technology is to provide a solution for extremely premature infants who would not survive in a traditional neonatal incubator. Viability for premature births (at or before 23 weeks) is a major area of interest.

Biomimetic Systems: Artificial wombs are being engineered using biomimetic systems that replicate the uterine environment, including amniotic fluid, temperature, and nutrient delivery. Such systems require highly controlled bioreactors and sophisticated monitoring systems to ensure foetal health and development. ([BORN et al., 1955](#))



Applicable Models and Simulations

To study molecular bioengineering and artificial womb systems, *in silico* models (computer simulations) and *in vitro* models are commonly used:

Computational simulations model molecular dynamics, nutrient exchange, and the biochemical environment in an artificial womb, helping predict foetal responses to factors like temperature and oxygen. These models also simulate protein and biomolecule behaviour to optimise conditions for foetal development.

Organs-on-chips and 3D stem cell cultures, such as liver, kidney, or heart organoids, are used to mimic tissue growth and development outside the womb, helping researchers study how organs form in artificial womb-like settings.

Bioreactor simulations replicate womb conditions by modelling mechanical and biological factors like nutrient flow, waste removal, and oxygen levels. Mathematical models optimise these processes to improve artificial womb designs and assess the feasibility of different prototypes for supporting foetal development. ([Sandle, E. 2017](#))

Monitoring foetal development in an artificial womb requires advanced technologies to observe and support cells at the molecular level. Live-cell imaging techniques like confocal microscopy allow researchers to track cell behaviour, gene expression, and protein production in real time. Single-cell RNA sequencing maps active genes in individual cells, providing insight into how cells differentiate and develop. Microfluidic devices offer precise control of the microenvironment, continuously monitoring factors such as oxygen levels, pH, and waste removal to maintain optimal conditions for healthy foetal growth. By analysing the metabolites and proteins present in the artificial womb environment, researchers can gain insights into the health of the foetus and how it is responding to its surroundings at the molecular level. These techniques can help identify biomarkers of developmental progress or stress. ([Partridge, EA. et al., \(2017\)](#))

Results and Progress:

Platform for Delivery of Targeted Molecular Therapies: Progress is being made in creating safe, effective ways to deliver molecular therapies that target genetic disorders, cancers, and other complex diseases. Advances in technologies like lipid nanoparticles, viral vectors, and nanocarriers are helping deliver genetic material—such as RNA and CRISPR—directly into cells. Many gene therapies have successfully moved from clinical trials to real-world use, treating conditions like spinal muscular atrophy and some cancers. While success rates are improving, ensuring these treatments remain safe and cause no harmful side effects remains a key challenge. ([Wired. 2023](#))

Prevention of Developmental Diseases: Progress is focused on using molecular therapies to prevent developmental diseases before they start through early genetic screening, gene editing, and stem cell treatments. Research into CRISPR technology is particularly promising, allowing precise edits to genes linked to disorders like Duchenne muscular dystrophy and cystic fibrosis. While studies show potential in reducing or preventing these diseases by targeting embryos or early development, the approach is still experimental, with important ethical, regulatory, and technical hurdles to overcome.

Testing New Molecular Drugs: Recent advances in biotechnology and high-throughput screening are speeding up the development and testing of new molecular drugs. These technologies allow scientists to quickly study how compounds interact with genes or proteins involved in diseases. As a result, many promising drug candidates—including small-molecule inhibitors, monoclonal antibodies, and RNA-based therapies—are now in clinical trials. ([Wilkinson, M. 2024](#))

Success in Gene Editing (e.g., CRISPR): Gene editing, particularly with tools like CRISPR-Cas9, is transforming how genetic diseases are treated by precisely targeting and fixing faulty genes. This approach has shown promise in conditions like sickle cell anaemia and beta-thalassaemia, using advanced methods such as base and prime editing. While clinical trials report encouraging results, ongoing research is essential to fully understand the long-term safety and effectiveness of these therapies. ([Cheng, Y., et al. 2023](#))

Challenges and Future Direction

Ensuring molecular therapies are safe and precise is crucial, as off-target effects and unwanted mutations remain major concerns. Regulatory agencies often lag behind rapid technological advances, potentially delaying new treatments. Ethical debates especially surround gene editing of embryos and germline cells, balancing benefits like disease prevention against moral boundaries. Social challenges, such as equity and discrimination, will grow as therapies become widespread. Collaboration among biologists, bioinformaticians, clinicians, and computer scientists is essential but complicated by differing language and perspectives. Handling complex multiomics data securely is necessary, yet adoption of technologies like blockchain is slow due to trust, regulatory, and technical hurdles. The regulatory framework must evolve rapidly to ensure molecular therapies are used safely, ethically, and equitably while managing risks inherent in gene modification. (Aiysha G. et al., 2024)

Conclusion

Molecular bioengineering and artificial womb technology promise to revolutionise foetal healthcare and targeted therapeutics. Advances in gene editing, synthetic biology, and computational modelling are creating unprecedented opportunities to precisely replicate and control the uterine environment, enabling healthier foetal development outside the body. Significant progress has been made from molecular delivery systems to early disease prevention and novel drug development. Addressing safety, ethical considerations, regulatory frameworks, and interdisciplinary collaboration will be vital to responsibly translating these technologies from research into clinical practice.

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From *Leduc* to Systems Medicine: The Mathematical Bridge in Synthetic Biology

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Introduction

Many acknowledge synthetic biology to have originated from Stéphane Leduc in 1912, who introduced the term "biologie synthétique" in French. However, its real implication is quite different and has little or no relation to today's well-developed field. (Leduc, 1912)

On the contrary, "synthetic biology," unlike other famous yet fancy terms, doesn't have a single clear originator but rather multiple significant contributors who reshaped and redefined the entire domain of systems biology... a domain that closely relates to synthetic biology.

According to many, one of the first uses of the phrase in its current sense was in 2000, when Stanford University's Eric Kool used it to refer to the engineering of biological systems. (Kool, 2000) Following this, in around 2003 to 2005, Drew Endy of MIT (now at Stanford) was instrumental in popularizing and defining the area, establishing synthetic biology as a separate engineering discipline devoted to the design and construction of biological components, technologies, and systems. (Endy, 2005) (Benner & Sismour, 2005) The modern conception of synthetic biology as an engineering approach to biology—Involving standardized biological parts, rational design principles, and bottom-up construction of biological systems—further crystallized through the work of multiple researchers in the early 2000s, including **Endy**, **Tom Knight** at MIT, and others in the emerging field. (Pottage, 2006)

This burgeoning area called synthetic biology now creates sophisticated biological systems by fusing genetic engineering with engineering concepts. It uses biological processes and genetic alterations to create useful goods. Synthetic biology uses technologies such as DNA synthesis and design to create bioparts or biocomponents that provide beneficial biofeatures, increasing the sustainability and efficiency of biological systems. Its practical uses, however, have just been made feasible in the last 20 years, necessitating substantial preparatory study, mathematical modeling, and technical advancements in DNA synthesis and sequencing to comprehend the functioning of cells and biological systems.

Mathematical modelling and Systems Biology

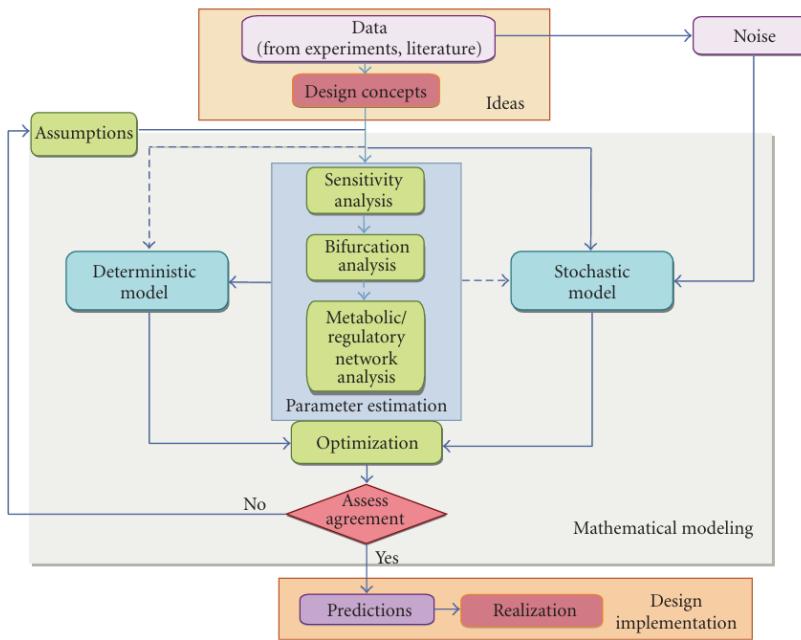


Fig.1: Overview of Mathematical Modeling

Reference: Zheng, Y., & Sriram, G. (2010). *Mathematical Modeling: Bridging the Gap between Concept and Realization in Synthetic Biology*. *BioMed Research International*, 2010, 541609. <https://doi.org/10.1155/2010/541609>

Mathematical modeling plays a crucial role in synthetic biology, connecting design concepts to realization. (Pasotti et al., 2014) It involves estimating parameters, which are then formulated based on assumptions and can be deterministic or stochastic. The process involves sensitivity analysis, bifurcation analysis, and metabolic and transcription network analysis. The dashed line from design concepts to deterministic models indicates that parameter estimation may be trivial or bypassed. A stochastic models use statistical functions to mimic system dynamics and consider data fluctuations. Parameter estimation may also provide information for selecting statistical functions in stochastic models. Optimization is necessary for both models and is complete when the model exhibits goodness of fit with experimental data. A good agreement allows for reliable prediction of system behavior and further biological realization, while unsatisfactory agreement necessitates revision of initial assumptions and the start of the next modeling cycle. (Zheng & Sriram, 2010)

However, mathematical modelling does exhibit certain limitations. Biological systems are challenging to model and simulate due to their complexity on multiple scales. These systems include metabolites, metabolic fluxes, proteins, RNA, and genes, which can form feedback loops that respond at various time scales. (Zheng & Sriram, 2010) Living systems are also highly sensitive to time-variant environmental conditions, leading to biological errors. This makes it difficult to predict the output of a biological system, unlike mechanical or electrical systems. However, simplifying a biological system can provide insights into synthetic circuit construction. Simplification of a model requires making various assumptions, such as homogeneity within the cell and within a cell population. Spatially homogeneous time-variant systems can be modeled using ordinary differential equations, while time-variant systems with compartmentation, spatial segregation, or intracellular gradients may require partial differential equations. (Zheng & Sriram, 2010)

Bridging gap between therapeutics and synthetic biology

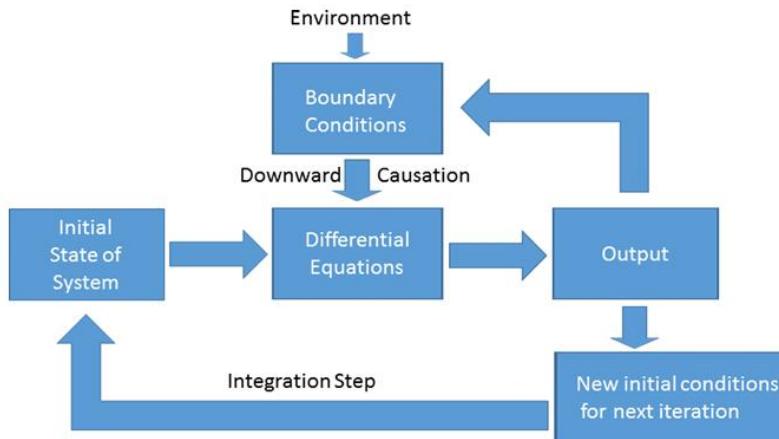


Fig.2: Integration Motif

Maguire G. (2014). *Systems biology approach to developing "systems therapeutics"*. ACS medicinal chemistry letters, 5(5), 453–455. <https://doi.org/10.1021/ml5000614>

Even after systems biology was introduced to the domains of biology and therapeutic development, the approach used in therapeutic development has frequently remained focused on using systems biology to identify the single target or pathway that may be disturbed most effectively in order to generate a treatment. The phrase "finding the magic bullet" is frequently used to characterize this prevalent issue. The proper method of thinking must instead change to one of identifying the bare minimum of targets or pathways to disrupt utilizing the "minimum molecule set" in order to create a therapy that works optimally. (Maguire G., 2014)

It's a well – known fact that human diseases and drug response are complex traits involving molecular networks driven by genetic and environmental perturbations. These changes can induce changes in biochemical processes or broader molecular networks that affect cell behavior, leading to pathophysiological states at the organism level. However, the concept of downward causation is often overlooked in models, and understanding disease requires multiple levels of understanding, such as protein, lipid, metabolic, tissue, and environmental networks. Causation flows in all directions among these networks. (Maguire, 2014)

A mathematical perspective can describe every component of a biological system in kinetic terms, such as the Motif at the level of DNA. A difference in DNA sequence can have various phenotypic effects until boundary conditions are set, including the actions of other genes, metabolic states, and the environment. Considering a disease state with data at only one level, including DNA sequence, will result in no predictability of the disease. In analogy with differential equations, understanding the necessary components and functions requires integrating data sets, including downward causation. Incorporating all these data sets into a predictable model is a classic big data problem. (Maguire, 2014)

From Leduc's visionary "biologie synthétique" to today's engineered biological circuits, synthetic biology has transformed from ambitious concept to predictable science through mathematical precision. No longer chasing pharmaceutical "magic bullets," we now orchestrate biological symphonies—targeting minimum molecule sets that harmonize with life's complex networks. Mathematical models serve as our conductor's baton, translating biological chaos into therapeutic melody. As DNA becomes programmable code and cells become living factories, we stand at the threshold of rewriting life itself. The convergence of mathematical rigor and biological creativity promises not just new medicines, but a fundamental reimaging of what it means to heal.

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Article 10:



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Exosome-Mediated Therapeutics for Neurodegenerative Disorders: Crossing the Blood–Brain Barrier at the Molecular Scale.

Exosomes are tiny, nano-sized extracellular vesicles that facilitate cell-to-cell communication and regulate a variety of physiological and pathological processes by transporting bioactive macromolecules like DNA (degraded fragments of about 200bp), mtDNA, mRNA, miRNAs, ncRNA, piRNA, lncRNAs, snRNAs, proteins, lipids, and more to recipient cells ([Record et al., 2013](#)). They originate from the endosomal system through a complex endocytic pathway that carries cell-specific cargos, which eventually fuse with the plasma membrane and are released into the extracellular space ([Zhang et al., 2019](#)). Initially thought to be mere cellular waste bags, exosomes are now an emerging revolutionary breakthrough in bioengineering. Specifically, in drug delivery, this method offers higher biocompatibility (from the patient's own cells), a bilayered lipid structure, lower toxicity, and the ability to diffuse through the blood and cross the blood-brain barrier. Its capacity to bypass the P-glycoprotein drug efflux system and provide tissue specificity highlights its potential for targeted drug delivery through engineered exosomes. Based on the surface recognition pattern, they can be effortlessly delivered to any type of cell. Exosomes carry various types of cargo, 80% of which are highly conserved. Some of these cargoes can be used as non-invasive diagnostic biomarkers or as nano-delivery systems.

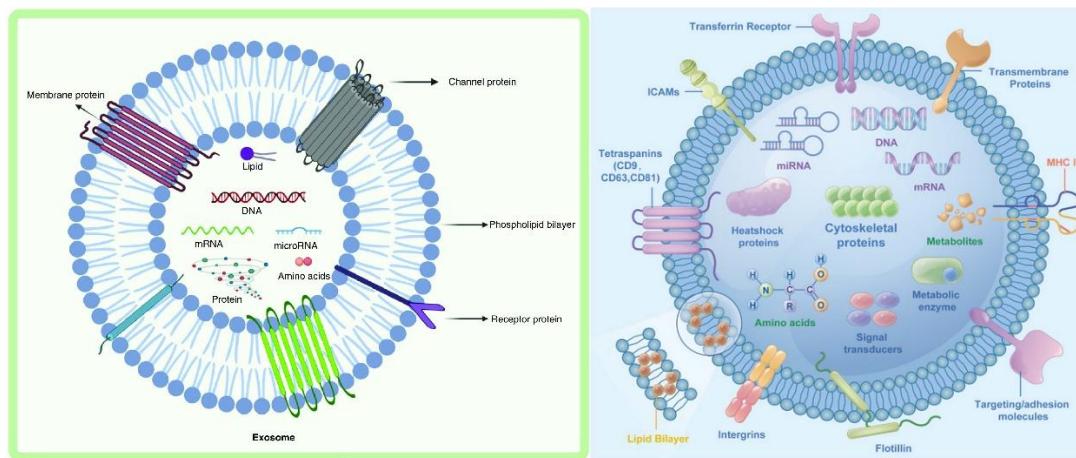


Figure 1: A. Framework of Exosomes ([Dilsiz, 2021](#)). B. Detailed composition of the exosome membrane and immunoregulatory molecules ([Si et al., 2023](#)).

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From Toxin Clearance to Biomarkers: Exosomes' Functions in Neurology

Neurological diseases affect approximately 10 million people worldwide, and their severe pathological conditions are characterized by immune cell-mediated reactions and protein aggregation in the brain. This highlights its role in regulating a wide range of neurodegenerative diseases such as Alzheimer's, Parkinson's, and Amyotrophic Lateral Sclerosis (ALS) ([Singh et al., 2024](#)). A stable internal environment,

or microenvironment, is maintained by the brain's interstitial fluid and cerebrospinal fluid (CSF) together to support brain cells. The brain's interstitial fluid is crucial for intercellular communication, waste removal, and nutrient supply. Despite having minimal reserves of fatty acids, brain cells are highly metabolically active and produce various wastes, including byproducts of cellular processes and neuronal activity (amyloid- β (A β), tau, neurotransmitter metabolites, lactate, alpha-synuclein, etc.). Exosomes have a dual role: propagating signals like A β and α -synuclein between cells and being involved in disease pathogenesis; they also assist in clearing accumulated toxins. Neurons, oligodendrocytes, astrocytes, and microglia all produce exosomes to deliver neurotrophic factors that are vital for brain repair, synaptic plasticity, and overall development. For example, exosomes from microglia carrying lactate during synaptic activity help maintain energy balance. Exosomes produced during hypoxia, oxidative stress, or circadian rhythm disruption can contribute to various neurological disorders and tumor progression ([Aryani & Denecke, 2016](#); [Yakovlev, 2023](#); [Singh et al., 2024](#)). Phagocytosis of these cells is prevented because of their natural origin, which gives them a "I am yours-Don't eat me" signal. The cell's composition, specific transporters, and membrane structure help identify the cell's origin, serving as important diagnostic biomarkers with specific proteins such as the cell adhesion protein L1, HSC70, subunits of the AMPA glutamate receptor, miR-1246, and tetraspanins, among others ([Yakovlev, 2023](#)).

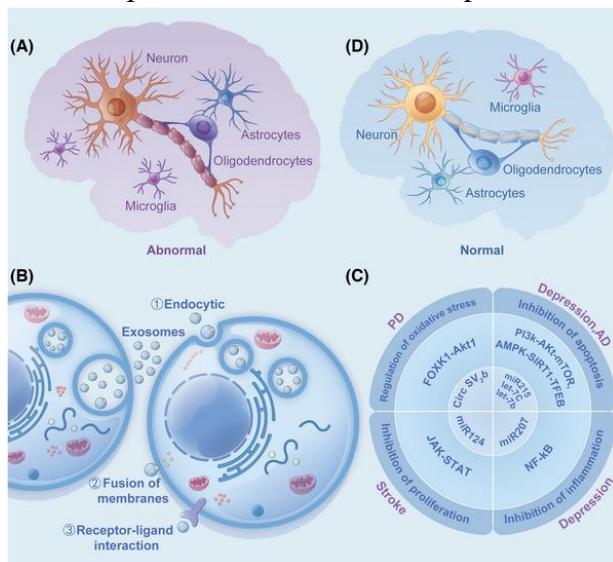


Figure 2: Mechanistic Overview of Exosome-Mediated Modulation of Neuroinflammation. **A.** Nerve cells that undergo inflammation and oxidative stress; **B.** Exosomes interact with target cells; **C.** Exosomes mediate intracellular signaling pathways; **D.** Nerve cells that have experienced biological effects ([Si et al., 2023](#)).

<https://cdn.ncbi.nlm.nih.gov/pmc/blobs/464d/10258444/26cb6c1bb31d/MCO2-4-e287-g003.jpg>.

From Blood-Brain-Barrier Penetration to CRISPR: Expanding Exosome Therapeutic Frontiers

Vesicles with desired properties can be generated to express specific ligands, signals, and proteins through selective engineering of exosomes. ([Khongkow et al.](#)) demonstrated that exosomes engineered with rabies viral glycoprotein (RVG) paved the way for neurodegenerative disease therapies by enabling the delivery of RNA therapeutic molecules to neuronal targets, successfully crossing the blood-brain barrier. Jia et al. highlighted the effectiveness of donor cell-engineered exosomes carrying ligands that can specifically bind to neuropilin-1, which is expressed by glioblastoma cells, thereby revealing enhanced targeting of brain tumors([Alvarez-Erviti et al.](#)). showcased how modified dendritic cells carrying siRNA targeting the BACE1 gene successfully silenced the intended gene ([Mehdizadeh et al., 2025](#)). The groundbreaking discovery of CRISPR/Cas9 can be harnessed to develop highly precise and accurate therapeutic strategies. Exosomes derived from donor cells, engineered or encapsulated with CRISPR/Cas9 targeting specific

genes such as PCSK9, have shown high specificity in genome editing in preclinical models ([Duan et al., 2021](#)). These exosome-mediated therapies are not limited to neurological disorders but hold significant potential for treating a wide range of diseases, including cancer, cardiovascular diseases, and inflammatory conditions ([Rezaie et al., 2022](#)). Advancing from laboratory research to clinical application is formidably complex. Advances in techniques that can produce heterogeneous exosome forms could provide transformative solutions to overcome major obstacles in treating neurological diseases, opening new prospects and enabling cutting-edge applications ([Mehdizadeh et al., 2025](#)).

Conclusion

Exosomes are emerging as powerful tools for modulating neuroinflammation at the molecular level, serving as nanoscale carriers for therapeutic cargo such as miRNAs and gene vectors. Advancements in standardization, isolation, characterization, and quantification techniques—combined with innovative bioengineering approaches—can address existing challenges and enhance their clinical utility. Furthermore, their potential as non-invasive biomarkers offers opportunities for early detection and prognosis of neurological disorders.

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Article 11:



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Chromosomal Therapies: Revolutionizing Down Syndrome Treatment

Introduction

Down syndrome, characterized by trisomy 21, an extra copy of chromosome 21 that affects approximately 1 in 700 newborns globally, leading to developmental delays, cognitive impairments, and health complications due to the overexpression of chromosome 21 genes (Antonarakis et al., 2020). Traditional interventions focus on symptom management through therapies and medical care, but they do not address the genetic root of the condition. The advent of next-generation therapeutics, particularly genome editing technologies, offers transformative potential by targeting the extra chromosome itself. This article explores chromosomal therapies for Down syndrome, emphasizing CRISPR-Cas9-based chromosome elimination, XIST-mediated silencing, and gene-specific modulation. These innovations, still in preclinical stages, highlight biotechnology's capacity to redefine genetic disorder treatment, aligning with the theme of cutting-edge therapeutics.

CRISPR-Based Chromosome Elimination

A groundbreaking study by Hashizume et al. (2025) at Mie University demonstrated the use of CRISPR-Cas9 to selectively eliminate the extra chromosome 21 in human induced pluripotent stem cells (iPSCs) and skin fibroblasts derived from individuals with Down syndrome. The approach employs allele-specific guide RNAs to target unique DNA sequences on the extra chromosome, inducing double-strand breaks that destabilize it during cell division. This technique achieved a chromosome elimination rate of up to 37.5%, restoring disomy in treated cells. Functional outcomes included normalized gene expression, enhanced cell proliferation, and reduced oxidative stress, which are hallmarks of trisomy 21's cellular pathology. Corrected cells also exhibited improved nervous system gene activity and reduced metabolic gene overexpression, suggesting a reversal of trisomic defects at the molecular level. However, challenges persist, including off-target effects that may damage healthy chromosomes and the technique's limitation to *in vitro* settings. Scaling this approach to *in vivo* applications requires overcoming delivery barriers and ensuring long-term safety, underscoring the need for further research (Hashizume et al., 2025).

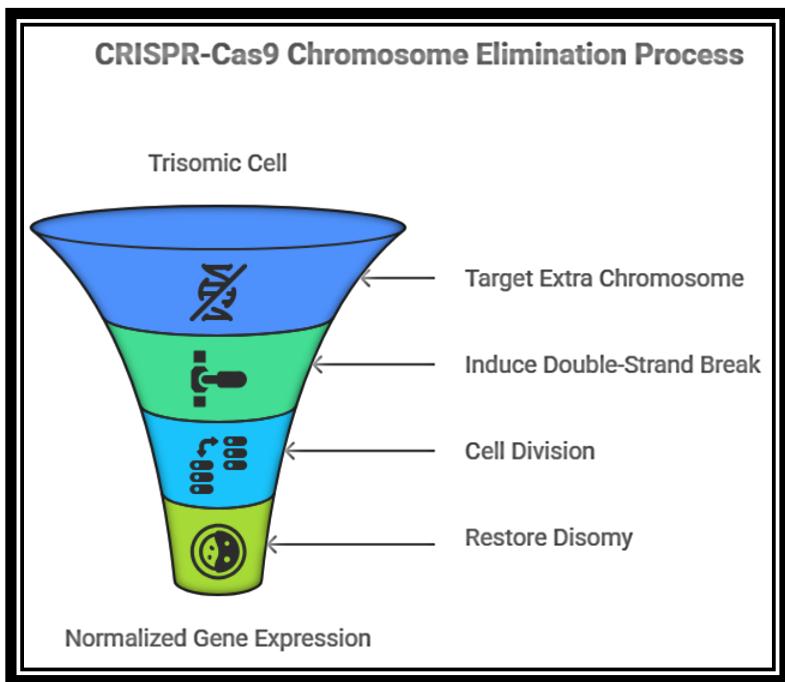


Diagram 1

XIST-Mediated Chromosome Silencing

An alternative strategy involves silencing the extra chromosome 21 without removing it, using the X-inactive specific transcript (XIST) gene. In 2014, researchers at the University of Massachusetts Medical School inserted XIST into iPSCs from Down syndrome patients, inducing epigenetic silencing by coating the extra chromosome with RNA, mimicking natural X-chromosome inactivation in females (Jiang et al., 2013). This reduced the expression of trisomic genes by up to 85%, restoring cellular phenotypes without altering the chromosome's structure. Recent studies have extended XIST silencing to mouse models of Down syndrome, achieving partial normalisation of neural function, though challenges remain in scaling to human tissues (Czermiński & Lawrence, 2020). Unlike CRISPR, XIST offers a non-destructive approach, potentially safer for postnatal applications. However, its efficacy depends on stable XIST expression and tissue-specific delivery, which are active areas of investigation. This method complements chromosome elimination by providing a less invasive therapeutic option.

Gene-Specific Modulation

Targeted modulation of overexpressed chromosome 21 genes offers another therapeutic avenue. Genes like DYRK1A, APP, and SOD1, linked to cognitive deficits and Alzheimer's-like phenotypes in Down syndrome, are prime targets. A 2025 study by Assamy used CRISPR to silence DYRK1A in Down syndrome cell models, improving neurogenesis and cellular phenotypes (Assamy, 2025). Earlier research demonstrated that normalising OLIG1 and OLIG2 expression in mouse models enhanced neural development (Chakrabarti et al., 2010). Alternative tools, such as zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs), have also been explored to downregulate specific genes or regions like the Down Syndrome Critical Region (DSCR) (Huang et al., 2024). These targeted approaches are more precise than whole-chromosome interventions, potentially reducing off-target risks, but they address only specific aspects of the syndrome's pathology.

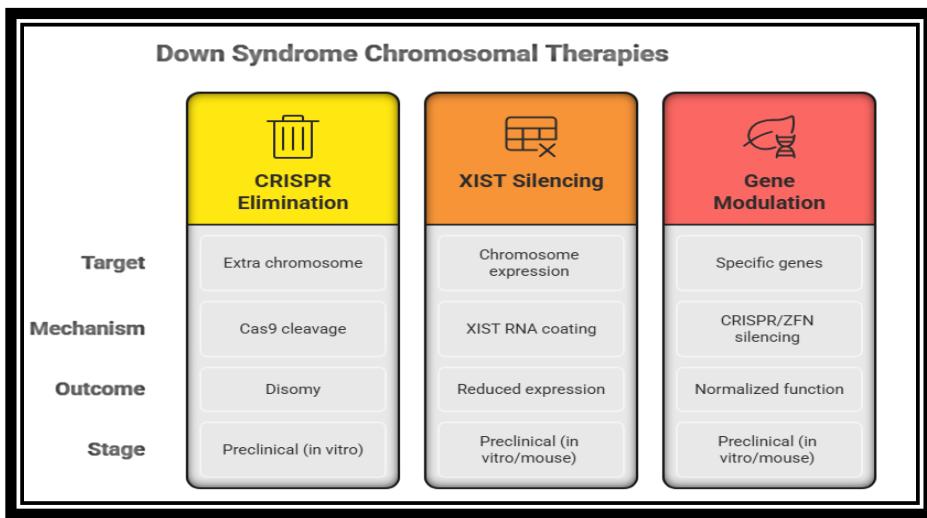


Diagram 2

Challenges and Future Directions

Chromosomal therapies hold immense promise but face significant hurdles. Off-target effects in CRISPR and ZFN/TALEN applications risk unintended genetic alterations, necessitating improved targeting precision. Delivery remains a critical barrier, as editing trillions of cells in a living organism, particularly non-dividing cells like neurones, is complex. Nanotechnology, such as PLGA nanoparticles, shows potential for enhancing delivery to specific tissues, but these systems are still in early development (Hussein et al., 2019). Ethical considerations are equally pressing. While some view chromosomal therapies as empowering, advocacy groups argue that framing Down syndrome as a condition to “cure” risks devaluing neurodiversity (Antonarakis et al., 2020). Engaging stakeholders like scientists, patients, and families—is essential to balance innovation with societal values. Future research will focus on refining delivery, ensuring safety, and exploring combination therapies, such as integrating XIST silencing with gene modulation.

Conclusion

Chromosomal therapies, from CRISPR-based chromosome elimination to XIST-mediated silencing and gene-specific modulation, represent a frontier in next-generation therapeutics for Down syndrome. By targeting the genetic basis of trisomy 21, these approaches offer hope for mitigating its effects at a molecular level, moving beyond symptom management to transformative care. While preclinical, their progress underscores biotechnology’s potential to address complex genetic disorders. For the biotechnology community, these innovations inspire continued exploration of genome editing’s therapeutic horizons, paving the way for a future where precision medicine redefines treatment possibilities.

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Aptamers: Pioneering Therapeutics in Wound Healing and Skin Regeneration
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Introduction

Aptamers are short, single-stranded DNA or RNA molecules that can fold into unique three-dimensional shapes, granting them the ability to bind selectively and with high affinity to a wide array of biological targets such as proteins, peptides, small molecules, and even whole cells. Their unique properties—high specificity, low immunogenicity, and ease of chemical synthesis—make them powerful tools in the development of next-generation therapeutics. These oligonucleotides have garnered significant attention for roles spanning diagnostics, targeted drug delivery, and therapeutic intervention (Keefe, Pai, & Ellington, 2010).

Why Aptamers Represent the Next Therapeutic Evolution

Several attributes make aptamers particularly attractive for therapeutic applications, especially in complex and sensitive tissue environments such as skin wounds:

- Rapid and scalable synthesis: Unlike protein-based biologics, aptamers are chemically synthesized with high reproducibility and at lower cost, enabling scalable manufacturing (Bouchard, Hutabarat, & Thompson, 2010).
- Low immunogenicity: Aptamers' nucleic acid structure, combined with chemical modifications, minimizes the risk of immune activation (Ng et al., 2006).
- Versatility in function: Aptamers can act as inhibitors, activators, or delivery vehicles, tailored precisely to interact with chosen molecular pathways (Zhu & Chen, 2018).
- SELEX technology: The systemic evolution of ligands by exponential enrichment (SELEX) allows rapid and precise identification of aptamers that bind nearly any molecular target, including those challenging to drug by conventional means (Sun et al., 2014).

These qualities equip aptamers to serve as highly specific, tuneable therapeutics with adjustable pharmacodynamics—perfect for dynamic environments like wound sites where controlled and localized intervention is crucial.

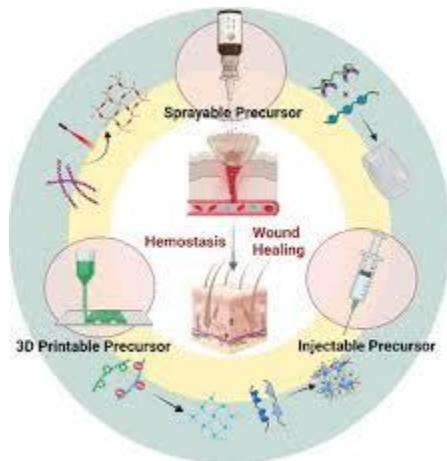
Application of aptamers for infectious disease control



Aptamer role in theranostic applications.

Aptamers in Wound Healing: Emerging Therapeutic Solutions

Chronic wounds and difficult-to-heal skin injuries represent a significant clinical challenge with large impacts on patient quality of life and healthcare resources. Recent advances highlight aptamers as innovative agents that can promote wound repair through precision targeting of biological pathways essential for skin regeneration.



In situ forming hydrogels

- **Growth Factor Delivery via Aptamer-Functionalized Hydrogels**

Vascular endothelial growth factor (VEGF) is a crucial protein that stimulates angiogenesis and tissue regeneration during wound healing. Direct administration of VEGF faces challenges such as rapid degradation and poor retention at injury sites. To overcome these issues, researchers have developed hydrogels functionalized with VEGF-specific aptamers. These aptamer-modified biomaterials enable sustained and localized VEGF release, markedly enhancing tissue revascularization and accelerating wound closure compared to conventional dressings (Kim et al., 2014). The aptamers stabilize VEGF in the hydrogel and mediate controlled release kinetics suited to natural healing timelines.

- **Targeted Recruitment of Regenerative and Antimicrobial Cells**

Beyond growth factor delivery, aptamers integrated into wound dressings can selectively bind and recruit regenerative progenitor cells and immune cells that fight infection. This targeted cell recruitment accelerates the healing process and reduces the risk of microbial colonization—a common impediment to chronic wound resolution. By enhancing the cellular microenvironment, these aptamer-enhanced dressings support more organized and robust tissue repair.

Preclinical Evidence and Future Directions

Animal models of skin injury treated with aptamer-functionalized materials have demonstrated significantly faster wound closure, improved neovascularization, and enhanced tissue architecture quality relative to controls. These promising results suggest aptamers could become foundational components of next-generation wound care products, with the potential for customization to diverse wound types, including diabetic ulcers, burns, and surgical incisions.

The modularity and specificity of aptamers also enable combination approaches—where aptamers deliver multiple bioactive agents or simultaneously modulate inflammation, infection, and tissue regeneration—helping to address the multifactorial nature of chronic wounds.

Conclusion

Aptamer-based therapeutics offer exciting new avenues for wound healing and skin regeneration through their unique combination of specificity, stability, and tunability. By facilitating sustained growth factor delivery and targeted cell recruitment, they overcome many limitations of conventional wound care. Continued development and clinical translation of aptamer-functionalized biomaterials are poised to revolutionize treatment paradigms, enhancing patient outcomes for a variety of challenging skin injuries.

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WHAT IF CANCER PRETENDS TO BE VIRUS!

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July 24, 2025

Hacker of our immune system!

Cancer is a disease in our body that hacks and tricks our immunity. Cancer cells grow uncontrollably, evade death, and escape the surveillance of our immune system ([Hanahan & Weinberg, 2011](#)). As they originate from the body's own tissue, they are often undetected by our immune system, and hence, today, it is the biggest challenge. But what if we "mark" those cells as foreign, so that our immune system sees that as a threat? Recent advances in gene-editing technology, particularly using CRISPR-Cas9, have opened the door to an innovative strategy: editing cancer cells to mimic virus-infected cells, thus alerting the immune system to eliminate them ([Zhao et al., 2020](#)).

So, what is CRISPR?

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is a gene-editing technology derived from a natural defense system found in bacteria. With the help of a protein called Cas9, scientists can target and precisely cut DNA at specific locations ([Jinek et al., 2012](#)). This allows for either disabling, repairing, or inserting genes, offering powerful tools to alter cellular behavior.

It was originally used to fix genetic mutation, but now it is notably used to cure -cancer ([Manguso et al., 2017](#)).

Blind spot of our Immune System!

Our immunity is very well precise and highly effective. Under a normal situation, i.e, whenever our body gets exposed to foreign particles like viruses or bacteria, it responds quickly. Why does it respond quickly? Because all those viral and bacterial substances have an antigen on their surface, which serves as a "red flag" to our immune system, and hence the immune system releases Cytotoxic T lymphocytes (CTL), which recognize the antigens and destroy the viral and bacterial material which is exposed to our body ([Janeway et al., 2001](#)).

But things are different incase of Cancerous cells! As the cancerous cells are a mutated version of our body cells, they do not raise enough "red flags" to be noticed by our immune system. Moreover, some tumors even create an immunosuppressive environment, actively blocking the immune system's activity ([Whiteside, 2006](#)).

The CRISPR Strategy: Viral Mimicry

What if our immune system recognizes the cancerous cells as any viral particle and not as its own body cells? And here comes CRISPR technology, which helps us to trick our own immunity. How can it be done? By editing the specific genes of cancerous cells, we can program them to display viral-like features, particularly viral-associated molecular patterns such as double-stranded RNA or specific proteins normally found during viral infection ([Chuon et al., 2017](#)).

One promising approach involves activating the interferon response pathway, which is typically triggered when a virus is detected. CRISPR can be used to activate dormant parts of the genome that resemble viral sequences, called endogenous retroelements. When these elements are expressed, the cancer cell begins to look, at least on a molecular level, like a cell infected by a virus. This alerts the immune system to its presence ([Roulois et al., 2015](#)).

This process is called Viral mimicry. Essentially, CRISPR turns cancer cells into decoys—cells that mimic infected ones, which immune cells are programmed to attack. Once the immune system detects these altered cells, it launches a powerful immune response that can selectively target and kill the tumor ([Park et al., 2021](#)).

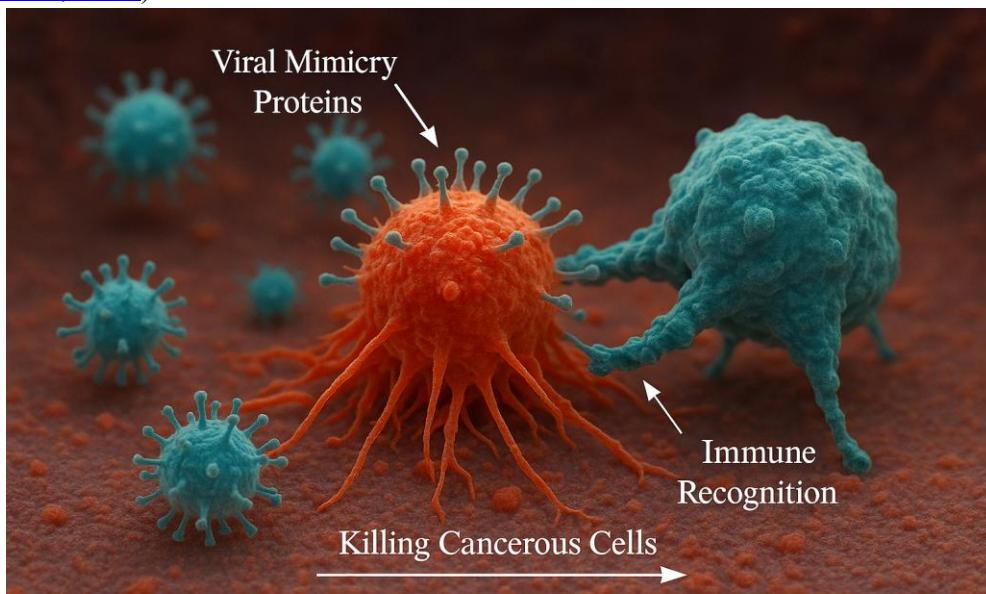


Figure 1. The cancerous cell mimicking as viral cells because of CRISPR technology

Advantages of Viral mimicry -

- Unlike chemotherapy and other radiation therapy, which harm healthy cells in our body, this method is more specific and targets cancerous cells ([Roulois et al., 2015](#)).
- This also helps to boost our immune system naturally instead of external therapies and medicines ([Chow et al., 2018](#)).
- Sometimes cancerous cells create self-resistance to the external drugs, but by using this technique, they will not be able to create resistance toward the immune system if the immune system is properly invaded ([Zhao et al., 2020](#)).

Though technology has advanced incredibly, it still hasn't matched the complexity, precision, and intelligence that already exists within our body's natural system.

Hence Challenges-

- It is important that CRISPR only targets the cancerous cells and not the healthy cells, for which it is necessary to introduce CRISPR safely and precisely into the tumor cells directly ([Zhang et al., 2019](#)).
- Overreaction of the immune system may happen due to which can also lead to autoimmune diseases ([Zhang et al., 2019](#)).
- It also depends on the body of the person whether the cancerous cells are growing fast or the immune system is working slowly, so according to the different body type, different doses need to be customized ([Topalian et al., 2016](#)).

Conclusion:

The use of CRISPR to induce viral mimicry in cancer cells represents a fascinating convergence of genetic engineering and immunotherapy. By making cancerous cells appear as viral cells, we are helping our body by naturally killing the cancerous cells with the help of the body's own

immune system. By using this technique, we will let our body suffer less and will save our body from harmful and painful radiation and therapy. This strategy could become a cornerstone of personalized cancer treatment—targeted, immune-driven, and minimally invasive. CRISPR, which was just a defense system used by bacteria, is now used to fight the war against cancer cells and hence it has now become a revolutionary tool to fight not just against cancer but with many more diseases and genetic disorders.

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“Next-Gen Therapeutics: Bioengineering at the Molecular Scale.”

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Date: July 2025



“Nanomedicine and Nano Drugs: Shaping the Future of Precision Therapeutics.”

Abstract

Nanomedicine, a rapidly evolving field within biotechnology and pharmaceutical sciences, focuses on using nanoscale materials for the diagnosis, treatment, and monitoring of diseases. Nano drugs, engineered at the molecular scale, enable targeted drug delivery, controlled release, and reduced systemic side effects. This article explores the basic concepts, mechanisms, applications, and future prospects of nanomedicine, particularly in cancer therapy, infectious diseases, and chronic conditions. With advances in bioengineering and the fusion of artificial intelligence, nanomedicine holds the potential to redefine personalized healthcare in the coming decade. ([Pan, 2024](#))

Introduction

Traditional drug therapies often face challenges such as poor bioavailability, nonspecific targeting, and adverse side effects. Nanomedicine addresses these issues by introducing nano-sized drug carriers—typically ranging from 1 to 100 nanometres—that can navigate biological barriers and deliver therapeutic agents precisely to the site of action (National Cancer Institute, 2023) ([Patra et al., 2018](#)). The unique physical and chemical properties of nanoparticles, such as large surface area, enhanced reactivity, and the ability to be functionalized, make them ideal tools for next-generation drug development.

What are Nano Drugs?

Nanodrugs are already in use for several diseases, including cancer, cardiovascular disorders, and microbial infections. The integration of nanotechnology with biotechnology, materials science, and computational modelling is pushing the boundaries of what medicine can achieve at the cellular and molecular levels. (Indian Council of Medical Research, 2022). *Nanomedicine Research in India – Current Trends.* www.icmr.gov.in)

Nano drugs are pharmaceutical compounds formulated with nanocarriers like liposomes, dendrimers, polymeric nanoparticles, micelles, and carbon nanotubes. These carriers encapsulate the active drug, protect it from degradation, and ensure its efficient delivery to the target tissue. (What is nanomedicine? <https://etp-nanomedicine.eu/about> -nanomedicine/what-is-nanomedicine)

Key features of nano drugs include:

- Targeted Delivery: Surface modification allows selective binding to diseased cells.
- Controlled Release: The drug can be released slowly over time to maintain therapeutic levels.
- Enhanced Solubility: Poorly water-soluble drugs can be made more bioavailable.
- Reduced Toxicity: Minimal exposure to healthy tissues lowers the risk of side effects.

Applications in Therapeutics

1. Cancer Treatment

Nanomedicine has shown exceptional promise in oncology. Nano drugs like Doxil (liposomal doxorubicin) and Abraxane (albumin-bound paclitaxel) are FDA-approved and used to treat breast, ovarian, and lung cancers. These formulations improve drug accumulation in tumours via the Enhanced Permeability and Retention (EPR) effect and minimize harm to healthy tissues. ([Gavas et al., 2021](#))

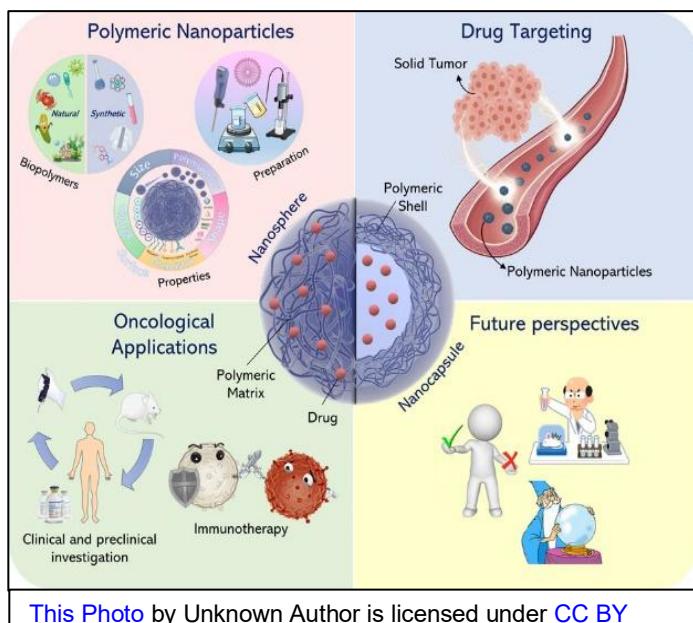


Figure 1. Polymeric nanoparticles for targeted drug delivery and cancer treatment with future biomedical applications.

2. Infectious Diseases

Nanoparticles can improve antibiotic delivery and help combat drug resistance. Silver and gold nanoparticles also show antimicrobial activity, disrupting bacterial membranes and biofilms. Nanocarriers are being investigated for efficient vaccine delivery, as seen in mRNA-based COVID-19 vaccines using lipid nanoparticles. ([Sobhani-Nasab et al., 2024](#))

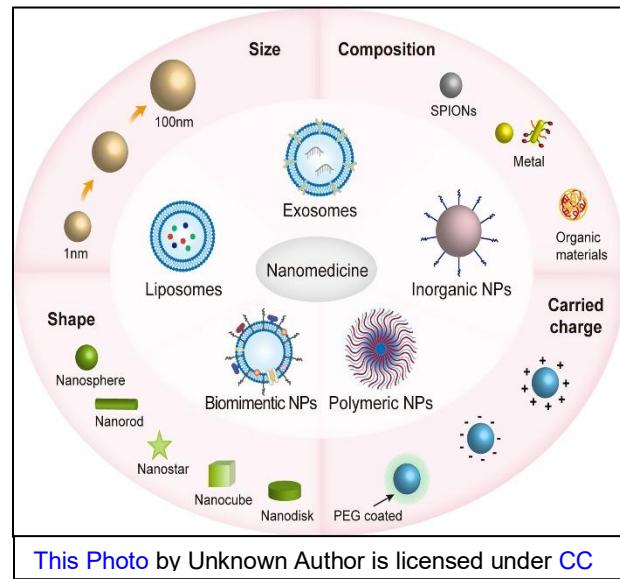


Figure 2. Classification of nanoparticles based on size, shape, composition, and surface properties used in nanomedicine.)

3. Neurological Disorders

Crossing the blood-brain barrier has been a major hurdle in treating diseases like Alzheimer's and Parkinson's. Nanoparticles functionalized with specific ligands can help transport drugs into the central nervous system with precision. (Recent Advances in Nanotherapeutics for Neurological Disorders. ([Vashist et al., 2023](#))

4. Cardiovascular and Chronic Diseases

Nano drugs are being designed to treat atherosclerosis by targeting plaque buildup in arteries. Similarly, in diabetes, insulin-loaded nanoparticles offer sustained glucose control with fewer injections. ([Omidian et al., 2023](#))

Recent Innovations

Nanomedicine is being elevated through AI-powered modelling, 3D bioprinting, and biosensor integration. Researchers are now developing smart nanocarriers that respond to pH, temperature, or specific enzymes within diseased tissues to release drugs only when needed.

A breakthrough in nanorobotics is also underway, where programmable nano-devices are expected to perform tasks like repairing tissues or removing clots at the microvascular level. The combination of bioinformatics and nanomedicine allows personalized therapy designs based on genomic or proteomic data. (Indian Council of Medical Research, 2022). *Nanomedicine Research in India – Current Trends.* www.icmr.gov.in)

Challenges and Limitations

- Despite remarkable progress, nanomedicine faces several hurdles:
- Toxicity Concerns: Some nanoparticles can trigger immune responses or accumulate in organs.
- Regulatory Approval: There is a lack of standardization for testing and approving nano drugs.
- Manufacturing Complexity: Scale-up of nanoparticle synthesis is still cost-intensive.
- Limited Public Awareness: There is a need for better communication between scientists, clinicians, and patients.

These challenges must be addressed through interdisciplinary collaboration, responsible innovation, and robust clinical trials.

Future Prospects

The future of nanomedicine lies in precision therapeutics, where treatments are tailored for individual patients. Developments in CRISPR gene editing, Nano vaccines, and RNA therapeutics will further expand the scope of nano drugs. In low-resource settings, cost-effective nano-formulations could bridge healthcare disparities.

India, too, is contributing to this revolution. Institutions like the Indian Institute of Science (IISc), IIT Bombay, and National Institute of Pharmaceutical Education and Research (NIPER) are conducting cutting-edge research in nano-based drug delivery and diagnostics. Indian biotech startups such as Bugworks, Molbio Diagnostics, and CuraTeQ Biologics are paving the way forward. (Indian Council of Medical Research. (2022). *Nanomedicine Research in India – Current Trends*. www.icmr.gov.in)

Conclusion

Nanomedicine is a game-changer in the quest for effective and personalized healthcare. With the growing need for safer, faster, and smarter therapies, nano drugs stand at the frontier of biomedical innovation. Continued research, ethical regulation, and collaboration across scientific domains will be key to unlocking their full potential. (Indian Council of Medical Research. (2022). *Nanomedicine Research in India – Current Trends*. www.icmr.gov.in)

The convergence of nanotechnology, biology, and artificial intelligence is not just a possibility—it's the next big leap in therapeutics.

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POSEIDON: A Nature-Inspired, Synthetic Biology Approach for Water Bioremediation Using Engineered Peptides

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Introduction

Water contamination has always been a sensitive issue due to the dangers it poses to civilization as well as natural ecosystems. Metals like iron, cadmium, nickel, arsenic, chromium, mercury and many others are being found in ever-increasing amounts in various rivers across India (**Govil and Krishna, 2018**) and the world (**Fischer et al., 2021**). With the extent of industrialization, unplanned urbanization, and lack of proper environmental standards to curb its negative effects, this problem shows no signs of slowing down. Despite the gravity of this issue, existing filtration solutions are often non-specific, expensive, or difficult to deploy, which results in a compromise on the filtration capability. **The future of environmental health lies in molecular-scale solutions, not for human bodies, but for Earth's most vital resource: water.** This ties into the **POSEIDON** project, which is short for ‘Phytoprotein Optimized System for Environmental Ion Detoxification,’ and it harnesses synthetic biology as the driving force behind its creation. This proposed solution not only serves as an efficient filtration module but also promises to be convenient to use and easy to deploy.

Societal and Environmental Impact

Water samples collected by the team from three geographically diverse locations revealed contamination levels significantly above the stipulated limits from the Central Pollution Control Board (CPCB). These locations are not only the site of industrial dumping but also the lifeline of several cities and villages that depend on their water. Mercury contaminations were as high as 0.895 ppm, nearly 900 times the permissible threshold of 0.001 ppm! Iron and aluminum levels also exceeded acceptable limits, underscoring the need for site-specific remediation.

POSEIDON is designed with the goals of community empowerment and sustainability in mind-values that are essential for rural and resource-constrained areas. Additionally, the project aims to support -

- **Metal reuse** - feeding into circular economy frameworks
- **UN SDGs alignment** - contributing to clean water access, responsible consumption, and climate action
- **Public health** - reducing the strain on healthcare resources and preventing humanitarian crises.

Additionally, the global biofilter market is projected to grow at over 9.5% Compound Annual Growth Rate (CAGR) and is estimated at \$3.7 billion USD in 2024. This indicates a fertile opportunity for real-world application and bio-entrepreneurship while mitigating societal and environmental handicaps. (**Biofilter Report 2025 - 2030**)



Figure 1: Schematic representation of the most important natural (rectangles bordered by solid black lines) and anthropogenic (rectangles with dashed black lines) sources of metal contamination, with metal transfer pathways (ovals) in the environment as well as into the human food chain, and on-site and off-site approaches to remediate metal-contaminated soils.

(Ondrasek et al., 2025)

Our Approach for This Problem

POSEIDON is built on engineered phytoproteins, namely metallothioneins (MTs) and phytochelatins (PCs). These are two classes of cysteine-rich peptides known for their metal sequestering ability. (Agarwal et al., 2025). A computational pipeline was designed that screened over 6,500 candidate sequences retrieved from gene databases. These were filtered down to a few dozen based on molecular docking and binding energy predictions, and engineered MTs were optimized for iron, aluminum and chromium ions. After running simulations, engineered peptides demonstrate higher binding efficiency and selectivity compared to their native counterparts, especially for Iron and aluminum ions. The team plans to utilize a cell-free protein expression system that will enable the rapid production of peptides in vitro. This method allows for the construction of a prototype without a lot of hurdles and avoids regulatory and metabolic complexities associated with live-cell bioreactors that are often harder to maintain, difficult to scale up, and intricate to build.

Additionally, after the bioengineering pipeline, the second innovation of POSEIDON comes to light. Here, these designed peptides are embedded within a sodium alginate matrix in order to form stable hydrogel beads. The constituent of this matrix is a polysaccharide derived from brown algae, which designates an added layer of non-toxicity, affordability, and stability to this structure along with its ability to form ionically crosslinked gels when bathed with divalent crosslinking cations like calcium ions. (Zhang et al., 2021) To ensure long-term stability and prevent peptide leaching, the team implements EDC/NHS coupling chemistry, which enables covalent bonding between carboxyl groups in the alginate and amine groups on the peptide. This measure improves the mechanical robustness while

ensuring no detrimental side effects of their prototype on the environment.

In short, the peptides act as the molecular therapeutics, whereas the hydrogel serves as the delivery platform. The final filter design consists of layered peptide-embedded gel beads packed within a modular housing unit that allows customization based on regional contamination profiles. The gel matrix and bead structure can be fine-tuned based on its filtration capability to include more beads, have a stiffer mechanical nature, or display increased porosity to hold more peptides and allow easy diffusion of water.

Conclusion and Outlook

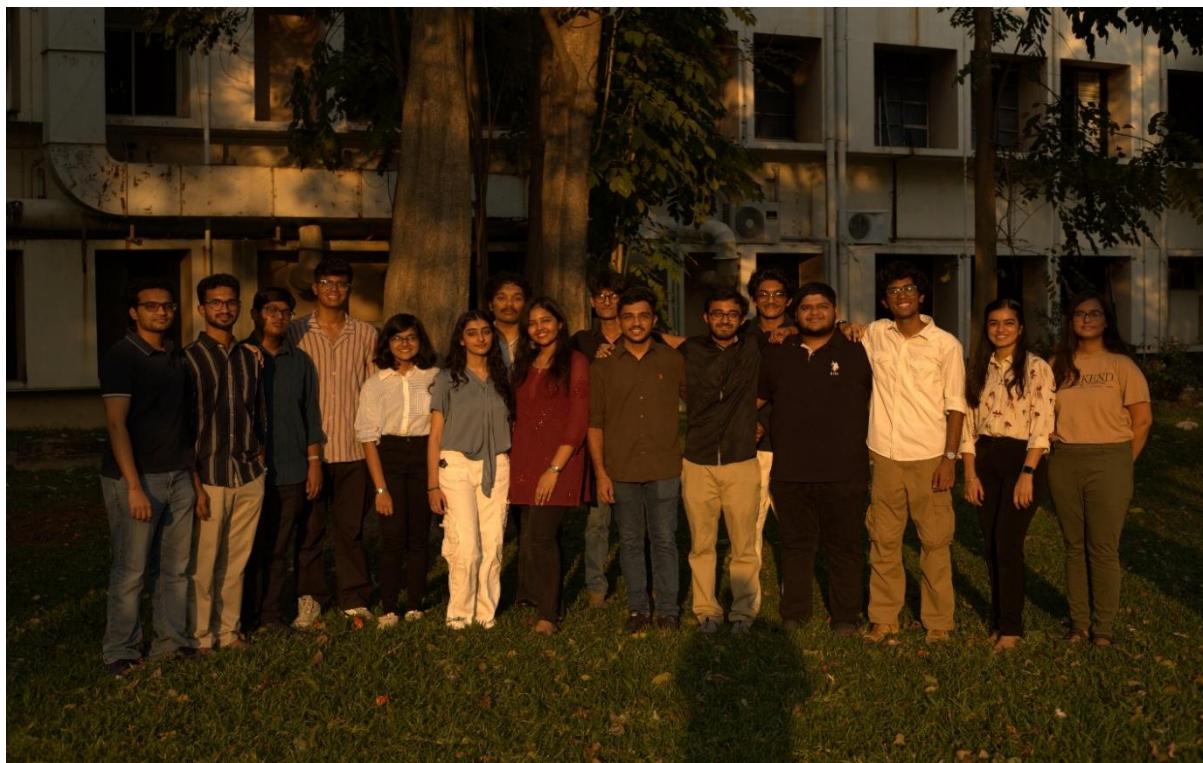
POSEIDON offers a compelling reason for the application of synthetic biology in environmental remediation. Its blend of protein engineering, biopolymer chemistry, and real-world applicability denotes it as a tool for addressing water contamination while simultaneously increasing the quality of life of multiple habitats as an unintended consequence. The next steps involve performance benchmarking under dynamic field conditions in order to explore IoT and integrated sensing features for on-site diagnostics- a feature that can prove to be very handy in remote regions. It is safe to say that with further development, POSEIDON could become a cornerstone technology for environmental resilience and sustainable development while uplifting ecosystems.

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Engineering E. coli for Sustainable Production of Ambrein: A Synthetic Biology Approach to Next-Gen Therapeutics

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Abstract:

Synthetic biology has opened doors to scalable, ethical, and sustainable production of high-value bioactive compounds. Our iGEM team at MIT-WPU Bharat focuses on bioengineering Escherichia coli to produce ambrein, a rare triterpenoid and the primary bioactive constituent of ambergris. Traditionally sourced from sperm whales, ambergris holds immense pharmacological potential but faces legal and ethical constraints. Our project leverages the metabolic versatility of E. coli and advanced molecular tools to establish a microbial biosynthesis platform for ambrein, highlighting the possibilities of therapeutic bioengineering at the molecular level.

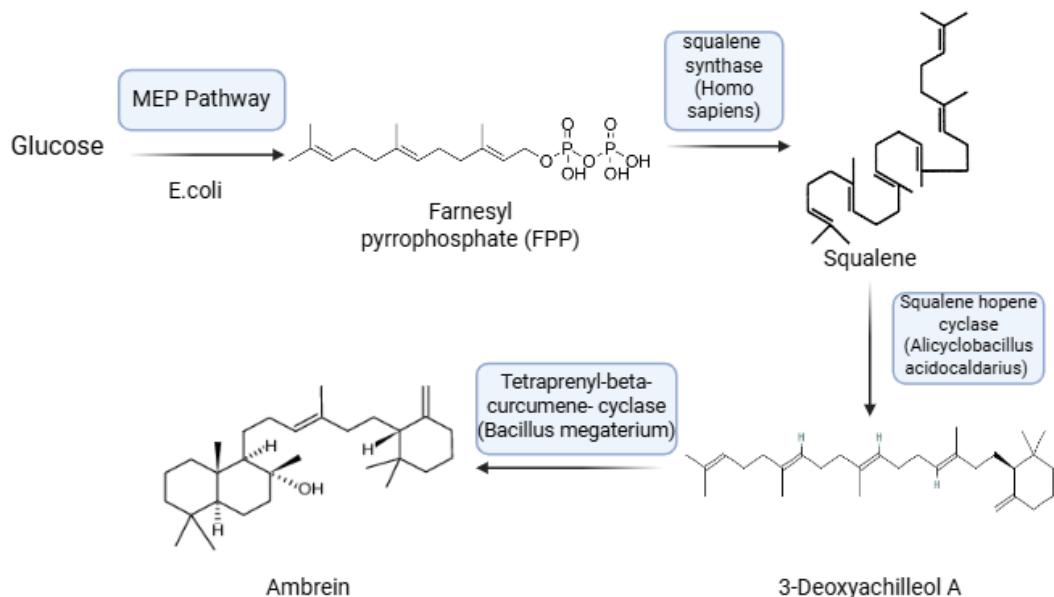
Introduction:

The landscape of medicine is evolving at an unprecedented pace, driven by the urgent need for precision, sustainability, and accessibility. As chronic diseases, antibiotic resistance, and neurodegenerative disorders rise, the limitations of conventional drug discovery are becoming more apparent. In this context, synthetic biology offers a transformative approach, one that operates at the molecular scale to reprogram living systems for therapeutic innovation. (Nielsen & Keasling, 2016; Bian et al., 2020)

Among the most compelling use cases of synthetic biology is the sustainable production of high-value natural compounds that are otherwise rare, ethically contentious, or environmentally damaging to harvest. One such compound is ambrein, the key bioactive constituent of ambergris, a waxy substance produced in the digestive system of sperm whales (*Physeter macrocephalus*). Historically prized in traditional medicine and perfumery for its fixative and medicinal properties, ambergris is now at the centre of legal and ethical debates. In India and many other countries, the trade and possession of ambergris are banned due to its association with endangered whale species protected under national and international conservation laws. (Indian Wildlife Protection Act, 1972)

Despite the restrictions on its source material, ambrein has shown significant pharmacological promise. Studies suggest it possesses anti-inflammatory, antioxidant, analgesic, neuroprotective, and quorum-sensing inhibitory properties, ‘making it a potential candidate for next-generation therapeutics. However, its rarity and reliance on illegal trafficking have hindered scientific and clinical exploration. (He, Yu, & Ye, 2024)

Design Overview:



We engineered *E. coli* BL21(DE3) to biosynthesize ambrein starting from glucose. The biosynthetic pathway involves multiple stages:

MEP Pathway for Isoprenoid Precursors:

The native *E. coli* MEP (methylerythritol phosphate) pathway was used to generate isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), the fundamental building blocks of terpenoids.

Farnesyl Pyrophosphate (FPP) Synthesis:

An overexpressed *ispA* gene ensures efficient conversion of IPP and DMAPP to FPP.

Squalene Synthesis and Cyclization:

FPP is then converted to squalene using a truncated squalene synthase (tSQS), followed by cyclization using squalene-hopene cyclase (SHC) or bacterial oxidosqualene cyclase analogs to produce 3-deoxyachilleol A, a known ambrein precursor. (Yamada et al., 2022)

Ambrein Synthase Expression:

Enzymatic conversion of the intermediate to ambrein is achieved through heterologous expression of ambrein synthase genes sourced from plant and animal databases.

Each gene in our construct is codon-optimized for *E. coli* and introduced using modular plasmid systems. Promoter tuning and ribosome binding site optimization allow precise control over enzyme expression levels, preventing metabolic burden and optimizing flux through the pathway. To ensure protein solubility and functionality, enzymes were tagged with fusion domains and chaperone systems.

Further, to facilitate downstream detection, we incorporated His-tags for western blotting and purification.

Applications and Therapeutic Potential:

Ambrein, a polycyclic triterpenoid and the principal bioactive compound in ambergris, has long been known for its fixative properties in the fragrance industry. However, recent advances in pharmacological research have revealed ambrein's multi-functional therapeutic potential, making it a compelling candidate for development as a next-generation therapeutic agent. (Indian Wildlife Protection Act, 1972)

1. Anti-inflammatory Effects:

One of the most well-documented biological effects of ambrein is its anti-inflammatory activity. It has been shown to inhibit the production of pro-inflammatory cytokines such as TNF- α and IL-6, both of which are implicated in autoimmune diseases, chronic inflammation, and metabolic disorders. Its ability to modulate oxidative stress pathways and suppress immune overactivation makes it a strong candidate for use in inflammatory conditions such as rheumatoid arthritis, Crohn's disease, and even long COVID. (Bian et al., 2020)

2. Analgesic (Pain-Relief) Properties:

Ambrein also exhibits central and peripheral analgesic activity, potentially by interacting with opioid and non-opioid receptors in the nervous system. In rodent models, ambrein has been shown to raise pain thresholds without the adverse effects commonly associated with traditional analgesics. This suggests that ambrein could serve as a non-addictive alternative to opioid-based painkillers, a major unmet need in global healthcare. (Ke et al., 2017)

3. Neuroprotective and Anti-Amyloid Activity :

One of the more cutting-edge therapeutic applications of ambrein is in the field of neurodegenerative diseases. Preliminary studies indicate that ambrein may inhibit the aggregation of β -amyloid plaques, one of the pathological hallmarks of Alzheimer's disease. It also exhibits antioxidant properties that protect neuronal cells from reactive oxygen species (ROS), suggesting it may be neuroprotective in conditions like Parkinson's disease, ALS, and age-related cognitive decline. (He, Yu, & Ye, 2024)

4. Antimicrobial and Anti-Quorum Sensing Effects;

Ambrein has shown inhibitory effects on quorum sensing, a bacterial communication mechanism crucial for biofilm formation and virulence factor expression. By interfering with these pathways, ambrein may serve as an anti-virulence agent that can disarm pathogens without exerting selective pressure for antibiotic resistance. This opens the door for ambrein-based therapies in hospital-acquired infections and chronic wounds, where biofilms are a major challenge. (Yamabe et al., 2020)

5. Antioxidant and Cytoprotective Effects:

Due to its robust antioxidant profile, ambrein is being explored for its ability to protect tissues from oxidative damage, a key mechanism in cardiovascular diseases, diabetes, and cancer. It scavenges free radicals and supports cellular redox balance, enhancing its utility as a cytoprotective adjunct in therapeutic regimens. (He, Yu, & Ye, 2024)

Conclusion:

By harnessing the power of synthetic biology, we have transformed *E. coli*, a humble microbial workhorse, into a living factory capable of producing ambrein, a compound historically sourced from an endangered marine species and locked behind ethical, legal, and environmental barriers. This is more than just a proof-of-concept. Our work illustrates a new model of ethical biomanufacturing, one that respects biodiversity while enabling biomedical innovation. It empowers research communities to revisit natural molecules that were once abandoned due to scarcity or controversy, and bring them into the fold of mainstream science through sustainable and reproducible biosynthesis. (Nielsen & Keasling, 2016; Bian et al., 2020)

On a molecular level, this project exemplifies how far synthetic biology has come, from simple gene editing to the design of entire biosynthetic pathways capable of executing multistep chemical transformations with enzymatic precision. From promoter tuning to enzyme solubility engineering and metabolic flux balancing, our journey with ambrein biosynthesis reflects the interdisciplinary synergy of molecular biology, metabolic engineering, systems biology, and bioethics. (Nielsen & Keasling, 2016; Bian et al., 2020)

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IIT Bombay iGEM Team



CalciCapture — Engineering Marine Algae for Climate Resilience

In our debut iGEM journey, Team IIT Bombay 2024 tackled one of humanity's greatest challenges: climate change, through a synthetic biology project titled CalciCapture. Despite being a first-time team and the newest technical entrant to iGEM, we proudly returned from the Grand Jamboree in

Paris with a Gold Medal and a nomination for Best Climate Crisis Project—an achievement that underscored the global relevance and innovation of our work.

CalciCapture was inspired by *Emiliania huxleyi*, a marine coccolithophore known for forming calcium carbonate (CaCO_3) shells that naturally sequester atmospheric CO_2 . Our project aimed to engineer microorganisms—specifically *E. coli*—to overexpress human calmodulin, a calcium-buffering protein, thereby enhancing the calcification pathway for efficient, long-term carbon storage. We used PET28a as our plasmid vector for efficient expression, verified by successful turbidity tests in the lab.

We complemented our wet lab work with population and kinetic modeling of *E. huxleyi* to understand how environmental factors like nitrate availability and light exposure affect bloom formation and calcification rates.

Why algae? Algal carbon capture accounts for more global CO_2 absorption than all tropical rainforests combined. Moreover, *E. huxleyi* plays a dual role—sequestering carbon as CaCO_3 and influencing cloud formation through sulfur emissions, contributing to global temperature regulation via the cloud-albedo effect.

Beyond just capturing CO_2 , our system is scalable and integrable with industrial applications, such as producing sustainable construction materials and ocean alkalinity enhancement. This circular approach not only mitigates climate change but also generates valuable byproducts like biofuels and biodegradable plastics.

Our Human Practices team worked hard to understand the varied aspects related to our problem statement. We met the climate activist Ridhima Pandey who was also part of the 2019 UN Climate Action Summit. Her words were an inspiration to us and have thus motivated us to conduct many such informative sessions regarding the climate crisis and approaches such as synthetic biology targeted towards school and college students, involving relevant professors and organisations as well. We participated in events like BSBE Alum Day, ChemTech World Expo to get more insights and contacts of domain experts and to gain exposure to the industrial perspective of bioreactors and interacting with industry professionals. We met Prof Reshamwala (Institute of Chemical Technology, Mumbai), Prof. PV Balaji (IIT Bombay) Prof. Amal Kanti Bera (Department of Biotechnology at the Indian Institute of Technology, Madras (IITM)), Prof. Rajesh Patkar (IIT Bombay) as part of our interactions with academicians. We learnt a lot of technical aspects from them that we applied in our project. As part of our Education Outreach, we conducted the INYAS (Indian Young Academy of Sciences) session hosted by professor Arnab Dutta on 7th of June, 2024 in IITB Campus and this was based on CCUS and BECCS, we organized AI Transformations in healthcare session in collaboration with the BioX Club of our college, we designed and conducted the SynBio101 course, which ran from June 27, 2024, for four weeks. This course was designed to introduce participants to the exciting and rapidly growing field of synthetic biology, a field that allows for the redesigning of organisms for useful purposes by programming them to perform new tasks and we also had the opportunity to interact with professors from IIT Jodhpur who were keen to understand the tech culture at IIT Bombay. We also conducted EO

activities like Biogenesis Symposium, rural outreach with The Centre for Technology Alternatives for Rural Areas (CTARA), Collaboration with NSS and several others.

As a first-year team, our ability to engineer, model, and communicate such a solution—while adhering to biosafety, sustainability, and stakeholder inclusion—demonstrates the impact that interdisciplinary synthetic biology can deliver when driven by purpose.

Galvanized by our first-year success in addressing an environmental challenge, Team IIT Bombay has taken a bold leap forward in 2025 by turning its attention to the healthcare domain—specifically, the global crisis of antibiotic-resistant infections. This year, our efforts culminate in a new synthetic biology project aimed at combating a hidden medical menace: biofilms.

Aureolyse: Redefining the Fight Against Biofilm Infections

Every year, over **1 million lives are lost to *Staphylococcus aureus* (S. aureus)** infections—yet the real culprit behind many of these deaths is not just the bacteria, but the **biofilms** they form. These **resilient microbial communities** adhere stubbornly to medical devices such as **catheters, contact lenses, and implants**, where they embed themselves in a protective matrix that shields them from antibiotics and immune responses, with **antibiotic resistance up to 1,000-fold higher** than their planktonic counterparts and display robust evasion of host immune mechanisms, including phagocytosis and complement activation.. Biofilms are not a minor complication—they are the **underlying cause of nearly 80% of chronic infections in hospitals**. Their presence makes treatment drastically more difficult, often leading to **persistent infections, prolonged hospital stays**, and invasive surgeries. In the U.S. alone, biofilm-associated infections contribute to an estimated **\$20 billion in annual healthcare costs**, not including productivity losses. The danger is especially clear in devices like catheters, where **catheter-related bloodstream infections (CRBSIs)** exhibit mortality rates ranging from **12% to 47.5%**, and in **prosthetic joints**, where biofilms necessitate complex and repeated revision surgeries. Despite decades of research, biofilms remain a **silent epidemic**, complicating modern medicine's most routine procedures and posing a severe threat to patient safety worldwide.

To address this crisis, **iGEM IIT Bombay** has developed **Aureolyse**—a synthetic biology project that leverages the natural biofilm-degrading enzyme **ESP protease**, produced by *Staphylococcus epidermidis*. We are engineering ESP for **enhanced selectivity** toward *S. aureus* biofilm proteins by **minimizing toxicity** to human extracellular matrix proteins and IL-33. Our **wet lab** is using **site-directed mutagenesis** and **protein expression in *E. Coli*** to generate scalable, safe enzyme variants. In parallel, our **dry lab** uses **computational modeling and docking** to design ESP mutants with improved stability, substrate specificity, and compatibility with immobilization platforms.

From **catheter coatings and lock therapies to wound dressings** and from **Atopic Dermatitis to orthodontic implant applications**, Aureolyse offers a **resistance-resilient solution** to one of medicine's most persistent threats. Our approach not only disrupts biofilms but also **prevents recurrence**, offering a long-term defense against device-associated infections.

Human Practices and Outreach team

Beyond the bench, the **Human Practices and Outreach team** at iGEM IIT Bombay has taken a deeply interdisciplinary and community-focused approach.

BioQuest

This year, the iGEM IIT Bombay team spearheaded **BioQuest'25**, a first-of-its-kind national initiative dedicated to introducing high school students to the transformative field of **Synthetic Biology (SynBio)**. Designed for students in **Grades 9–10**, BioQuest'25 aimed not just to educate, but to **inspire young minds to think scientifically and solve real-world problems** using interdisciplinary approaches.

What made this event even more impactful was our **collaboration with the iGEM MITWPU Bharat team**, whose insights, mentorship, and active participation played a vital role in the success of the program.

Program Structure and Reach

BioQuest'25 was structured as a **rigorous, three-tier competition**, combining conceptual learning, application of SynBio principles, and innovative problem-solving. The event saw **an overwhelming response, with over 1,500 students registering from across India** — representing a wide spectrum of schools, socio-economic backgrounds, and geographic regions.

Round 1 involved an **online screening test** covering Physics, Chemistry, Biology, and General Aptitude. From this, **450 students** advanced to Round 2.

Round 2 delved deeper into advanced biology and introduced students to the **core concepts of synthetic biology**, laying a strong academic foundation. From this stage, **60 students** were shortlisted as national finalists.

Round 3, conducted **offline at IIT Bombay**, was the heart of BioQuest'25. The 60 finalists were divided into **10 interdisciplinary teams**, each mentored by a member of the iGEM IIT Bombay team or iGEM MIT-WPU. Over **two intensive weeks**, the students worked on curated **problem statements in healthcare, agriculture, and environmental sustainability**, applying SynBio frameworks to devise innovative, technically grounded solutions — many of which demonstrated potential for real-world commercialization.

The Grand Finale: Innovation Meets Impact

On **July 13, 2025**, the program culminated in a **Grand Finale at IIT Bombay**, where student teams pitched their ideas in a format inspired by the **iGEM Jamboree** — complete with structured presentations, visuals, Q&A rounds, and scientific validation. Their work was evaluated by an esteemed jury from IIT Bombay's Department of Biosciences and Bioengineering:

- **Prof. Swapnil Shinde**
- **Prof. Rajesh Patkar**
- **Prof. Sanjeeva Srivastava**

The judges commended the students for their **depth of scientific thinking, creativity, and interdisciplinary engagement** — a testament to the power of early scientific exposure when guided by meaningful mentorship.

The event was livestreamed on YouTube, **amassing over 2500 views**, garnering an immense support and accolade from all our viewers!

Mentorship and Collaboration

BioQuest'25 would not have been possible without the unwavering support and mentorship of our **Primary Principal Investigators**,

Prof. Kiran Kondabagil and **Prof. Saket Choudhary**,

whose academic oversight and strategic vision ensured the scientific and logistical success of the program.

From the iGEM IIT Bombay team, key contributors who designed and executed the program included:

Arth Agrawal, Saanvi T.S., Angel Singhvi, Pari Soni, Shreya Agrawal, Jennifer Mary, Hitesh Meena, Deepan Balaji, and Riya Joglekar.

We also extend our heartfelt thanks to the **iGEM MITWPU Bharat team** for their collaboration in problem-statement development, content review, and event facilitation — embodying the true spirit of iGEM through **inter-team cooperation and shared impact**.

BioQuest'25 is more than a competition — it is a movement to **reshape how life sciences are taught and imagined in India**. By nurturing scientific curiosity at the school level, it lays the foundation for a new generation of innovators who see biology not just as a subject, but as a toolkit to engineer a better future.

As part of our further Education & Outreach efforts, iGEM IIT Bombay conducted **DNA & Science Day** at AECS, Mumbai, engaging over **320 students** through hands-on activities of **banana DNA extraction**, introducing them to genetics and synthetic biology. We also hosted a **Foldscope Workshop** at IIT Bombay for **80 students**, where participants assembled their own microscopes and explored plant and microbial samples. Both events emphasized **interactive, low-cost science education**, sparking curiosity and critical thinking. These initiatives reflect our commitment to making biology accessible and inspiring for school students across diverse educational backgrounds.

We also designed **age-appropriate modules and kits**, comic books and videos to make complex biology accessible to diverse audiences, bridging the gap between science and society.

We also conducted **SynBio Simplified**, a talk series aimed at demystifying synthetic biology for the general public and non-STEM audiences. In **Science-on-Wheels**, our team visited under-resourced schools and rural areas around Mumbai, distributing science kits, conducting experiments, and using comic books in regional languages to teach the basics of microbes, hygiene, and antibiotics. Through **interviews with clinicians, biomedical engineers, and industry mentors**, we ensured our project aligns with patient needs and regulatory expectations.

Through these efforts, iGEM IIT Bombay doesn't just aim to solve a scientific problem—we strive to create a culture where **science is participatory, accessible, and socially responsible**. Aureolyse is the embodiment of this philosophy: rigorous in the lab, responsible in society, and revolutionary in its potential.

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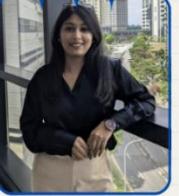
MEET *the* TEAM

 iGEM
MIT - WPU - BHARAT

Faculty Advisors


Dr. Anup Kale
Primary PI


Dr. Shilpa C.
Primary PI


Amrita S.
Secondary PI


Madhu C.
Secondary PI

PhD Supervisors

Student Team


Meetrayu


Arya


Animesh


Aarya


Sharvari


Ayushi


Rui


Sanskriti


Gargi


Dhruva

 @igem_mitwpubharat

 Team iGEM MITWPU Bharat

What is iGEM?



The International Genetically Engineered Machine (iGEM) competition is a worldwide synthetic biology event that unites thousands of participants from diverse backgrounds. What began as a course at MIT in 2003 has evolved into a global platform for high school students, university teams, entrepreneurs, and community labs.

iGEM challenges multidisciplinary teams to design, build, and test projects that use synthetic biology to solve real-world problems. Participants are given a kit of standard biological parts, called **BioBricks**, and can also design their own. Projects often address critical issues like climate change, food security, and health.

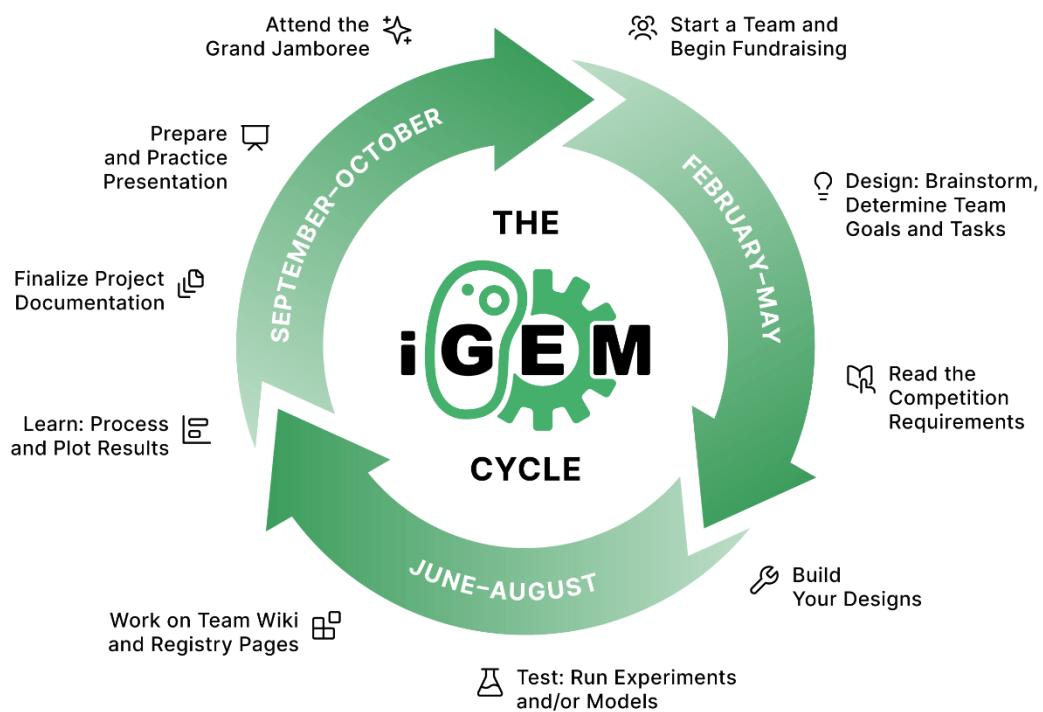
Participation in iGEM offers a unique and intensive learning experience that goes beyond the classroom. Teams develop essential skills in:

- **Teamwork and Project Management:** Tackling complex projects requires collaboration among students from various fields, including biology, engineering, computer science, and design.
- **Problem-Solving:** Teams must identify a societal need, design a biological solution, and work through the challenges of building and testing their prototype in a lab.
- **Scientific Communication:** A key component of the competition is clearly communicating the project's details to a broad audience through presentations, posters, and a team wiki.
- **Human Practices:** This crucial element of iGEM encourages teams to consider the ethical, social, and safety implications of their work. It teaches teams to think beyond the lab and consider how their innovations will impact the world.

iGEM provides a platform for students to innovate, develop invaluable skills, and contribute to the advancement of synthetic biology in a responsible and collaborative environment.



The iGEM cycle:



The iGEM cycle is a structured roadmap guiding teams through the stages of the International Genetically Engineered Machine (iGEM) competition. Starting in February, teams form, brainstorm ideas, set goals, and begin fundraising. By May, teams refine designs and familiarize themselves with competition requirements. From June to August, the focus shifts to experimental work, building and testing synthetic biology constructs, and updating team wikis. In September and October, teams analyze data, finalize project documentation, and practice presentations. The cycle culminates in the Grand Jamboree, where teams showcase their innovations and share their synthetic biology journeys with a global community.

The Grand Jamboree

The Grand Jamboree is the highlight event of the iGEM competition, serving as the world's largest gathering of the synthetic biology community. In 2025, it will take place from October 28 to 31 at the Paris Convention Centre. Thousands of students, researchers, and industry participants from around the globe will come together to present projects, attend talks, and celebrate advances in bioengineering. The event features presentations, poster sessions, startup competitions, and even playful activities, blending serious science with creativity and fun. The lively atmosphere fosters innovation, collaboration, and community among aspiring and established synthetic biologists.



About Team iGEM MIT – WPU Bharat



A Journey of Innovation and Impact

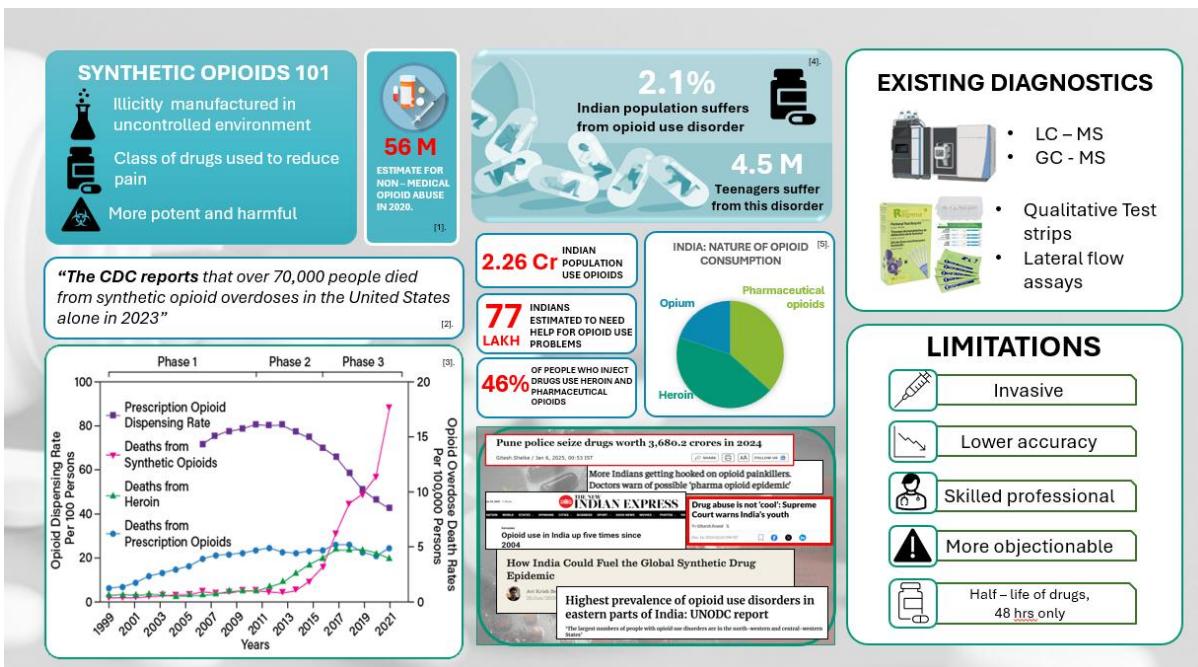
We are Team iGEM MIT – WPU Bharat, and our journey began on a national stage. After being recognized as one of the top 15 finalists out of 3,000 teams at the National Bio Entrepreneurship Competition 2024, we dedicated over a year to developing a novel biosensor to combat the critical societal issue of **opioid abuse**.

iGEM gave us more than a competition; it was a platform to represent our university and our country globally. We seized the opportunity to transform our prototype and research into a tangible solution for a crisis

that is quietly escalating, particularly among young people.

This journey wouldn't have been possible without the unwavering support of our incredible mentors, **Prof. Dr. Anup Kale** and **Dr. Shilpa Chapadgaonkar**. They were the strong pillars who guided us every step of the way. It was in those late-night meetings—troubleshooting critical challenges as a team—that our dream of making a real-world impact became a reality. Their constant support and belief in our potential fuelled our passion and pushed us to turn this vision into a testament of our dedication.

Our Project: A Ticking Clock We're Racing Against



The opioid pandemic is a devastating crisis that has ravaged our communities. In 2023, the U.S. alone saw approximately **105,000 overdose deaths**, with over 75% involving synthetic opioids. These aren't just statistics; they represent a tragic wave of human loss and fractured families. A major reason for this tragedy is a significant **detection gap**—our current methods for detecting opioid use are slow, invasive, and ineffective for real-time monitoring.

Existing solutions, such as lab-based blood and urine tests, are reactive. They can take days for results and are impractical for continuous, proactive care. This means we're always one step behind, unable to intervene when it matters most.

Our **iGEM project** tackles this problem head-on by using **synthetic biology** to create a novel, non-invasive diagnostic tool. We are engineering a biological system to detect opioids in on-site settings through a simple, non-invasive method. This technology shifts the paradigm from reaction to prevention. By providing a discreet "early warning system," we empower individuals and their support networks to act before it's too late. Our ultimate goal is to create a powerful, accessible tool that can help turn the tide on this public health emergency.

To help us make an even greater impact, we'd love your support—please take a moment to fill out our quick form below.



Follow us on linkedin!



"Hey! As part of our project, we'd really appreciate it if you could fill out this form. It



IGEM_MITWPUBHARAT

Hit up our Instagram to show some love!

BioQuest 2025: 1st edition

A collaborative spirit between iGEM MIT - WPU Bharat and iGEM IITB

By: Meetrayu Raut and Shreya Agarwal



This year, the iGEM IIT Bombay team in collaboration with iGEM MIT - WPU Bharat team spearheaded **BioQuest'25**, a first-of-its-kind national initiative dedicated to introducing high school students to the transformative field of **Synthetic Biology (SynBio)**. Designed for students in **Grades 9–10**, BioQuest'25 aimed not just to educate, but to **inspire young minds to think scientifically and solve real-world problems** using interdisciplinary approaches.

whose insights, mentorship, and active participation played a vital role in the success of the program.

Program Structure and Reach

BioQuest'25 was structured as a **rigorous, three-tier competition**, combining conceptual learning, application of SynBio principles, and innovative problem-solving. The event saw **an overwhelming response, with over 1,500 students registering from across India** — representing a wide spectrum of schools, socio-economic backgrounds, and geographic regions.

Round 1 involved an **online screening test** covering Physics, Chemistry, Biology, and General Aptitude. From this, **850 students** advanced to Round 2. The short - listed students then underwent rigorous revision sessions to make them ready for round 2.

Round 2 delved deeper into advanced biology and introduced students to the **core concepts of synthetic biology**, laying a strong academic foundation. From this stage, **60 students** were shortlisted as national finalists.

Round 3, conducted **offline at IIT Bombay**, was the heart of BioQuest'25. The 60 finalists were divided into **10 interdisciplinary teams**, each mentored by a member of the iGEM IIT Bombay team or iGEM MIT-WPU. Over the span of **two intensive weeks**, the students worked on curated **problem statements in healthcare, agriculture, and environmental sustainability**, applying SynBio frameworks to devise innovative, technically grounded solutions — many of which demonstrated potential for real-world commercialization. Along with the spontaneous team mentoring, multiple masterclass events were also conducted which involved a Genetic engineering simulation program to replicate critical processes of this complex process in real life i.e through a web based platform that duplicated formation of a recombinant plasmid to protein expression in the fermenters. Apart from this, both the teams also conducted a Commercialisation program where students were exposed to the commercialisation aspect of synthetic biology. This indeed created a lasting impact on the students, and fostered curiosity among these young minds enabling them to think and develop innovations that stand a stronger chance beyond research and pave way till the commercialisation step, enabling them to think more like an entrepreneur.

The Grand Finale: Innovation Meets Impact

On **July 13, 2025**, the program culminated in a **Grand Finale at IIT Bombay**, where student teams pitched their ideas in a format inspired by the **iGEM Jamboree** — complete with structured presentations, visuals, Q&A rounds, and scientific validation. Their work was evaluated by an esteemed jury from IIT Bombay's Department of Biosciences and Bioengineering:

- **Prof. Swapnil Shinde**
- **Prof. Rajesh Patkar**
- **Prof. Sanjeeva Srivastava**

Each group had to present in a span of 10 minutes followed by Q and A of another 5 minutes that tested their depth of knowledge and critical understanding on three significant parts: the scientific technicalities of the project followed by its feasibility, the impact and their commercialisation strategies. The bioethics, presentation skills and the various extra curricular programs conducted by the teams were also considered and complemented by the judges.

The judges commended the students for their **depth of scientific thinking, creativity, and interdisciplinary engagement** — a testament to the power of early scientific exposure when guided by meaningful mentorship.

The event was livestreamed on YouTube, **amassing over 2500 views**, garnering an immense support and accolade from all our viewers!

Winners list and special awards 

Medal	Group	Project	Mentor
Gold	Group 3	Oncology (Targeted Therapy)	Rui Agashe
Gold	Group 9	Diagnosis: Detection of non- infectious disease	Meetrayu Raut
Gold	Group 1	Coral care/ revival	Saanvi T
Silver	Group 2	Diagnosis: Host response markers	Sharvari Bhosale
Silver	Group 6	Sleep disruption and synthetic biology solution	Arth Agrawal
Silver	Group 7	Salinity shield	Ayushi Mishra
Bronze	Group 4	Sustainable Biofuels	Aarya Kunnure
Bronze	Group 5	Eco- compost	Riya Joglekar
Bronze	Group 8	Bioelectricity	Shreya Agrawal
Bronze	Group 10	Venom Shield	Angel Singhvi

Special prizes

Best Project Overall	Group 3
Most Innovative	Group 2
Most Creative	Group 3 and Group 9
Best Commercialisation	Group 7
Audience Choice	Group 3 and Group 6



ALL INDIA iGEM MEET



Team iGEM MIT WPU Bharat participated in the All India iGEM meet held at ICT Mumbai from 25th-27th July, 2025. The All India iGEM meet (AIIM) is a 3-day event designed to provide Indian iGEM teams with invaluable feedback and opportunities for idea exchange during the iGEM competition. AIIM is a platform for teams to interact with one another, fostering collaboration and networking opportunities. Over 14 teams from institutions like IISc, IIT Bombay, IIT Madras and IISER Kolkata participated in this year's meet.

iGEM stands for International Genetic Engineered Machine which is a prestigious international competition in synthetic biology where student teams design, test and build biological systems using standardised genetic parts known as Bio Bricks. This year, students from the department of Biosciences and Technology at MIT WPU, are proudly representing the institution as team iGEM MIT WPU Bharat.

Day 1 of the event featured workshops, guest lectures and engaging activities such as games and quizzes. A very important workshop on Dual-Use Research was held by the iGEM ambassadors on day 1 of the event to make the teams aware of the importance of biosecurity, biosafety, dual use research concern and their relevance in the iGEM competition. Team MIT-WU gained invaluable insights from this workshop and participated in the ensuing group discussion with great enthusiasm. This workshop was followed by a series of guest lectures on diverse topics. Dr. Subhojit Sen from UM-DAE CBS, Mumbai talked about synthetic models for epigenetic drug screens and how undergrad labs can be empowered to do groundbreaking research. Moving on, Dr. Prajakta Dandekar from ICT, Mumbai shared her work on 3D spheroid cultures and their significance in Anticancer Drug Development. Next, Ms. Tanvi Kale from IISER Pune gave insights of her research on viral RNA detection using a translational enhancer-based amplification for Toehold sensors. This was followed by a fascinating lecture by Dr. Amitesh Anand from TIFR in adaptive bacterial energetics. Next, Ms. Varsha Jaisimha from IISc interacted with the teams and spoke about community building in iGEM. This series of talks by eminent guests on diverse topics enlightened the students from team iGEM MIT WPU on the

interdisciplinary nature of synthetic biology and invoked great curiosity and inspiration. This was followed by practical experience from a computational biology workshop conducted by team IISER Berhampur.

Day 2 of AIIM was particularly impactful, wherein all teams presented their projects to an esteemed judging panel. The judges offered valuable critiques and feedback across multiple aspects of each team's project, including impact, presentation, engineering, and human practices. These sessions were crucial in guiding teams towards refining their projects. Team iGEM MIT WPU's project is dedicated to solving the social problem of Opioid overuse by a novel sensor. This sensor uses biological materials to detect the presence of drugs in bodily fluids. Through the use of aptamer technology, which are extremely versatile DNA and RNA sequences which can be programmed to identify a particular target molecule from a vast pool of others with high specificity.



Day 3 of AIIM began with a bang by a poster presentation from all the teams. All participating students and guests were greatly intrigued by team MIT WPU's iGEM project. The poster presentation was followed by a quiz competition from the IISc team. Team MIT-WU conducted a highly spirited game of scientific charades where randomly drawn teams of 5 took part. 1 person was nominated as the speaker and had to describe a given biological term in just 1 word. The remaining 4 team members had to guess the word. The team who guessed the maximum number of words in 3 minutes will win. iGEM ambassador and ICT team won the game with a whopping 12 words! The scientific charades game was a hit with all the participating teams and guests. The hosts ICT, Mumbai held a thrilling gene auction and team VIT conducted crisis comms. This exciting meet came to end with the prize distribution ceremony for the earlier presentations.

Team MIT WPU Bharat gained many new insights and inspiration from the AIIM. The team used this opportunity to connect with other teams to plan future collaborations. With renewed motivation, valuable feedback, and a spirit of collaboration, Team iGEM MIT WPU Bharat returns from AIIM 2025 inspired and better equipped to take their project to the global stage.

From DNA to Dreams: Inspiring Rustomjee Cambridge International School Students Through Synthetic Biology

Written by: Arya Bundi, Gargi Mulay, Aarya Kunnure
Team iGEM MIT WPU BHARAT



Team iGEM MIT WPU Bharat conducted a fascinating session for over 250 students for Class 8 at Rustomjee Cambridge International School, Mumbai introducing them to exciting concepts in modern life sciences. The interesting discourse was held on 11th July, 2025, team iGEM's educational initiative is to inculcate a passion for biosciences among school children and inspire them to various scientific paradigms.

iGEM stands for International Genetic Engineered Machine which is a prestigious international competition in synthetic biology where student teams design, test and build biological systems using standardised genetic parts known as BioBricks. This year, students from the Department of Biosciences and Technology at MIT-WPU, are proudly representing the institution as team iGEM MIT WPU Bharat.

In this engaging session of teaching students, key concepts of Synthetic biology, Genetic engineering, Recombinant DNA technology and microbiology were explained and simplified to stimulate the students curiosity. Tools like animations, figures and analogies like Captain America were used to make for a truly captivating and relatable session. By introducing these concepts and their diverse applications in an exciting way, team iGEM captured the students' imagination.

In addition to science education, the session also touched upon pressing societal issues. Around 2.1% of India's population- 26 million people-use opioids non-medically and synthetic opioids like fentanyl are frequently found in illegal drug supplies, increasing the risk of accidental drug overdoses. They also educated the students about the dangers of opioid abuse and the importance of saying no to peer pressure. As a part of their ongoing project, team iGEM MIT WPU is addressing this societal problem, by working on a novel sensor.

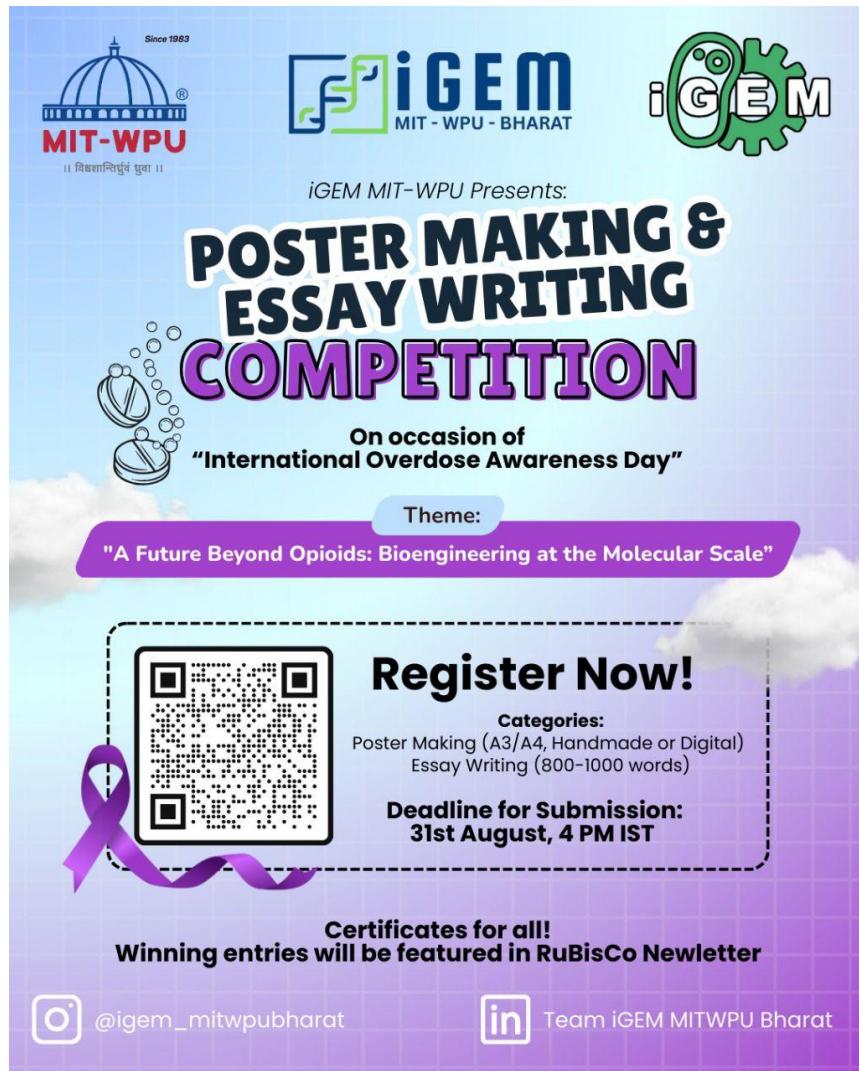
This sensor uses biological materials to detect the presence of drugs in bodily fluids. Through the use of aptamer technology, which are extremely versatile DNA and RNA sequences which can be programmed to identify a particular target molecule from a vast pool of others with high specificity.

To enhance interaction and assess understanding, this session also included various quizzes on nucleotides consisting of questions on base pairing in double stranded DNA. This activity sparked enthusiasm among the students and reinforced key concepts in a playful manner.

The feedback from the session was very positive and the students had a lot of fun learning about new ideas and terms. Everyone left with curiosity in their minds wanting to find out more about synthetic biology and genetic engineering.

Through initiatives like these, **Team iGEM MIT WPU Bharat** continues to nurture the next generation of scientists and changemakers, making an impact on the future of Biosciences in India.

Poster making and essay writing competition on occasion of “International Overdose Awareness Day”



The iGEM MIT-WPU Bharat team organized a **Poster Making and Essay Writing Competition** exclusively for school and high school students on the occasion of *International Overdose Awareness Day*. The event aimed to spread awareness about opioid overdose and encourage young minds to explore innovative solutions in line with the theme **“A Future Beyond Opioids: Bioengineering at the Molecular Scale.”** Through this initiative, students were given a platform to showcase their creativity and scientific thinking, while also learning about the role of bioengineering in addressing global health challenges. These are the winners of the competition, whose outstanding contributions have been recognized and featured by the team.



X
International Overdose
Awareness Day



Winners

Poster Making & Essay Writing Competition
organized by iGEM MIT-WPU Bharat



Rachita Alavani

SoSES, MIT-WPU



Md.Kashif Khan

Bhavan's R.K. Sarda Vidya Mandir



Vidhita M. Ghadi

Abhyudaya Nagar Mumbai Public School (A.B.M.P.S)



Ishwari K. Joshi

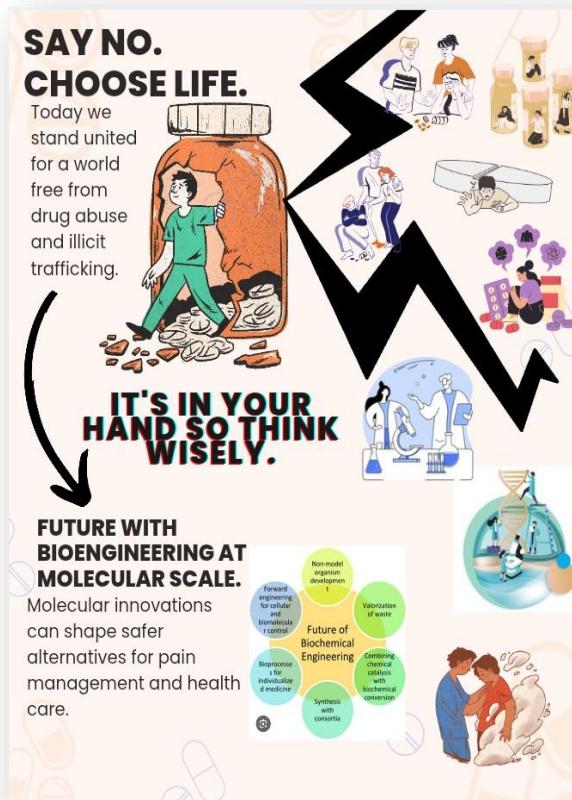
SoSES, MIT-WPU

You all captured the spirit of our theme, "**A Future Beyond Opioids: Bioengineering at the Molecular Scale**," incredibly well!

Congratulations!

Find your Essays and Posters published in the latest edition of
RuBisCo Newsletter

By, Vidhita Mangesh Ghadi



By, Ishwar Kedar Joshi



A FUTURE BEYOND OPIOIDS BIOENGINEERING AT THE MOLECULAR SCALE

Submitted by: Md.Kashif Khan

Institution: Bhavan's R.K. Sarda Vidya Mandir

Theme: "A Future Beyond Opioids: Bioengineering at the Molecular Scale"

Abstract

The opioid crisis represents one of the most devastating public health emergencies of our time, claiming over 80,000 lives annually in the United States alone and affecting millions worldwide^{1 2}. Yet, within this darkness lies an unprecedented opportunity for innovation. As we commemorate International Overdose Awareness Day, the convergence of bioengineering and molecular-scale technologies offers a transformative vision for pain management—one that promises effective relief without the specter of addiction, tolerance, or fatal overdose.

The devastating reality of opioid dependence

The scope of the opioid crisis defies comprehension. According to the World Health Organization, approximately 125,000 people died from opioid overdose in 2019, with close to 80% of all drug-related deaths involving opioids

¹. In Canada alone, over 52,544 apparent opioid toxicity deaths occurred between January 2016 and December 2024, with 74% involving fentanyl—a synthetic opioid up to 100 times more potent than morphine^{1 3}. These statistics represent not merely numbers, but shattered families, lost potential, and communities in crisis.

The physiological dangers of opioid use extend far beyond overdose risk. Opioids function by binding to μ -opioid receptors in the brain, triggering massive releases of endorphins that create intense euphoria⁴. However, this same mechanism leads to rapid tolerance, requiring increasingly higher doses to achieve the same effect^{2 5}. The body's breathing centers become suppressed, leading to the characteristic "opioid overdose triad" of pinpoint pupils, unconsciousness, and respiratory depression⁵. Even medically prescribed opioids can cause cardiovascular changes, immune system suppression, and paradoxically, increased pain sensitivity over time².

Perhaps most insidiously, opioids hijack the brain's reward pathways, creating powerful psychological dependence that persists long after physical withdrawal symptoms subside⁴. The transition from legitimate medical use to addiction can occur within days, leaving patients trapped in a cycle where the medication meant to heal becomes the source of destruction.

Molecular engineering precision solutions for complex problems

The limitations of traditional pharmacotherapy have catalyzed a revolutionary shift toward bioengineering solutions that operate at the molecular scale. These approaches represent a fundamental departure from the "one-size-fits-all" paradigm, instead targeting specific cellular mechanisms underlying pain perception and transmission.

Nanotechnology-Based Drug Delivery Systems

Nanotechnology-based drug delivery systems represent the vanguard of this revolution. Advanced nanocarriers, including liposomes, biodegradable polymers, and mesoporous silica particles, can encapsulate analgesic compounds and deliver them precisely to affected tissues 6 7. These systems achieve sustained, controlled release over days to weeks, dramatically reducing dosage requirements and systemic side effects. The FDA approved Posimir™ system, which uses poly(lactide-caprolactone) microparticles to provide 72-hour controlled release of bupivacaine, exemplifies this approach's clinical potential 8. Recent innovations have incorporated stimulus-responsive elements, allowing drug release to be triggered by specific pH changes, enzyme activity, or inflammatory markers—essentially creating "smart" medications that activate only when and where needed 6

Gene Therapy and CRISPR Technology

Gene therapy and CRISPR technology offer even more precise interventions at the genomic level. Recent breakthroughs have demonstrated the feasibility of using CRISPR-dCas9 systems to temporarily suppress pain-related genes without permanent genomic alterations 9 10. Researchers have successfully targeted the SCN9A gene encoding Nav1.7 sodium channels, which are crucial for pain signal transmission. Intrathecal delivery of CRISPR-dCas9 constructs provided significant pain relief in multiple preclinical models, including carrageenan-induced inflammatory pain and paclitaxel-induced neuropathic pain, without impairing normal sensory functions 10 11. This approach addresses pain at its molecular origin while preserving the body's ability to respond to genuine threats.

The University of North Carolina's recent development of chemogenetic tools represents another quantum leap in precision medicine 12 13. By engineering modified receptors that respond only to inert, non-psychoactive compounds, researchers can create "molecular switches" that allow patients to control their own pain relief by simply taking an inactive pill that becomes therapeutic only in cells expressing the engineered receptor.

Advanced Biosensor Networks

Advanced biosensor networks are revolutionizing pain assessment and monitoring. Wearable and implantable biosensors can continuously monitor physiological markers associated with nociception, including heart rate variability, electrodermal activity, and specific biomarkers like inflammatory cytokines 14 15. These systems enable real-time pain assessment and personalized treatment adjustments, moving beyond subjective patient reports to objective, quantifiable measurements 16.

Regenerative medicine and tissue engineering

Beyond symptom management, bioengineering approaches increasingly focus on addressing the root causes of chronic pain through tissue regeneration. Advanced biomaterials incorporating growth factors, stem cells, and bioactive scaffolds can repair damaged tissues that generate pain signals 8. Researchers have developed injectable hydrogels that promote neural regeneration while simultaneously delivering anti-inflammatory agents, offering the potential for permanent pain resolution rather than temporary masking 8.

The Northwestern University team's biocompatible, dissolving implant represents a paradigm-shifting innovation 17. This device wraps around nerves to deliver precise, targeted cooling that blocks pain signals without drugs, functioning like a programmable, localized anesthetic system. After treatment completion, the device naturally dissolves and is absorbed by the body, eliminating the need for surgical removal.

Artificial intelligence and predictive medicine

The integration of molecular-scale sensors with artificial intelligence creates unprecedented opportunities for predictive pain management. Machine learning algorithms can analyze complex patterns of biomarker expression, genetic variants, and environmental factors to predict pain episodes before they occur ¹⁴. This enables preemptive interventions using targeted molecular therapies, potentially preventing chronic pain syndromes from developing.

Challenges and future horizons

Despite these remarkable advances, significant challenges remain in translating molecular-scale solutions to clinical practice. The complexity of pain pathways means that single-target approaches often fail due to compensatory mechanisms ¹⁸. Future success likely depends on multi-target strategies that simultaneously address multiple pain mechanisms. Additionally, the high development costs and regulatory complexities of personalized medicine present substantial barriers to widespread adoption.

However, the potential benefits justify these challenges. Early clinical trials of molecular-targeted therapies show promise for achieving effective pain relief without addiction potential ^{19 20}. As our understanding of pain genetics deepens and manufacturing costs decrease, these precision approaches may become accessible to patients worldwide.

Conclusion engineering hope at the molecular scale

The opioid crisis has demonstrated the devastating consequences of relying on crude pharmacological approaches to complex biological problems. However, the emergence of molecular-scale bioengineering offers genuine hope for a future beyond opioids. By harnessing the power of nanotechnology, gene editing, regenerative medicine, and artificial intelligence, we can envision pain management systems that are simultaneously more effective and infinitely safer than current approaches.

The path forward requires sustained investment in research, thoughtful regulatory frameworks, and collaborative efforts between engineers, clinicians, and patients. As we honor the memory of those lost to overdose, we must commit to building a future where effective pain relief never again comes at the cost of human life. Through bioengineering at the molecular scale, that future is not merely possible—it is inevitable. The question is not whether we will achieve this vision, but how quickly we can make it reality for those who suffer today.

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A Future Beyond Opioids: Bioengineering at the Molecular Scale

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Introduction

Opioids seem like the real-life Ambrosia, the mythical nectar of the gods. These are synthetic or natural substances that can reduce or even stop pain by interacting with the nerve cells in the body and brain. Opioids in various forms have been used in medicine as painkillers since the era of the Sumerian civilisation. "Milk of poppy" was known as an analgesic as far back as 4000 B.C. Ancient philosophers like Hippocrates praised opium as a useful narcotic and anaesthetic. Later in the 19th century, newer forms of opioids emerged, such as morphine in 1804 and heroin in 1897. In the 20th century, synthetic opiates like methadone and fentanyl were created, which opened new avenues for better pain management. So, on paper, opioids sound like a dream come true for anyone seeking pain relief. But unfortunately, just as any fulfilled fantasy has risks, the use of opiates as painkillers carries heavy dangers.

Opioids work by binding to and activating opioid receptors in neural cells present in the brain, spinal cord, and any other organs involved in sensations of pain and pleasure. Once the chemicals bind to the opioid receptors, they block pain signals and release large amounts of dopamine throughout the body, giving the user a feeling of a "high," making them feel relaxed. This reinforces them to keep taking these drugs, often in excess and for non-medical use. But regular use of opioids leads to the user developing a tolerance to the drug. Meaning they can no longer produce the endorphins naturally, leading to the regular dose feeling "not as good". This is called opioid use disorder or opioid addiction.

Current issues with opioid addiction

There have been three major waves of opioid addiction, especially in Western countries. First, in the late 19th century, due to the development of hypodermic needles and the overprescription of narcotics. Second, in the 1990s, when people often turned to cheaper heroin to quell their painkiller addiction. And third in 2013, with the illicit manufacturing of stronger drugs like fentanyl.

In the USA, there were about 81000 opioid related deaths in 2022. According to a 2019 survey in India, there is a high prevalence of opioid abuse, with about 2.1% of the population using opioids like heroin. While this number is less than that of the USA, there is a possibility of this increasing because of amendments in the Narcotic Drugs and Psychotropic Substances Act (2014), which allows easier access to essential drugs. Along with that, pharmaceutical companies and governments are increasing the types of available opiates in third-world markets.

Current and future solutions

In India, the current solutions include prevention methods like opioid availability control, Awareness generation, and treatments like opioid substitution therapy. Opioid substitution

therapy involves replacing short-acting and illicit opioids with safer medications like methadone. These medications reduce withdrawal symptoms and cravings, allowing individuals to stabilise and rebuild their lives.

However, recent advancements in biotechnology and drug design open new possibilities to improve existing treatments and develop innovative ones for opioid addiction. Opioids trigger dopamine release in the brain's reward pathway via opioid receptors that are part of the G-protein-coupled receptors (GPCRs) family. This process reinforces drug-seeking behaviour and promotes addiction. Therefore, by targeting the molecular pathways involved, we can preserve the analgesic effects while minimising the harmful side effects of opioid use.

When opioids bind to mu opioid receptor (MOR) and delta opioid receptor (DOR), the receptors are pulled inside the cell and stop working properly. This is called downregulation, which builds tolerance to opioids. In some cases, cells might reduce the rate of transcription and translation in the genes coding for the receptors. The development of tolerance can be prevented by designing drugs that only activate the G protein signalling pathway, which is often referred to as the "pain relief" part, but not the beta-arrestin signalling pathway, which causes tolerance in cells. These drugs are called biased agonists. These chemicals selectively activate one GPCR pathway while leaving the others inactive. Some examples include TRV130 (oliceridine) and PZM21, which are still in development

Kappa Opioid receptor, another G-protein-coupled receptor in the nervous system, is more potently analgesic and is involved in hallucinations, dissociation, stress, depression, and anxiety. When activated continuously, it can lead to severe depression and a risk of relapse when sober. However, KOR blockers, called antagonists, can be created. These target only the areas of the brain involved in emotional distress. This can be done by either genetic therapy, where genes coding for KOR are modified, or by slow-release implants, which release the medication for blocking KOR over the course of weeks or months. The slow-release implants can prevent severe withdrawals in opioid users, and also release biased antagonists, which prevent triggering addiction while providing pain relief.

KoR is embedded within the cell membrane, and with the help of advanced techniques like cryo-EM, we have been able to visualise its structure. Molecules can be designed to specifically activate only the useful pathways. One such molecule is a de novo cyclic peptide-β-naloxamine conjugate, which demonstrated potent KOR agonism and MOR antagonism.

Another way to help treat opioid addiction is Transcranial Magnetic Stimulation. This is an FDA-approved method usually used for treating neuropsychiatric disorders. TMS is a non-invasive technique that uses magnetic pulses to create electrical currents in the brain. It is currently in the beginning stages of its use in addiction treatment. TMS can be used to treat opioid addiction by stimulating the prefrontal cortex to modulate the reward and inhibition control centre of the brain. This works by reversing the neuroadaptations that take place due to chronic opioid abuse, leading to a reduction in drug-seeking behaviour and relapse.

Finally, going even beyond the molecular engineering aspects of possible treatments, an upcoming treatment is pharmacogenomics. Pharmacogenomics uses an individual's genetic profile to personalise opioid-based pain management and opioid addiction treatment by predicting how their body will metabolise and respond to these drugs. Important genes

include CYP2D6 and OPRM1, which are involved in opioid receptor sensitivity and drug metabolism. This helps design tailored dosing and medication choices, promoting safer and more effective opioid management and addiction treatment.

Thus, with the help of genetic and molecular engineering, scientists can develop safer and more effective methods of opioid addiction treatment. This will not only prevent deaths by overdose but also help reduce the stigma, helping addicts recover safely and with dignity.

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