

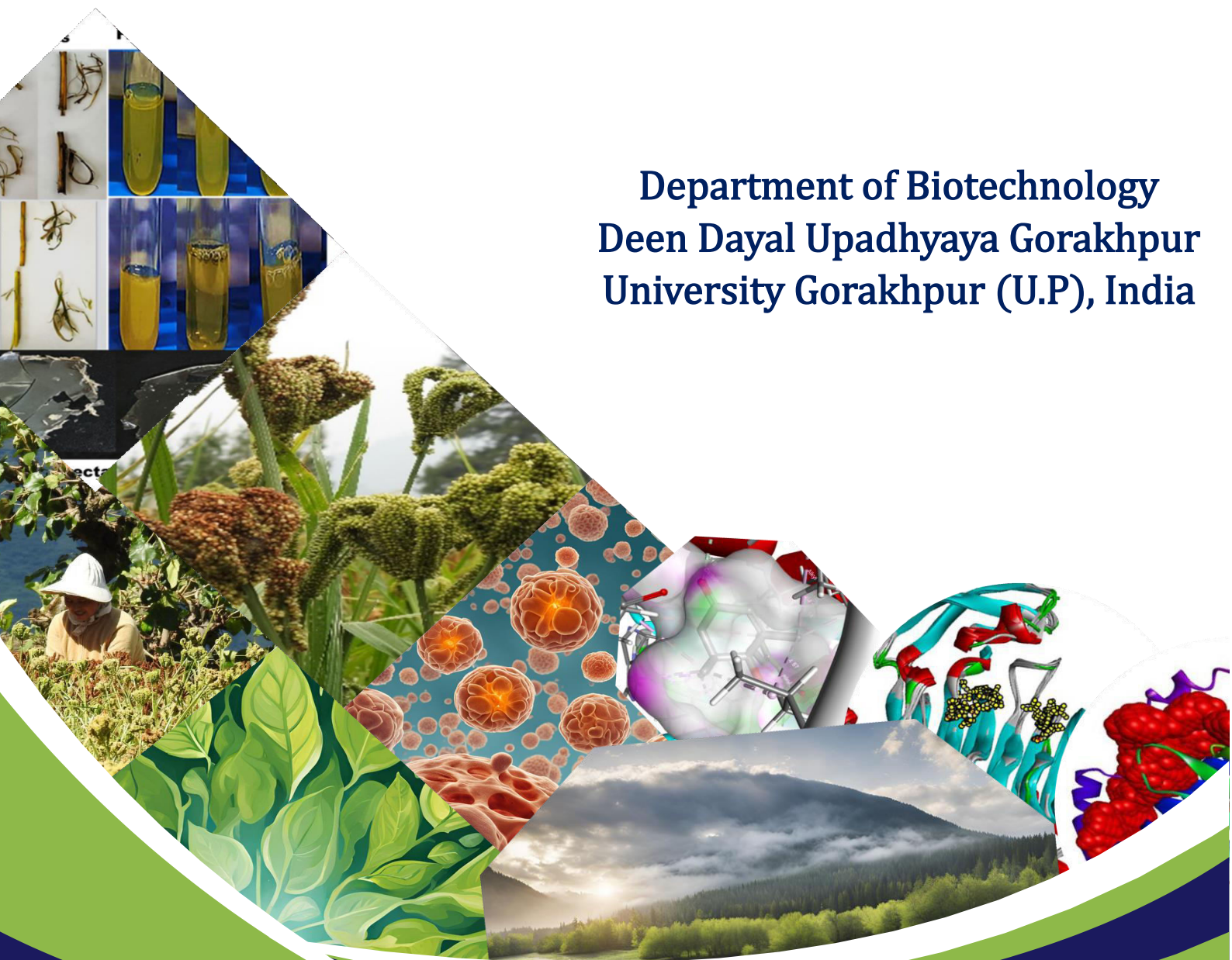
July 2024

VOLUME 1: ISSUE:2 (SIX MONTHLY)

BIOTECH INNOVATORS

Magazine

Department of Biotechnology
Deen Dayal Upadhyaya Gorakhpur
University Gorakhpur (U.P), India



Biotech Innovators
VOLUME 1: ISSUE:2 (SIX MONTHLY)
July 2024

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MESSAGES

From The Patron Desk



It is really a great pleasure to see the second issue of “**BIOTECH INNOVATORS**” by the Department of Biotechnology. The continuity of the issues with contributions from faculty members and students is appreciated. The Department of Biotechnology is contributing immensely in enhancing the academic profile of the University and recently filing of 12 patents reveals the potential of the faculty members and students. The purpose of the magazine is to provide opportunity to young minds especially students to develop skill in scientific writing and I hope students and faculty members will come forward to contribute regularly for the continuity of this magazine.

Best wishes to faculty members and students of Department of Biotechnology

Prof. Poonam Tandon

Vice-Chancellor

Message from Chief Editor

It is a matter of satisfaction that we are coming with second issue of “**BIOTECH INNOVATORS**” with substantial changes in the overall content. Efforts have been made to prepare an instruction to authors with several well-defined sections like featured articles, review articles, research communications, research highlights, departmental achievements and photo gallery. An advisory board has been framed to enhance the quality of the magazine gradually. I would like to sincerely thank all the contributors for this issue and hope the journey continues with further improvements. The guidance and motivation of our Hon’ble Vice-Chancellor Prof. Poonam Tandon for such academic activity which ultimately enhances the visibility of the Department is sincerely acknowledged.



With best wishes

Prof. Dinesh Yadav

2. Stem Cell Therapy in Regenerative Medicine

Stem cells are the cornerstone of regenerative medicine, thanks to their unique ability to differentiate into various cell types and self-renew. This section explores the current applications, challenges, and future perspectives of stem cell therapy in regenerative medicine.

Types of Stem Cells

Our bodies hold two main types of stem cells: embryonic and adult. Embryonic stem cells, found in early embryos, are the most versatile, able to morph into any of the body's 200+ cell types. This makes them ideal for potential treatments, but ethical concerns surround their origin. Adult stem cells reside in various tissues like bone marrow and fat. They're more specialized than embryonic stem cells, but can still become several cell types within their tissue group. Additionally, scientists can create induced pluripotent stem cells (iPSCs) by reprogramming adult cells to behave like embryonic stem cells, offering another promising avenue for regenerative medicine.

2.1. Embryonic Stem Cells (ESCs):

Derived from the inner cell mass of the blastocyst, ESCs are pluripotent and can differentiate into any cell type in the body. Despite their potential, the use of ESCs raises ethical concerns due to the destruction of embryos. Moreover, the risk of teratoma formation (tumors consisting of multiple cell types) poses a significant challenge for clinical applications.

2.2. Adult Stem Cells:

Found in various tissues, adult stem cells are multipotent and can give rise to a limited range of cell types. Hematopoietic stem cells (HSCs), which generate all blood cell types, and mesenchymal stem cells (MSCs), which can differentiate into bone, cartilage, and fat cells, are the most studied adult stem cells. These cells are already used in clinical settings, such as bone marrow transplants for treating leukemia and other blood disorders.

2.3. Induced Pluripotent Stem Cells (iPSCs):

iPSCs are generated by reprogramming adult somatic cells to a pluripotent state using specific transcription factors (Takahashi and Yamanaka, 2006). iPSCs offer the benefits of ESCs without the ethical issues and can be derived from the patient's own cells, minimizing immune rejection risks. However, concerns about the potential for genetic mutations and tumor formation remain.

3. Current Applications of Stem Cell Therapy

Stem cell therapy is a rapidly evolving field offering hope for various conditions. One established application is in blood diseases like leukemia. Doctors use adult stem cells from bone marrow to replenish and restore blood cell production. Another area of progress is in treating damaged tissues. Stem cells can be used to regenerate skin after burns, potentially helping heal chronic wounds. Research is also underway for cardiovascular diseases, where stem cells might create new blood vessels to improve circulation. While not yet mainstream, scientists are exploring stem cells for neurodegenerative diseases like Parkinson's. The idea is to use them to replace lost brain cells and potentially slow disease progression. It's important to remember that stem cell therapy is still under development for many conditions. However, its potential to treat a wide range of diseases makes it a promising area of medicine. Some examples are provided below

3.1. Hematopoietic Stem Cell Transplantation:

HSC transplantation is the most established form of stem cell therapy, primarily used to treat hematological malignancies such as leukemia, lymphoma, and multiple myeloma. Autologous transplants (using the patient's own stem cells) and allogeneic transplants (using donor stem cells) have significantly improved survival rates for these conditions.

3.2. Cardiovascular Repair:

Stem cell therapy holds promise for repairing heart tissue damaged by myocardial infarction. Clinical trials using MSCs, cardiac stem cells, and iPSCs have shown potential in improving cardiac function and reducing scar tissue. However, challenges such as cell survival, integration, and potential arrhythmias need to be addressed.

3.3. Neurodegenerative Diseases:

Research is ongoing to develop stem cell therapies for neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis (ALS). For instance, dopaminergic neurons derived from iPSCs are being tested for their ability to restore motor function in Parkinson's disease models.

3.4. Diabetes:

Stem cell therapy holds promise as a treatment for type 1 diabetes by generating insulin-producing beta cells. Researchers are using induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) to create these functional cells, which have shown effectiveness in preclinical studies. Clinical trials are currently underway to assess the safety and efficacy of this approach in humans, offering a potential future where people with type 1 diabetes may no longer require daily insulin injections.

4. Challenges in Stem Cell Therapy

Stem cell therapy holds immense promise for treating a variety of ailments, but significant hurdles remain. One major challenge lies in controlling the differentiation, or specialization, of stem cells. These cells have the potential to become many different cell types, but coaxing them down the desired path is tricky. Additionally, ensuring the safety of stem cell transplants is crucial. There's a risk of tumor formation if the cells multiply uncontrollably. Furthermore, ethical concerns surround the use of embryonic stem cells, while harvesting adult stem cells can be invasive and yield limited quantities. Despite these challenges, research is ongoing to refine techniques and overcome these obstacles, paving the way for a future where stem cell therapy can revolutionize medicine.

4.1. Ethical and Regulatory Issues:

The use of ESCs is ethically controversial due to the destruction of embryos. Regulatory frameworks must balance scientific advancement with ethical considerations, ensuring patient safety and informed consent.

4.2. Immune Rejection:

Allogeneic stem cell transplants carry the risk of immune rejection and graft-versus-host disease (GVHD). Developing methods to reduce these risks, such as using iPSCs derived from the patient's own cells or engineering immune-compatible cells, is crucial.

4.3. Tumorigenicity:

The potential for stem cells, especially ESCs and iPSCs, to form tumors (teratomas) poses a significant challenge. Ensuring the safety and controlled differentiation of stem cells is essential for their clinical application.

4.4. Cell Survival and Integration:

Achieving long-term survival, integration, and functionality of transplanted stem cells in the target tissue remains challenging. Developing methods to enhance cell engraftment, vascularization, and integration with the host tissue is necessary.

The future of stem cell therapy holds immense promise for treating currently incurable diseases. Research on various stem cell types, like adult and induced pluripotent stem cells, is ongoing to refine their ability to differentiate into specialized cells for repair and regeneration. This could lead to breakthroughs in areas like neurodegenerative diseases, where new therapies could replace damaged tissues. While challenges like tumor formation and ethical considerations regarding embryonic stem cells remain, advancements in gene editing and personalized medicine offer solutions for targeted and safe treatments. With continued

research, stem cell therapy has the potential to revolutionize medicine, offering patients a chance to heal and restore lost functions.

<p>Stem Cell Therapy Protocol</p> <p>1. Patient Assessment Objective: To evaluate the patient's medical history, current condition, and suitability for stem cell therapy. Steps:</p> <p>1. Medical History Review:</p> <ol style="list-style-type: none"> 1. Collect comprehensive medical history, including past illnesses, surgeries, and treatments. 2. Document any allergies, current medications, and family medical history. <p>2. Physical Examination:</p> <ol style="list-style-type: none"> 1. Conduct a thorough physical examination to assess the patient's general health and specific issues related to the condition being treated. <p>3. Diagnostic Testing:</p> <ol style="list-style-type: none"> 1. Order necessary diagnostic tests (e.g., blood tests, imaging studies) to evaluate the patient's condition and establish baseline health metrics. <p>4. Eligibility Determination:</p> <ol style="list-style-type: none"> 1. Assess eligibility for stem cell therapy based on medical history, physical examination, and diagnostic test results. 2. Discuss potential risks and benefits with the patient. <p>5. Informed Consent:</p> <ol style="list-style-type: none"> 1. Provide detailed information about the stem cell therapy procedure, including potential risks, benefits, and alternatives. 2. Obtain written informed consent from the patient. 	<p>Stem Cell Therapy Protocol</p> <p>1. Patient Assessment Objective: To evaluate the patient's medical history, current condition, and suitability for stem cell therapy. Steps:</p> <p>5. Quality Control Objective: To test the expanded cells for safety, viability, and effectiveness. Steps:</p> <p>1. Sterility Testing:</p> <ol style="list-style-type: none"> 1. Conduct sterility tests to ensure the absence of microbial contamination. <p>2. Viability Testing:</p> <ol style="list-style-type: none"> 1. Assess cell viability using appropriate assays (e.g., trypan blue exclusion, flow cytometry). <p>3. Functional Testing:</p> <ol style="list-style-type: none"> 1. Perform functional assays to evaluate the therapeutic potential of the stem cells (e.g., differentiation potential, cytokine production). <p>4. Release Criteria:</p> <ol style="list-style-type: none"> 1. Establish criteria for the release of stem cells for clinical use, including sterility, viability, and functional test results. <p>6. Preconditioning of Patient Objective: To prepare the patient to receive the stem cells. Steps:</p> <p>1. Pre-Treatment Evaluation:</p> <ol style="list-style-type: none"> 1. Conduct a pre-treatment evaluation to assess the patient's current health status and readiness for stem cell administration. <p>2. Preconditioning Regimen:</p> <ol style="list-style-type: none"> 1. Administer a preconditioning regimen to enhance stem cell engraftment and therapeutic efficacy (e.g., immunosuppressive drugs, radiation therapy).
<p>2. Stem Cell Collection Objective: To collect stem cells from the patient (autologous) or a donor (allogeneic). Steps:</p> <p>1. Selection of Stem Cell Source:</p> <ol style="list-style-type: none"> 1. Determine the appropriate source of stem cells based on the patient's condition and treatment plan (e.g., bone marrow, adipose tissue, umbilical cord blood). <p>2. Preparation for Collection:</p> <ol style="list-style-type: none"> 1. Prepare the patient or donor for the collection procedure, including any necessary pre-collection medications or fasting requirements. <p>3. Collection Procedure:</p> <ol style="list-style-type: none"> 1. Perform the stem cell collection procedure using aseptic techniques to minimize contamination risk. <ol style="list-style-type: none"> 1. Bone Marrow Aspiration: Collect bone marrow from the iliac crest or other suitable site. 2. Adipose Tissue Harvesting: Perform liposuction to obtain adipose tissue. 3. Umbilical Cord Blood Collection: Collect blood from the umbilical cord and placenta after childbirth. <p>4. Post-Collection Care:</p> <ol style="list-style-type: none"> 1. Monitor the patient or donor for any immediate complications following the collection procedure. 2. Provide instructions for post-collection care and follow-up appointments. 	<p>3. Monitoring:</p> <ol style="list-style-type: none"> 1. Monitor the patient for any adverse reactions or complications during the preconditioning phase. <p>7. Cell Administration Objective: To introduce the prepared stem cells into the patient. Steps:</p> <p>1. Administration Route:</p> <ol style="list-style-type: none"> 1. Determine the appropriate route of administration based on the patient's condition and treatment plan (e.g., intravenous infusion, direct injection into the target tissue). <p>2. Administration Procedure:</p> <ol style="list-style-type: none"> 1. Perform the stem cell administration procedure under sterile conditions. <ol style="list-style-type: none"> 1. Intravenous Infusion: Infuse stem cells through a vein, typically over a period of 30-60 minutes. 2. Direct Injection: Inject stem cells directly into the target tissue (e.g., joint, heart muscle). <p>3. Post-Administration Care:</p> <ol style="list-style-type: none"> 1. Monitor the patient for any immediate reactions or complications following stem cell administration. 2. Provide instructions for post-administration care and follow-up appointments.
<p>3. Cell Processing Objective: To isolate, purify, and prepare the collected stem cells for expansion. Steps:</p> <p>1. Transport to Processing Facility:</p> <ol style="list-style-type: none"> 1. Transport the collected stem cells to a laboratory or processing facility under controlled conditions to maintain cell viability. <p>2. Isolation of Stem Cells:</p> <ol style="list-style-type: none"> 1. Isolate stem cells from the collected material using appropriate techniques (e.g., density gradient centrifugation, magnetic-activated cell sorting). <p>3. Purification:</p> <ol style="list-style-type: none"> 1. Purify the isolated stem cells to remove any unwanted cells or contaminants. <p>4. Preparation for Expansion:</p> <ol style="list-style-type: none"> 1. Prepare the purified stem cells for the expansion process, including resuspension in suitable culture media. <p>4. Cell Expansion Objective: To culture and expand the processed stem cells to obtain a sufficient quantity for therapy. Steps:</p> <p>1. Culture Conditions:</p> <ol style="list-style-type: none"> 1. Maintain stem cells in a controlled environment with optimal culture conditions (e.g., temperature, humidity, CO₂ levels). <p>2. Expansion Protocol:</p> <ol style="list-style-type: none"> 1. Follow standardized protocols for stem cell expansion, including regular media changes and monitoring for cell growth and viability. <p>3. Harvesting Expanded Cells:</p> <ol style="list-style-type: none"> 1. Harvest the expanded stem cells once the desired cell quantity and quality are achieved. 	<p>Stem Cell Therapy Protocol</p> <p>8. Monitoring and Follow-Up Objective: To continuously monitor the patient to assess therapy effectiveness and manage any adverse effects. Steps:</p> <p>1. Regular Follow-Up Visits:</p> <ol style="list-style-type: none"> 1. Schedule regular follow-up visits to monitor the patient's progress and response to therapy. <p>2. Clinical Assessments:</p> <ol style="list-style-type: none"> 1. Conduct clinical assessments to evaluate the therapeutic outcomes (e.g., symptom improvement, functional recovery). <p>3. Laboratory Tests:</p> <ol style="list-style-type: none"> 1. Perform laboratory tests to monitor biomarkers of treatment response and detect any potential complications. <p>4. Imaging Studies:</p> <ol style="list-style-type: none"> 1. Use imaging studies (e.g., MRI, CT scans) to assess structural changes and treatment efficacy. <p>5. Adverse Event Management:</p> <ol style="list-style-type: none"> 1. Monitor for and manage any adverse events or complications related to stem cell therapy. <p>6. Long-Term Follow-Up:</p> <ol style="list-style-type: none"> 1. Continue long-term follow-up to assess the durability of the treatment response and identify any late-onset complications.

Figure 2. Protocol outline of stem cell therapy

5. Future Perspectives of Stem Cell Therapy

5.1. Enhanced Reprogramming Techniques:

Improving the efficiency and safety of iPSC generation through non-viral and integration-free methods will enhance their clinical applicability. Advances in understanding the molecular mechanisms of reprogramming will lead to more reliable and safe iPSC production.

5.2. Organoid Development:

Using stem cells to create organoids—miniaturized, three-dimensional versions of organs—offers exciting possibilities for disease modeling, drug testing, and potentially developing transplantable organs. Organoids can mimic the structure and function of real organs, providing valuable insights into disease mechanisms and therapeutic responses.

5.3. Immune System Modulation:

Combining stem cell therapy with immune-modulating strategies, such as regulatory T cells or immune checkpoint inhibitors, could enhance transplant success and treat autoimmune diseases. Understanding the interactions between stem cells and the immune system will pave the way for more effective and safer therapies.

5.4. Personalized Medicine:

Stem cell therapy offers the potential for personalized medicine, where treatments are tailored to the individual patient's genetic makeup and disease profile. Advances in genomic and proteomic technologies will enable the identification of patient-specific markers, guiding the development of targeted therapies.

6. Tissue Engineering in Regenerative Medicine

Tissue engineering is a field that aims to repair or replace damaged tissues. There are three main components involved in this process: cells, biomaterials, and signaling molecules. Cells, often stem cells, provide the building blocks for new tissue. Biomaterials, which can be natural or synthetic, act as a scaffold to support the cells and guide their growth. Signaling molecules, such as growth factors, help to instruct the cells on how to behave and organize themselves into functional tissue. By carefully combining these components, scientists hope to create new tissues that can improve people's lives. **The Key Components of Tissue Engineering are discussed below.**

6.1. Scaffolds:

Scaffolds provide a three-dimensional framework for cell attachment, proliferation, and differentiation. They can be made from natural materials (e.g., collagen, alginate) or synthetic materials (e.g., polylactic acid, polyglycolic acid). The choice of scaffold material depends on

the target tissue and desired properties, such as biodegradability, mechanical strength, and biocompatibility.

6.2. Cells:

Various cell types can be used in tissue engineering, including primary cells, stem cells, and differentiated cells relevant to the target tissue. Stem cells, particularly MSCs and iPSCs, are widely used due to their ability to differentiate into multiple cell types.

6.3. Bioreactors:

Bioreactors provide a controlled environment for the cultivation of tissue-engineered constructs. They supply necessary nutrients, oxygen, and mechanical stimuli to promote cell growth and tissue development. Bioreactors can mimic the physiological conditions of the target tissue, enhancing the maturation and functionality of the engineered tissue.

7. Current Applications of Tissue Engineering

Tissue engineering is revolutionizing medicine by creating functional substitutes for damaged tissues. Skin grafts, for instance, are already used to treat burns and wounds. Beyond that, researchers are making progress on engineering more complex tissues like cartilage for knee injuries and even tracheas for breathing problems. While still in development for some organs, tissue engineering holds immense promise for regenerating lost tissue function and improving patient lives.

7.1. Skin Grafts:

Engineered skin is used to treat burn victims, chronic wounds, and diabetic ulcers. Products such as Apligraf and Dermagraft, composed of living cells and scaffolds, are already in clinical use. These skin substitutes promote wound healing by providing a biologically active environment that supports cell migration and tissue regeneration.

7.2. Cartilage Repair:

Tissue-engineered cartilage is being developed for joint repair and the treatment of osteoarthritis. Autologous chondrocyte implantation (ACI) and matrix-induced autologous chondrocyte implantation (MACI) are techniques that use the patient's own cartilage cells, seeded onto scaffolds, to repair cartilage defects. These approaches aim to restore the functionality and integrity of damaged cartilage.

7.3. Bone Regeneration:

Bone tissue engineering aims to create constructs that can promote bone regeneration and repair. Scaffolds loaded with osteogenic cells and growth factors are used to treat bone defects and non-unions. Advances in 3D printing and bioprinting technologies have enabled the creation of complex, patient-specific bone constructs that mimic the architecture and mechanical properties of natural bone.

7.4. Vascular Grafts:

Engineered blood vessels are being developed for use in bypass surgery and the treatment of vascular diseases. Tissue-engineered vascular grafts (TEVGs) can provide a viable alternative to autologous grafts, reducing the risk of complications and improving patient outcomes. These grafts are designed to integrate with the host tissue and promote endothelialization, ensuring long-term patency.

7.5. Organoids:

Organoids are miniaturized, simplified versions of organs grown in vitro from stem cells. They are used for disease modeling, drug testing, and potential future organ replacement. Organoids can replicate the cellular diversity and architecture of real organs, providing valuable insights into developmental biology and disease mechanisms. Advances in organoid technology may lead to the development of transplantable tissues and organs for regenerative medicine applications.

8. Challenges in Tissue Engineering

Tissue engineering, though promising, faces hurdles. Creating ideal scaffolds that mimic natural tissues and support cell growth is difficult. We also need better control over stem cell differentiation to ensure they become the desired cell type. Additionally, engineered tissues often lack proper vascularization, limiting nutrient and oxygen delivery. These limitations are actively being researched, but overcoming them is key to bringing this technology to the forefront of medicine. Some identified challenges are discussed below:

8.1. Vascularization:

One of the major challenges in tissue engineering is achieving adequate vascularization of the engineered tissue. Without a blood supply, cells in the interior of the construct may suffer from hypoxia and nutrient deprivation, leading to cell death and tissue necrosis. Developing techniques to promote angiogenesis and integrate the engineered tissue with the host vasculature is essential for the success of tissue-engineered constructs.

8.2. Immune Response:

The immune response to implanted biomaterials and cells can affect the success of tissue-engineered constructs. Immune rejection, inflammation, and fibrosis can compromise the functionality and longevity of the engineered tissue. Strategies to modulate the immune response, such as using immunomodulatory biomaterials and cells, are being explored to improve the biocompatibility and integration of tissue-engineered constructs.

8.3. Mechanical Properties:

Replicating the mechanical properties of native tissues is crucial for the success of tissue-engineered constructs. Scaffolds must provide the necessary structural support and withstand physiological loads without deforming or failing. Developing biomaterials with tunable mechanical properties and incorporating mechanical stimuli during the cultivation process can enhance the functionality and durability of the engineered tissue.

8.4. Scale-Up and Manufacturing:

Scaling up tissue-engineered constructs for clinical use presents significant challenges. Standardizing production processes, ensuring quality control, and meeting regulatory requirements are essential for the commercialization of tissue-engineered products. Advances in bioreactor design, automation, and bioprinting technologies can facilitate the large-scale production of tissue-engineered constructs, making them more accessible to patients.

9. Future Perspectives of Tissue Engineering

Tissue engineering is poised to revolutionize medicine by growing replacement tissues and organs. Imagine damaged bones healing with your own cells, or 3D-printed skin for burn victims. Advancements in biomaterials, stem cells, and bioprinting hold immense potential. This field could overcome donor shortages and revolutionize treatment for diseases and injuries.

9.1. 3D Bioprinting:

3D bioprinting allows for the precise layering of cells, biomaterials, and growth factors to create complex tissue structures. This technology enables the fabrication of patient-specific constructs with high spatial resolution and reproducibility. Advances in bioprinting techniques, such as multi-material printing and microfluidics, will expand the possibilities for tissue engineering, enabling the creation of functional tissues and organs for transplantation.

9.2. Smart Biomaterials:

The development of smart biomaterials that can respond to environmental cues or deliver bioactive molecules will enhance tissue integration and healing. These materials can release growth factors, drugs, or genetic material in response to specific stimuli, promoting tissue

regeneration and reducing the risk of complications. Advances in nanotechnology and material science will drive the development of next-generation biomaterials with improved functionality and biocompatibility.

9.3. Personalized Tissue Constructs:

Combining patient-derived cells with tissue engineering techniques can lead to the development of customized grafts and implants tailored to individual patients. Advances in stem cell technology, genetic engineering, and biomaterials will enable the creation of personalized tissue constructs that match the patient's genetic profile and disease state. This approach has the potential to improve the success rates of tissue-engineered therapies and reduce the risk of immune rejection.

9.4. Integration with Regenerative Medicine:

Integrating tissue engineering with other regenerative medicine approaches, such as stem cell therapy and gene editing, will enhance the efficacy of tissue-engineered constructs. Combining these technologies can create synergistic effects, promoting tissue regeneration and repair. For example, using gene-edited stem cells seeded onto engineered scaffolds can enhance the functionality and longevity of the tissue-engineered constructs.

10. Gene Therapy and Gene Editing in Regenerative Medicine

Gene therapy and gene editing are powerful tools for treating genetic disorders and enhancing the regenerative potential of cells and tissues. This section explores the current status, applications, and future directions of gene therapy and gene editing in regenerative medicine.

10.1 Gene Therapy

Gene therapy offers a revolutionary approach to medicine by directly targeting the root cause of diseases at the genetic level. It involves modifying genes or cellular behavior to treat or prevent illness. This can be achieved through several methods, such as replacing faulty genes with healthy copies, inactivating malfunctioning genes, or introducing entirely new genes to equip cells with the ability to fight disease. This holds immense promise for a wide range of conditions, from genetic disorders like cystic fibrosis to cancers caused by mutated genes. While still a developing field, with most applications currently undergoing clinical trials, gene therapy has already seen its first successes in approved treatments for certain cancers and genetic diseases. This exciting field holds the potential to transform medicine by offering permanent cures or significantly improved management of diseases that were previously untreatable.

10.2 Types of Gene Therapy:

Gene therapy tackles diseases by modifying a patient's DNA. There are two main categories: somatic and germline. Somatic gene therapy, the focus of current research, targets body cells

(not sperm or egg cells) and changes only affect the individual treated. Germline therapy alters genes in sperm or egg cells, which can be passed to future generations, but due to ethical concerns, it's not currently used in humans. Within somatic gene therapy, there are different approaches like adding a healthy gene, editing a faulty one, or using RNA therapy. These approaches aim to address the underlying cause of a disease and offer exciting possibilities for treating various conditions.

10.2.1. In Vivo Gene Therapy:

In vivo gene therapy involves delivering the therapeutic gene directly into the patient's body. Viral vectors, such as adeno-associated virus (AAV) and lentivirus, are commonly used to deliver the gene to the target cells. Non-viral methods, such as nanoparticles and liposomes, are also being developed to improve the safety and efficiency of gene delivery.

10.2.2. Ex Vivo Gene Therapy:

Ex vivo gene therapy involves modifying the patient's cells outside the body and then transplanting the genetically modified cells back into the patient. This approach is commonly used for hematopoietic stem cell (HSC) transplantation, where the patient's HSCs are harvested, genetically modified, and then re-infused.

10.3 Current Applications of Gene Therapy:

Gene therapy is a rapidly evolving field that introduces genetic material to treat or prevent diseases. While still in its early stages for many conditions, it's already showing promise. Currently, approved gene therapies target certain blood cancers and rare genetic illnesses. For instance, it can modify immune cells to attack cancerous B-cells or deliver functional copies of missing genes. Additionally, researchers are actively exploring gene therapy for diseases like cystic fibrosis, heart disease, and blindness. Though challenges like unintended side effects and ensuring long-term effectiveness remain, gene therapy holds immense potential for revolutionizing medicine by tackling diseases at their genetic root.

10.3.1. Inherited Genetic Disorders:

Gene therapy has been approved for several inherited genetic disorders, including spinal muscular atrophy (SMA) and Leber congenital amaurosis (LCA). For example, Zolgensma (onasemnogene abeparvovec) is an AAV-based gene therapy approved for the treatment of SMA, delivering a functional copy of the SMN1 gene to the patient's motor neurons.

10.3.2. Cancer Treatment:

Gene therapy techniques, such as chimeric antigen receptor (CAR) T-cell therapy, are used to reprogram a patient's immune cells to attack cancer cells. CAR-T cells are engineered to express receptors that recognize and bind to specific antigens on the surface of cancer cells, leading to their destruction. This approach has shown remarkable success in treating certain

types of blood cancers, such as acute lymphoblastic leukemia (ALL) and diffuse large B-cell lymphoma (DLBCL).

10.3.3. Blood Disorders:

Gene therapy is being investigated for the treatment of blood disorders such as hemophilia, sickle cell anemia, and beta-thalassemia. Clinical trials using gene therapy to deliver functional copies of the clotting factor genes (FVIII or FIX) for hemophilia, or to correct the defective hemoglobin gene in sickle cell anemia and beta-thalassemia, have shown promising results.

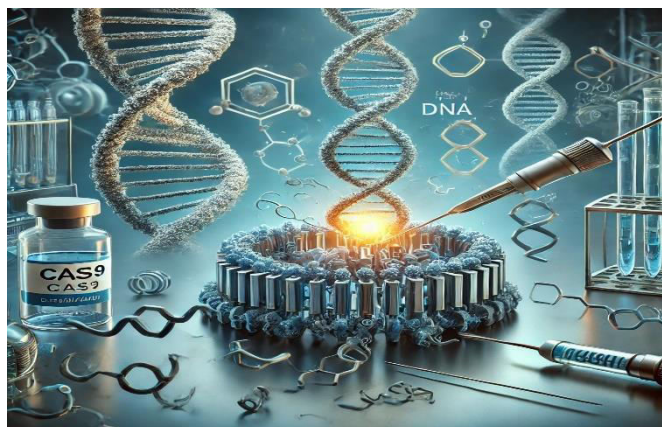


Figure 3. Gene editing is one of powerful tool in regenerative medicine, advent of CRISPR technology empowers the scientist to develop a better therapy for incurable diseases.

11. Gene Editing

Gene editing offers the ability to make precise alterations directly within an organism's DNA, potentially correcting genetic disorders or introducing beneficial traits for therapeutic purposes (Figure 3). The most prevalent method for this is CRISPR-Cas9. CRISPR-Cas9 acts as a sophisticated molecular scalpel, allowing scientists to target specific locations on the genome. With this pinpoint accuracy, researchers can snip out unwanted genetic mutations, insert healthy genes to counteract diseases, or even fine-tune gene expression to achieve desired therapeutic effects. This revolutionary technology holds immense promise for revolutionizing medicine, potentially leading to cures for currently untreatable illnesses.

11.1. Mechanism of CRISPR-Cas9:

CRISPR-Cas9 consists of two key components: the Cas9 protein, which acts as a molecular scissor to cut DNA, and a guide RNA (gRNA) that directs Cas9 to the target DNA sequence. Once the DNA is cut, the cell's repair mechanisms can be harnessed to introduce specific genetic changes (Figure 4).



Figure 4. Steps involved in gene therapy

11.2. Current Applications of Gene Editing:

Gene editing is revolutionizing various fields. In medicine, researchers are using CRISPR, a powerful editing tool, to develop potential cures for genetic diseases. They've made progress in correcting mutations responsible for illnesses like cystic fibrosis and hemophilia in lab models. Additionally, scientists are engineering immune cells with CRISPR to target and destroy cancer cells, marking a new era in personalized cancer therapy. Gene editing is also impacting agriculture. Scientists are creating crops resistant to diseases and harsh environments, contributing to food security. For instance, CRISPR-edited rice varieties show resistance to bacterial blight, and brown button mushrooms have been modified to resist browning. These applications hold immense promise, but there are ongoing discussions about the ethical implications of altering human genes and the potential unintended consequences in ecosystems when it comes to edited crops.

11.2.1. Monogenic Disorders:

Gene editing is being explored for the treatment of monogenic disorders, where a single gene mutation causes the disease. For example, CRISPR-Cas9 is being used to correct the genetic mutations responsible for cystic fibrosis, Duchenne muscular dystrophy, and Huntington's disease in preclinical models.

11.2.2. Hematological Disorders:

Gene editing is being investigated for the treatment of hematological disorders such as sickle cell anemia and beta-thalassemia. Clinical trials using CRISPR-Cas9 to correct the defective hemoglobin gene in patient-derived HSCs have shown promising results, with patients achieving normal or near-normal hemoglobin levels.

11.2.3. Cancer Immunotherapy:

Gene editing is being used to enhance the efficacy of cancer immunotherapy. For example, CRISPR-Cas9 is used to knock out immune checkpoint genes, such as PD-1, in T cells, enhancing their ability to attack cancer cells. This approach is being tested in clinical trials for various cancers, including lung cancer and melanoma.

12. Challenges in Gene Therapy and Editing

Gene therapy and editing hold immense promise for treating a vast array of diseases, but significant hurdles remain. Delivering the corrective genetic material to the right cells and ensuring it functions properly are ongoing challenges. Our immune system, designed to fight off invaders, can recognize the viral vectors often used for delivery as foreign, potentially hindering or eliminating the treatment. Additionally, gene therapy can unintentionally disrupt healthy genes or cause uncontrollable overexpression of the introduced gene, leading to serious side effects. Even if these technical hurdles are cleared, the high costs of gene therapy development and treatment pose a major barrier to widespread application, especially for rare genetic disorders.

12.1. Delivery Efficiency:

Efficient and targeted delivery of therapeutic genes or gene-editing components to the target cells is a major challenge. Viral vectors, while effective, can induce immune responses and have size limitations. Developing non-viral delivery methods, such as nanoparticles and liposomes, can improve the safety and efficiency of gene delivery.

12.2. Off-Target Effects:

Ensuring the specificity of gene editing and minimizing off-target effects is crucial for the safety of gene-editing therapies. Advances in CRISPR technology, such as high-fidelity Cas9 variants and base editors, are being developed to improve the precision and reduce the risk of unintended genetic changes.

12.3. Long-Term Safety and Efficacy:

The long-term safety and efficacy of gene therapy and gene editing must be thoroughly evaluated. Potential risks include immune responses, insertional mutagenesis, and the

durability of the therapeutic effect. Long-term follow-up studies and rigorous preclinical testing are essential to ensure the safety and efficacy of these therapies.

13. Future Perspectives of Gene Therapy and Editing

The future of gene therapy and editing holds immense promise for revolutionizing medicine. With CRISPR and other tools becoming more precise and efficient, researchers are optimistic about tackling a vast array of diseases. Imagine a world where cystic fibrosis, sickle cell anemia, and even some cancers are treatable by correcting the underlying genetic errors. Gene therapy for rare genetic disorders affecting the brain and nervous system is already on the horizon. However, challenges remain. Ensuring the safety and efficacy of these interventions in the long term is crucial. Additionally, ethical considerations regarding the potential for human enhancement and unintended consequences require careful discussion. Public education and open dialogue will be vital for navigating the ethical complexities and ensuring equitable access to these transformative therapies. If these hurdles can be overcome, gene therapy and editing have the potential to usher in a new era of preventative and curative medicine, offering a future free from the burden of many debilitating genetic diseases.

13.1. CRISPR and Beyond:

Ongoing improvements in CRISPR technology, such as prime editing and epigenome editing, will enhance the precision and efficiency of gene-editing therapies. These advancements will expand the range of treatable conditions and reduce the risk of off-target effects.

13.2. In Vivo Gene Editing:

Advances in delivery methods, such as viral vectors and nanoparticles, will make in vivo gene editing more feasible, allowing for the direct modification of genes within the patient's body. This approach has the potential to treat a wide range of genetic disorders without the need for ex vivo manipulation.

13.3. Synthetic Biology:

Integrating synthetic biology with gene editing will lead to the creation of novel therapeutic approaches, such as programmable cells that can sense and respond to disease states. This field holds promise for developing highly specific and adaptable treatments for complex diseases.

13.4. Regulatory and Ethical Considerations:

Addressing regulatory and ethical challenges will be crucial for the widespread adoption of gene therapy and editing. Developing clear guidelines for the approval and monitoring of these therapies will ensure patient safety and promote innovation. Ethical considerations, such as informed consent and equitable access to treatments, must be addressed to gain public trust and support.

Conclusion

Regenerative medicine is at the forefront of medical innovation, offering the potential to revolutionize healthcare by repairing or replacing damaged tissues and organs. The current status of regenerative medicine includes significant advancements in stem cell therapy, tissue engineering, and gene therapy. These technologies are already making an impact in clinical settings, offering new treatment options for a wide range of diseases and injuries.

Looking ahead, the future of regenerative medicine is bright, with continued research and development driving the field forward. Advances in stem cell therapy, tissue engineering, and gene editing will lead to more effective and personalized treatments. The integration of these technologies with other emerging fields, such as synthetic biology and nanotechnology, will further enhance their potential.

However, addressing regulatory, ethical, and economic challenges will be crucial for realizing the full potential of regenerative medicine. Developing clear guidelines, ensuring patient safety, and promoting equitable access to treatments will be essential for gaining public trust and support.

Therefore, regenerative medicine holds tremendous promise for transforming healthcare and improving patient outcomes. By addressing the challenges and leveraging the latest advancements in technology, we can unlock the full potential of regenerative medicine and usher in a new era of medical innovation.

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REVIEW ARTICLES

ROLE OF COMPUTER DOCKING IN PLANT DISEASE MANAGEMENT

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Abstract

Computational methods offer novel approaches to tackle plant diseases with minimal environmental impact by simplifying drug discovery efforts and offering molecular insights into plant-pathogen interactions. The application of computational biology to agricultural methods could transform crop protection strategies and secure food production for future generations, provided that research in this area continues to advance.

Introduction

Plant diseases affect agricultural productivity, quality, and economic stability, which make them serious challenges to global food security. Chemical interventions are frequently used in traditional illness control techniques, which may have negative effects on the environment and human health (Ristaino 2021). On the other hand, developments in computational methods, especially computer docking, present encouraging paths for more focused and long-term approaches to plant disease control. The use of computer docking to study plant-pathogen interactions, medication discovery to fight plant diseases, and possible agricultural applications are all covered in this article (Satpathy 2022).

Perceptive of Plant-Pathogen Interactions

In order to understand the molecular mechanics behind plant-pathogen interactions, computer docking is essential. Docking techniques simulate the pathogen protein binding to plant receptors or enzymes, allowing for the prediction of the specificity and strength of these interactions (Mustafa et al., 2022). Finding possible targets for disease prevention initiatives is made much easier with the use of this information (Figure 1). Researchers can prioritize candidate proteins or tiny compounds that break important connections, preventing pathogen virulence or strengthening plant defense mechanisms, by using computer modeling (Rasheed et al., 2024).

ecologically sustainable and efficacious. Additionally, by reducing the need for traditional chemical pesticides, virtual screening can identify new therapeutic targets and compounds, lowering the danger of resistance development and environmental pollution. In the end, farmers can implement more precision-driven methods of managing diseases by utilizing computational biology, which will enhance crop yields, improve food security, and have a smaller negative environmental impact (Marwal et al., 2017).

Conclusion

The use of computer docking in plant disease management has many potential benefits, but there are drawbacks as well. Depending on the system under study, the precision of computational algorithms and the quality of structural data are critical to the accurate prediction of protein-ligand interactions. Furthermore, it can take a lot of time and resources to conduct thorough experimental validation in order to translate *in silico* predictions into practical solutions. It will take interdisciplinary cooperation between computational biologists, plant pathologists, and agricultural scientists as well as ongoing developments in computational techniques to address these issues. One effective weapon in the toolbox for managing plant diseases is computer docking (Srivastava et al., 2024).

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LIFE IS BECAUSE OF PHOTOSYNTHESIS

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We have to be thankful to Photo-autotrophs that produce oxygen, directly related to the survival of all creatures on the earth. Photo-autotrophs are groups of organisms, able to synthesize their food in the presence of light *viz.*, photosynthetic bacteria, algae, and plants. Synthesis of own food in the form of sugar using light and carbon dioxide is called photosynthesis.

Science of Photosynthesis

Photosynthesis consists of a complex series of both physical and chemical reactions, but it could be divided into 3 key stages:

- 1) Light absorption in which photon of sunlight is absorbed by photosystems (I and II) that contains photosynthetic pigments releases electron. This electron is passed through a series of protein molecules embedded in the thylakoid membrane until it is used to convert chemical energy in the form of NADPH (Nicotinamide adenine dinucleotide phosphate).
- 2) Splitting of the water molecule, in which PS II is used to break water molecule into hydrogen ion and oxygen molecule as a byproduct. The produced hydrogen ion is used to synthesize chemical energy in form of ATP (Adenosine triphosphate).
- 3) Atmospheric carbon dioxide is fixed into carbohydrates by utilizing energy that is produced in chemical form along with the most abundant enzyme *i.e.*, RuBisCO (Ribulose-1,5-bisphosphate carboxylase oxygenase).

Significance of Photosynthesis

Therefore, it is a unique process on the earth in which light energy converts to chemical energy, and oxygen is produced as a byproduct, essential for the survival of living organisms. It does not only supply oxygen, but it also provides food and energy to all. No other living creatures can synthesize their food except Photo-autotrophs. Due to the ability of photosynthesis these groups of organisms, are primary producers in all different ecosystems and key players to maintain the flow of energy from one trophic level to the other which leads to the integrity of the system. Ecological integrity means optimizing the maintenance of equilibrium to ensure a constant flow of food for socioeconomic significance. In the aquatic ecosystem, the food web starts from phytoplankton these are producers, consumers *viz.*, zooplankton, small and big fish, and ends with decomposers. Similarly, in terrestrial ecosystems, energy flow begins from plants and end-up with microorganisms through different intermediates as consumers. We human beings are consumers that benefit from all different types of yummy foods and oxygen that photosynthesis creates. Sometimes few people argue that they eat meat and other animal products, not plants but they should understand these animals also depend on plants. So plants

are the ultimate source of food and energy for all other living organisms. We expel lots of carbon dioxide into the atmosphere in the process of breathing, which provides essential components for photosynthesis to synthesize more food. Therefore, all living organisms are connected in a continuous cycle of dependencies. The cycle continues as long as all the essential components are available.

Recently an article was published in Speaking Tree, Times of India entitled “Beauty is an Outcome of Photosynthesis” by Prof. Vir Singh. He emphasized “beauty begins with photosynthesis; heterogeneity of life is more beautiful than uniformity of life. Since light through photosynthesis diversifies life by evolving innumerable species with diversified genetic traits, communities, ecosystem, living landscape, and biome, beauty itself evolutionary.”

Based on all the above facts, it is evident how photo-autotrophs play a crucial role in the regulation of the life cycle and diversity of organisms in all different ecosystems of planet earth, and life without photosynthesis would be impossible. In the terrestrial ecosystem, humans are most intelligent because of our 1400 cc brain capacity, we must realize the importance of plants every time we breathe in and out, and protect against deforestation to save our life. The only protection from deforestation does not fulfill our requirement but we need to plant more and more plants for the survival of the growing population, projected 9 billion by 2050. Therefore,

Save Plants, Save Lives, and Save the Planet!!!

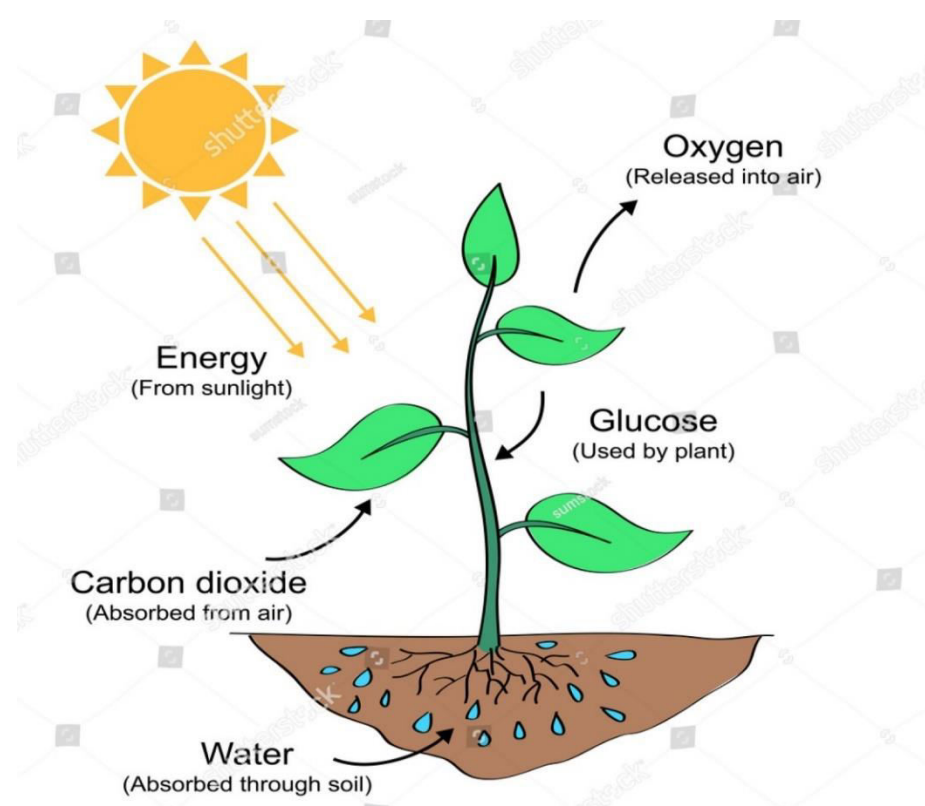


Fig 1: Science of Photosynthesis

Reference: <https://www.shutterstock.com/image-illustration/photosynthesis-process-labelled-illustration-535886347>



Fig 2: Protect deforestation and plant more trees

Reference: <http://www.edubilla.com/blog/plant-trees-to-save-future/>

BIOINFORMATICS INTERVENTION IN NEW DRUG IDENTIFICATION AND DESIGNING

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Abstract

Current drug discovery involves creating large quantities of compounds and quickly analyzing these extensive libraries. This demand for efficient storage, management, and analysis has led to the development of computer-aided drug design (CADD). Computational methods are invaluable in interpreting and directing experiments, speeding up the process of designing antibiotic drugs. There are two primary types of CADD: structure-based drug design (SBDD) and ligand-based drug design (LBDD). CADD encompasses computational techniques and tools used to aid the discovery and creation of new therapeutic solutions. Digital repositories, which hold comprehensive information on drugs and other useful compounds, are essential for studying chemical reaction capabilities. Design libraries, capable of generating a wide range of molecular variants, allow for the selection and sampling of chemical compounds with varied properties. SBDD techniques analyze the three-dimensional structural information of macromolecular targets, typically proteins or RNA, to identify crucial sites and interactions necessary for their biological functions. This information is then used to design antibiotic drugs that can disrupt these essential interactions, thereby hindering the biological pathways crucial for the microorganism's survival. LBDD methods concentrate on known antibiotic ligands for a target, establishing a relationship between their physicochemical properties and antibiotic activities, known as structure-activity relationships (SAR). This information can be used to optimize existing drugs or guide the creation of new drugs with enhanced activity. Virtual screening, the digital equivalent of high-throughput screening, holds significant potential for systematically evaluating vast chemical libraries to identify promising lead candidates for synthesis and testing. This article provides an overview of the key data sources and computational methods for discovering new molecular entities. It discusses the entire workflow of a virtual screening campaign, from data collection to post-screening analysis.

Introduction

A typical drug discovery process, from lead identification to clinical trials, is estimated to take around 14 years and cost approximately 800 million US dollars. In the early 1990s, advances in combinatorial chemistry and high-throughput screening technologies aimed to speed up this process by allowing large libraries of compounds to be synthesized and tested quickly (DiMasi et al., 2003). Despite these efforts, the number of successfully launched new molecular entities did not increase and may have even decreased. The hit rates are often low, and many identified

hits fail to be further developed into actual leads and preclinical candidates (Oprea et al., 2001). A significant portion of recent failures, about 40-60%, is attributed to issues with absorption, distribution, metabolism, excretion, and toxicity (ADME/Tox) (Venkatesh et al., 2000, Hou et al., 2004).

A new paradigm in drug discovery has emerged, emphasizing the early evaluation of lead candidates for potency (activity), selectivity, and potential ADME/Tox liabilities. This approach aims to minimize expensive late-stage failures and expedite the successful development of new molecular entities. Central to this paradigm shift is the use of computational techniques in drug discovery. Computer-aided drug design (CADD) encompasses computational tools and resources for storing, managing, analyzing, and modeling compounds. This includes creating digital repositories for studying chemical interactions, developing software for designing compounds with desirable physicochemical properties, and employing tools for systematically assessing potential lead candidates before synthesis and testing. The foundations of CADD were established in the early 1970s with the use of structural biology to modify the biological activity of insulin and to guide the synthesis of human hemoglobin ligands (Beddell et al., 1976). However, at that time, X-ray crystallography was too costly and time-consuming for large-scale screening in industrial laboratories.

Over the years, new technologies like comparative modeling based on natural structural homologues have been developed and utilized in lead design. Alongside advances in combinatorial chemistry, high-throughput screening technologies, and computational infrastructures, these innovations have effectively bridged the gap between theoretical modeling and medicinal chemistry. This has led to numerous successful drug designs, including Dorzolamide for cystoid macular edema, Zanamivir for influenza treatment and prevention, Sildenafil for male erectile dysfunction, and Amprenavir for HIV infection (Grover et al., 2006, Von Itzstein et al., 1993).

Despite the availability and long-term use of numerous antibiotic drugs, the ongoing battle between humans and the bacteria causing infections continues and is expected to persist in the future. This is largely due to the increasing resistance to antibiotics, which necessitates the development of new ones (Walsh 2003). To design new antibiotics, computer-aided drug design (CADD) can be integrated with wet-lab techniques to understand drug resistance mechanisms, identify new antibiotic targets, and create novel antibiotics for both existing and new targets. CADD methods are particularly valuable because they can generate atomic-level structure-activity relationships (SAR), which streamline the drug design process, reducing both time and costs.

Understanding the atomic-level mechanisms behind antibiotic resistance helps identify the limitations of current antibiotics and informs the design of new drugs. For instance, molecular dynamics (MD) simulations to study mutations at the bacterial ribosomal A-site, uncovering the origins of bacterial resistance to aminoglycoside antibiotics (Panecka et al., 2014). Researchers have used bioinformatics approaches to computationally screen various databases, identifying seven enzymes involved in bacterial metabolic pathways and 15 non-homologous proteins located on the membranes of the gram-positive bacterium *Staphylococcus aureus* (SA) as potential targets (Hossain et al., 2013). These findings may help overcome SA's resistance to

common antibiotics like methicillin, fluoroquinolones, and oxazolidinones (O'Neill et al., 2013).

Computer-aided drug design now plays a crucial role in discovering new molecular entities. The current focus includes enhancing the design and management of data sources, creating computer programs to generate vast libraries of pharmacologically interesting compounds, developing new algorithms to evaluate the potency and selectivity of lead candidates, and designing predictive tools to identify potential ADME/Tox liabilities. In this article, we discussed the major tools and resources developed to accelerate the search for novel drug candidates.

Data sources available for new drug and disease identification

Data accessibility is vital for the success of drug discovery and development campaigns. Vast amounts of information on organic molecules, biological sequences, and related data have been accumulated in scientific literature and case reports. These data are systematically collected and stored in various databases. Each year, hundreds of biological databases are documented. Concurrently, computational algorithms are being actively developed to aid in the design of combinatorial libraries. This section reviews the most important data sources.

Database of genes and genomics or biological database

The sequencing of human and other model organism genomes has generated vast amounts of data relevant to the study of human disease. The international collaborative databases GenBank, DNA Data Bank of Japan (DDBJ), and European Molecular Biology Laboratory (EMBL) serve as global repositories for nucleotide sequences from various sources, synchronizing their records daily. Swiss-Prot and Protein Information Resource (PIR) offer comprehensive and expertly annotated protein sequence and functional information (O'Donovan et al., 2001). Swiss-Prot currently indexes more than 400,000 protein sequences. Translated EMBL (TrEMBL) complements Swiss-Prot by providing computer-annotated protein sequences from EMBL nucleotide sequences not covered in Swiss-Prot (Westbrook et al., 2002). The Protein Data Bank (PDB) is the primary global archive for structural data on biological macromolecules, housing thousands of structures.

Some of these pairwise relationships are abstracted into biologically relevant pathways and networks, accessible through resources such as the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and BioCarta pathways RESID (Lee et al., 2006, Farriol-Mathis et al., 2004, Kanehisa et al., 2004). These resources enable detailed analysis of specific biomolecules and their roles in disease-related molecular pathways. Further comprehensive reviews are available elsewhere.

Small molecules or compounds databases

Small compound or molecule databases are a crucial resource for studying biochemical interactions and are becoming increasingly important in modern drug discovery due to the accumulation of data. Various repositories of biologically interesting small molecules and their physicochemical properties have been compiled (Chen et al., 2005). These include databases of known chemical compounds, drugs, carbohydrates, enzymes, reactants, natural products, and

natural-product-derived compounds (Ortholand., 2004). PubChem, part of the National Institute of Health (NIH) Molecular Library Roadmap Initiative, provides information on the biological activities of over 40 million small molecules and 19 million unique structures.

The Available Chemicals Directory (ACD) from Molecular Design Limited serves as a key resource for docking studies. As this database provides information on over 600000 purchasable compounds, while its counterpart, the Screening Compounds Directory, holds over 4.5 million unique structures. ZINC, a free database of purchasable compounds, contains 20,089,615 3D structures of molecules annotated with biologically relevant properties such as molecular weight, calculated Log P, and the number of rotatable bonds. LIGAND provides records on 15,395 chemical compounds, 8031 drugs, 10,966 carbohydrates, 5043 enzymes, 7826 chemical reactions, and 11,113 reactants as of February 2009 (Irwin et al., 2005). DrugBank stores detailed information on nearly 4800 drugs, including more than 1350 FDA-approved small molecule drugs, 123 FDA-approved biotech drugs, 71 nutraceuticals, and over 3243 experimental drugs. ChemDB includes nearly 5 million commercially available compounds. Numerous other small molecule databases exist and have been reviewed elsewhere (Wishart et al., 2006).

Selection of ligand and its selectivity

The discovery of new molecules for drug development involves a highly complex process due to the vast diversity of protein targets and the immense variability among potential lead candidates. The theoretical number of natural proteins is estimated at around 250,000, while the number of real organic compounds with a molecular weight less than 2000 Da exceeds 10^{60} (O'Donovan et al., 2001).

Drug target or Receptor-based techniques

Having access to the structure of a protein target is typically advantageous for identifying potential ligand interactions. Such approaches often involve molecular docking of ligands into the receptor binding site, which generates a predicted binding mode for each candidate compound (Lyne., 2002). However, accurately predicting the preferred binding poses of ligands within a protein's active site poses challenges.

Firstly, knowing the precise location and geometry of the binding site can be a limitation, as these aspects may not always be fully resolved by X-ray crystallography or NMR studies (Fernandez-Recio et al., 2004). Secondly, the method must effectively determine the correct orientation of a compound within the protein's active site. Incremental construction algorithms are potentially valuable in guiding the search for optimal binding poses, where fragments are initially positioned within the protein's binding site and then expanded to occupy the available space (Taylor et al., 2002).

Researchers have explored the use of conformational ensembles and genetic algorithms to predict how flexible ligands bind to macromolecular targets. A comparative assessment of eight docking programs (DOCK, FlexX, FRED, GLIDE, GOLD, SLIDE, SURFLEX, and QXP) evaluated their ability to accurately predict the X-ray pose of 100 small-molecule ligands. Results showed that these programs achieved successful docking for up to 63% of cases at a 1Å root-mean-square deviation (r.m.s.d.) threshold, and up to 90% success at a 2Å r.m.s.d. threshold.

Thirdly, the system must assess the relative suitability of how well a compound can bind to the receptor compared to others. An early effort in this direction was described by Platzer and colleagues, who calculated the relative standard free energy of binding substrates to α -chymotrypsin (Platzer et al., 1972). Computational limitations at the time precluded the inclusion of solvation or entropic effects in simulations. Subsequent methods have since been developed to handle these aspects (Kitchen et al., 2004). Physical-based potentials utilize atomic force fields to model binding free energies and may integrate techniques like free energy perturbation (FEP) and thermodynamic integration (TI) for improved accuracy. Tools that implement these physical-based scoring methods include Assisted Model Building and Energy Refinement (AMBER), Chemistry at HARvard Molecular Mechanics (CHARMM), and DOCK (Case et al., 2005, Ewing et al., 2001).

Ligand-based techniques

At the core of ligand-based screening procedures lies the Similarity Property Principle, which suggests that molecules with similar structures tend to exhibit similar properties. This principle underpins many efforts in ligand-based screening, where descriptors of molecular structure and properties are used to identify other molecules with comparable characteristics. More recently, mapping methods have been introduced to transform molecular features into different representations. For example, Godden et al. introduced Dynamic Mapping of Consensus positions (DMC) to map consensus positions of specific compound sets into binary-transformed chemical descriptor spaces, and Distance in Activity-Centered Chemical Space (DACCS) to accurately identify molecular similarity relationships in high-dimensional 'raw' chemical spaces (Godden et al., 2004, Godden et al., 2006).

Eckert et al. introduced an extension of DMC known as DynaMAD, which maps compounds to descriptor values dependent on activity class using unmodified descriptor value distributions. Molecular fingerprints based on 2D or 3D descriptors are also employed in virtual screening applications, such as MOLPRINT 2D (Bendel et al., 2004), Property Descriptor value Range-derived FingerPrint (PDR-FP) (Eckert et al., 2006), Rapid Overlay of Chemical Structures (ROCS) (Rush et al., 2005), shape fingerprints (Haigh et al., 2005), and 3D pharmacophore fingerprints. Recent advancements have also led to hybrid techniques integrating both structure-based and ligand-based methods.

ADME/Tox properties assessment

The pharmacokinetic or ADME properties of a pharmaceutical compound describe its disposition within the body (Tetko et al., 2006). To exert its pharmacological effects, a compound must traverse physiological barriers like the gastrointestinal, blood-brain, and microcirculatory barriers to reach the bloodstream. It then distributes to tissues and organs, undergoes enzymatic degradation, and is ultimately eliminated through excretion. Genetic variability in drug-metabolizing enzymes can lead to metabolic activation of certain compounds, potentially causing adverse reactions or toxicity in humans (Gardiner et al., 2006). Therefore, the ADME/Tox characteristics of a compound directly influence its effectiveness and safety

The ability of a compound to permeate membranes depends on several factors, such as its size, aqueous solubility, ionizability (pKa), and lipophilicity (log P). Studies have shown that polar

surface area (PSA) is inversely related to lipid penetration capability (Palm et al., 1997). Compounds with a PSA value exceeding 140 \AA^2 are typically absorbed by less than 10% in humans, whereas those with PSA values under 60 \AA^2 tend to be completely absorbed. Lipinski et al. analyzed the physicochemical properties of 2245 drugs from the World Drug Index (WDI) and identified molecular weight $<500 \text{ g/mol}$, $\text{Clog P} < 5$, less than 5 hydrogen bond donors, and less than 10 hydrogen bond acceptors as predictors of poor absorption and permeation (Lipinski et al., 2000). These findings led to the formulation of the "rule of five" for drug-likeness. Subsequent researchers, including Ghose et al. 1999, and Oprea., 2000, extended and refined these rules (Ghose et al., 1999, Oprea et al., 2001).

Conclusion

Since the inception of discovery by design more than thirty years ago, there has been a remarkable proliferation in both the quantity and sophistication of resources and analytical tools. Computer-aided drug design (CADD) is now widely acknowledged as a viable complement to and alternative for high-throughput screening. The pursuit of novel molecular entities has prompted the development of high-quality datasets and design libraries that can be tailored for either maximizing molecular diversity or similarity. Meanwhile, advancements in molecular docking algorithms, coupled with enhancements in computational infrastructure, are facilitating substantial increases in screening efficiency. Fueled by increasingly robust technology, distributed computing is gaining traction in large-scale screening endeavors. Notable recent examples include the WISDOM project, funded by the European Union, which screened over 41 million malaria-relevant compounds in less than a month using 1700 computers across 15 countries (Ananthula et al., 2008), and the Chinese-funded Drug Discovery Grid (DDGrid) for anti-SARS and anti-diabetes research, boasting a calculation capacity exceeding 1 Tflops per second. These developments, alongside concerted efforts to refine physical models such as solubility and protein solvation, promise to fully unleash the potential of lead discovery by design for the first time.

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BIOREMEDIATION: PRINCIPLES AND APPLICATIONS IN ENVIRONMENTAL MANAGEMENT- A REVIEW

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1. Bioremediation

Bioremediation is defined as a process that utilizes living organisms, mainly microorganisms, green plants, and their enzymes, to remove, degrade, mineralize, transform, and detoxify the environmental pollutants and hazardous components of the environmental waste into innocuous or less toxic forms during the treatment of contaminated sites in order to return them to their original condition (Azubuiké et al., 2016). The bioremediation process has been used to reduce the concentration and toxicity of various chemical pollutants, such as pesticides, polyaromatic hydrocarbons, halogenated petroleum hydrocarbons, nitroaromatic compounds, metals, and industrial solvents. The field of bioremediation comprises basic research areas (cometabolism, biotransformation kinetics, biotreatment, and biogeochemical modeling) and field application research areas (biogeochemical assessment techniques, environmental attenuation, fate modeling, and cometabolic techniques) (Harekrushna and Kumar, 2012). The bioremediation process has been used successfully in large- and smallscale applications; Alaska oil-spill cleanup is one of the good examples of bioremediation application for the treatment of pollutants. Bioremediation techniques can be applied in the cleanup of contaminated groundwater, soil, lagoons, waste streams, and sludge. With the proper utilization of natural and modified microbes and their processes and appropriate engineering models or designs to provide a favorable growth environment, the bioremediation techniques can be successfully implanted in the contaminated field. The main objective of this report is to highlight the silent features of bioremediation and its principles, the various methods of bioremediation, that is, in situ and ex situ remediation categories of bioremediation technique, their advantages and limitations, their prospects, and the possible solution of bioremediation techniques.

1.1 Principles of bioremediation

In bioremediation, living organisms, such as microorganisms (bacteria, fungi, and algae) or plants, are used to degrade and detoxify the hazardous pollutants present in the environment and convert them into CO₂, H₂O, microbial biomass, and metabolites (by-products which are less toxic than the parent compound), as shown in Fig. 1. These microorganisms can be indigenous to that contaminated site or may be isolated and brought from outside to that contaminated site for bioremediation. Microorganisms degrade and transform these pollutants through their metabolic reactions and utilize them for their growth. Complete degradation of a pollutant requires the action of several microbes, therefore sometimes potential microbes can be added to the contaminated site for the effective degradation process and this process is

called bioaugmentation. The biodegradation process depends on favorable environment conditions, the pollutant type and solubility, and the bioavailability of the pollutant to the microbes, therefore the environmental conditions are controlled or manipulated to allow sufficient microbial growth and thus fast and effective biodegradation.



Figure 1 -Illustration of bioremediation principle.

1.1.1 Microorganisms used in bioremediation

Microbes inhabit varied environments such as thermal springs, desert, glaciers, saline lakes, and oceans. Microbes with degradation potential can be isolated from contaminated environments, such as heavy metal-polluted sites, landfills, petroleum-contaminated sites, from pesticides-contaminated sites due to agricultural activities, and wastewater treatment plant, for the degradation of variety of pollutants. Microbes use the hazardous pollutant as their energy and carbon source in either aerobic and anaerobic conditions, and thus via metabolic activity can degrade or convert the pollutant to less or nontoxic metabolites (Tiwari and Singh, 2014). Soil microbes and pollutants are not distributed uniformly in the soil, therefore the pollutant should be available or in contact with the microbes for the effective degradation of the pollutant and it can be done by the application of surfactants. Aerobic bacterial species such as *Mycobacterium*, *Alcaligenes*, *Sphingomonas*, and *Pseudomonas* are known for their aerobic degradation of hydrocarbons (alkanes and polycyclic aromatic hydrocarbons) and pesticides. Along with that, a few of the aerobic methylotrophs are also recognized for the degradation of dichloroethane and trichloroethylene (chlorinated aliphatics). Some of the anaerobic bacterial species are known for the degradation of PCBs, chloroform, and trichloroethylene (chlorinated solvent). Beside the bacterial species, a few of the fungal species, such as *Phanerochaete chrysosporium*, also have been reported to be effective in the remediation of a variety of toxic and persistent pollutants (Harekrushna and Kumar, 2012).

1.2 Types of bioremediations

The bioremediation process is broadly categorized into ex situ remediation and in situ bioremediation, based on the origin, transportation, and removal of pollutants from contaminated sites, as shown in Fig. 2.

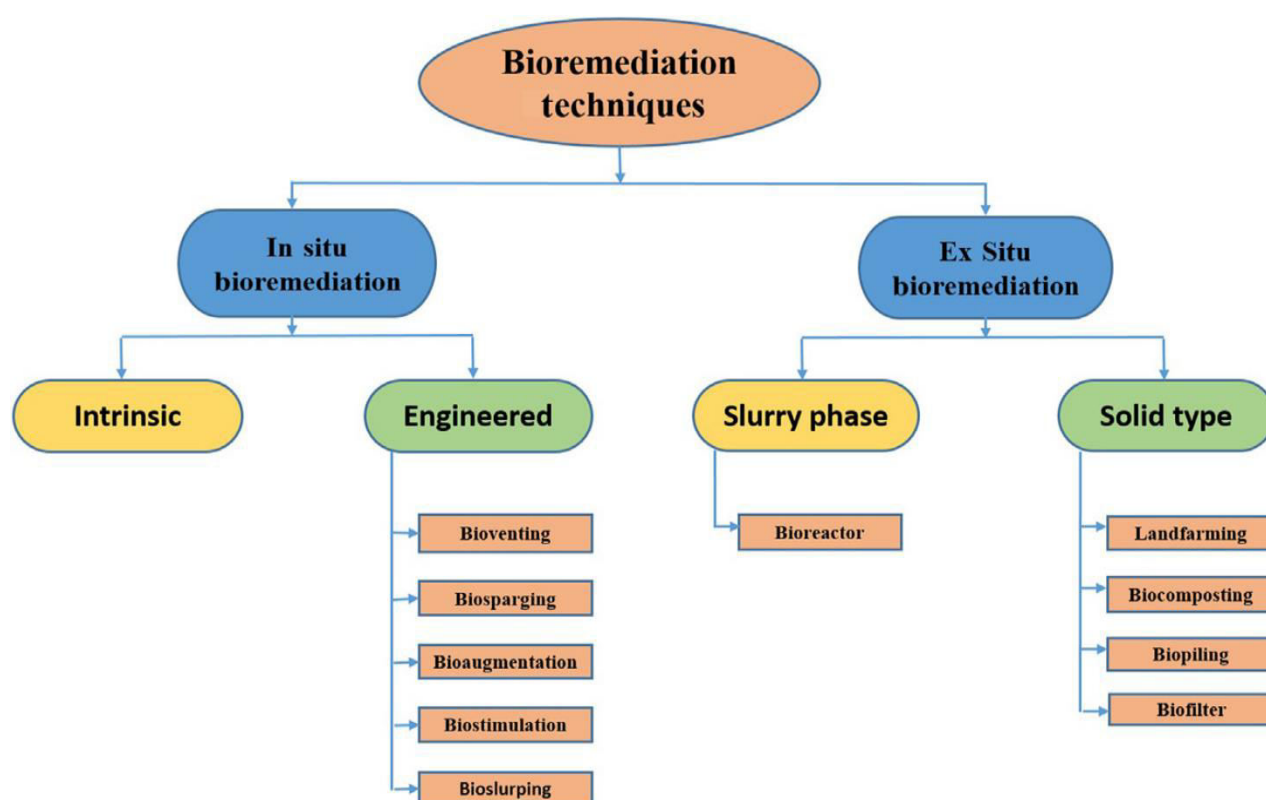


Figure 2. Types of bioremediation technique.

Table 1: The basic idea of the types of bioremediations, their mechanisms, advantages, and disadvantages

Bioremediation techniques	Types	Technique details	Advantages	Disadvantages
<i>In situ</i>	Bioventing	Air and nutrients are supplied through well	Low cost of operation	Environmental limitation
	Biosparging	Air is injected under pressure to enhance microbial activity	Relatively passive	Extended time period of treatment
	Bioaugmentation	Specialized and genetically modified microbes are supplied to target specific pollutants	Noninvasive	Difficulties in monitoring

	Biostimulation	Nutrients are supplied to optimize the growth and activity of the natural microbial population	Natural attenuation process	
<i>Ex situ</i>	Landfarming	Topsoil is tilled and water and nutrients are added to it	Low cost of operation	Space requirements
	Biocomposting	Decomposition of organic waste in the presence of microbes under high nutrient and aerobic condition	Rapid reaction rate	Need to control abiotic loss
	Biopiles	It is a combination of composting and landfarming	Low groundwater contamination	Bioavailability limitation
	Bioreactors	In a tank, microorganisms carry out the biological reaction	Provides a favorable environment for indigenous microbes . Better rate of degradation	Problem in mass transfer

1.3 Pollutants and types of bioremediation techniques involved

Table 2: Nature of pollutants with their sources, types of bioremediation techniques involved and types of microbial process

Nature of the pollutants	Pollutant examples	Major sources of the pollutant	Type of the bioremediation technique involved for removal	Type of microbial process
BTEX	Benzene, toluene, ethylbenzene, and xylene	Paint manufacture, gas working station, chemical manufacture, oil production and storage	Soil scrubbing, bioreactors, biopiling, bioventing, phytoremediation	Both aerobic and anaerobic
Pesticides	Carbofuran, atrazine, diazinon, parathion, 2,4-D, carbaryl, and glycofosphate	Agriculture, landfill sites, and pesticides manufacturing	Landfarming, soil scrubbing, bioreactors, bioslurping, and phytoremediation	Both aerobic and anaerobic
Polyaromatic hydrocarbons	Naphthalene, anthracene, phenanthrene,	Biodiesel and oil production and storage, engine	Landfarming, soil scrubbing, bioreactors, biopiling,	Aerobic

	fluorene, pyrene, and benzo(a) pyrene	works, coke plants, landfill sites, and gas work sites	bioventing, biosparging, bioslurping, and phytoremediation	
Heavy metals	Pb, Co, Cd, As, Ni, Hg, Zn, and Cr	Agriculture, landfill sites, mining area	Power station and electrical equipment manufacturing	Both aerobic and anaerobic
Chlorinated solvents	Trichloroethylene and perchloroethylene	Chemical manufacture, dry cleaners	Landfarming, phytoremediation	Anaerobic
Polychlorinated biphenyls	4-Chlorobiphenyl and 4,4-chlorobiphenyl	Power station and electrical equipment manufacturing	Soil scrubbing, bioreactors, landfarming	Anaerobic

1.4 Factors affecting bioremediation

The bioremediation process is affected by several factors which include scientific or environmental factors and nonscientific factors.

Table 3. Major factors affecting the bioremediation process.

Factors	Effects	References
Scientific/technical factors		
Microbial factor	Microbial growth until critical biomass is achieved Microbial population diversity Induction of enzymes Toxic metabolite formation Enrichment of efficient microbes Mutation and horizontal gene transfer	Boopathy (2000)
Environmental factor	Inhibition of favorable environment conditions (pH, temperature, moisture present, carbon, and energy sources, and Eh) Nutrient deficiency Preferential substrates deficiency	Boopathy et al. (2018)
Substrate	Chemical composition of contaminants Toxicity of contaminants Very low concentration of contaminants	Boopathy (2000)
Aerobic/ anaerobic process	Types of the microbial population at the contaminated site Oxidation/reduction potential Electron acceptors availability	Boopathy et al. (2018)
Growth substrate	The type of pollutants present	Blackburn and

	Concentration of pollutant An additional carbon source present Interaction between microbes	Hafker (2019)
Bioavailability of pollutants	Equilibrium sorption Irreversible sorption Pollutant interaction with humic materials	Manning et al. (2005)
Mass transfer limitations	Diffusion and solubility of oxygen Nutrients diffusion The solubility of pollutants in water	Boopathy (2000)
Nontechnical factors		
Regulatory factors	Controlling usage of the genetically modified organisms in bioremediation Market for bioremediation program Controlling the introduction of marketed products and human food and soil pathogens Controlling the process involved in the waste cleanup objective	Day (2013)
Research and technical factors	Diminishing of funds for research on bioremediation work Maintenance of instruments used in bioremediation techniques	Boopathy (2000)
Human resource factors	Lack of trained human resources Requirement for a multidisciplinary and integrated approach	Boopathy (2000)
Economic and liability factors	Scrutinization of bioremediation techniques rather than conventional techniques by regulatory agencies Imposition of tight regulation and performance standards on bioremediation techniques as compared with other remediation techniques	Day (2013)

1.5 Application of bioremediation in environmental management

- Bioremediation of organic pollutant.
- Bioremediation of metal
- Bioremediation of polycyclic aromatic hydrocarbons
- Bioremediation of rubber waste
- Bioremediation of agricultural waste

1.6 Biotechnology and bioremediation

The use of biotechnological approaches in bioremediation has several advantages over the physicochemical approaches as they are based on the natural activity of microbes and may achieve the complete degradation of pollutant. Some of the biotechnological tools, such as genetic engineering, enzyme tailoring and DNA shuffling, probe and biosensors development, and biosurfactant-mediated bioremediation, can be successfully applied to increase the slow biodegradation rate of microbe-mediated remediation of waste, and thus can improve the efficacy of bioremediation techniques in waste treatment.

2. Future aspects of the bioremediation technique

From the above comprehensive discussion of bioremediation, one can easily understand that ex situ and in situ bioremediation techniques are widely using for waste minimization and the cleanup of contaminated soil and water. Further advances in genomic, molecular, and biotechnological techniques may aid in the expansion of bioremediation approaches. In spite of individual bioremediation technique use, the application of various bioremediation techniques simultaneously can be a more efficient, promising, and cost-effective solution to the pollution problem. The application of biosurfactant-mediated bioremediation to clean hydrocarbons-contaminated sites in order to improve the solubilization and bioavailability of pollutants to the microbes is gaining interest nowadays. This can be possible due to the low cost of biosurfactant production using microbes supplemented with agroindustrial waste and the biodegradable nature. Furthermore, with the help of bioaugmentation and biostimulation techniques, the biodegradation potential of the indigenous microbes can be enhanced. On the other side, the emerging advanced molecular techniques (metagenomics, genomics, metabolomics, transcriptomics, and proteomics) have resolved the problems associated with microbial culturing and provide better knowledge of microbial diversity and their functions, and the metabolic and catabolic pathways present at a given polluted environmental site, which contribute to enhancing the mitigation of emerging pollutants and related problems. New emerging technology, such as microbial fuel cells inoculated with microbes (*Shewenwlla* sp. and *Pseudomonas* sp.), may be considered as potential candidates for the bioremediation of polyaromatic hydrocarbons (phenanthrene)-contaminated sites. Also the application of genetically engineered microbes in bioremediation is a promising and advanced technique which facilitates the effective degradation of a recalcitrant pollutant by utilizing the novel and efficient catabolic pathways, increasing the substrate domain for degradation process, and increasing the stability of the degradation activity of microbes. The improvement in nanoscience and technology has resulted in numerous nanomaterials which act as biocatalysts and improve the surface area and decrease the activation energy for the biodegradation process.

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RESEARCH COMMUNICATION

IN-SILICO INVESTIGATION TO IDENTIFY PHYTOCHEMICALS AS ANTICANCER AGENTS TARGETING EGFR

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Background:

Cancer is a major health concern and a leading cause of death worldwide, accounting for nearly 10 million deaths in 2020 (Siegel et. al., 2023). According to GLOBOCAN 2022, breast cancer is the most commonly diagnosed cancer followed by (2.26 million cases); lung (2.21 million cases); colon and rectum (1.93 million cases); prostate (1.41 million cases); skin (non-melanoma) (1.20 million cases); and stomach (1.09 million cases) (Siegel et. al., 2023).

Increasing report demonstrates the pivotal role of Epidermal Growth Factor Receptor (EGFR) signaling in various cancers. EGFR, a transmembrane protein, acts as a receptor for the epidermal growth factor family of extracellular protein ligands (Sigismund et.al., 2018). Mutations in the EGFR gene can lead to altered expression or activity, contributing to oncogenesis (Patel et. al., 2020). Therefore, targeted therapies against EGFR have been developed and approved for clinical use, however, resistance mutations in the EGFR gene often result in treatment failure (Patel et.al., 2020, Verma et.al., 2023, Abourehab et.al., 2021). Additionally, these EGFR targeted therapies exhibit adverse side effects. Hence, there is a pressing need to identify novel EGFR inhibitors for clinical application (Purawarga et.al., 2020)

Given the rich repertoire of bioactive compounds found in plants, we propose exploring plant-based natural compounds as potential EGFR inhibitors. Plants have long been recognized as valuable sources of molecules with anti-cancer properties (Zubair et.al., 2017). By tapping into this resource, we aim to uncover novel inhibitors that could offer improved efficacy and reduced side effects compared to existing therapies.

Materials and Methods:

Protein structure for EGFR and ligand (phytochemicals) structures were retrieved from PDB (Protein Database) and IMPPAT database, respectively. Docking was performed using Auto Dock vina-based PyRx software. To visualize the interactions between the protein and ligands, the BIOVIA Discovery Studio Visualizer was used. Furthermore, ADME (Absorption, Distribution, Metabolism, Excretion) analysis was also analyzed by SWISS ADME.

Result:

Based on insilico analysis and molecular modeling of EGFR (PDB ID: 4HJO) with 60 different phytochemicals identified from eight Indian medicinal plants. A molecular docking study revealed that several phytochemicals bind strongly to the EGFR, with strong binding affinities. Manogenin (-9.6), Withasomidienone (-9.7), Viscosalactone B (-9.5), and Cedeodarin (-9.5) have the highest binding affinity with drug-likeness properties (Table 1). These compounds

were also compared with known TKI (Tyrosine kinase inhibitor) erlotinib. Manogenin and Withasomidienone could be effective therapeutic agents for cancers possessing enhanced EGFR activity (Figure 1). The naturally occurring phytochemicals are considered less toxic or have less side effects in contrast to synthetic drugs. However, there are also challenges associated with screening phytochemicals as EGFR inhibitors. These include issues related to compound availability, standardization of extracts, potential off-target effects, and the need for rigorous preclinical and clinical testing to establish safety and efficacy.

Overall, while screening phytochemicals as EGFR inhibitors through molecular docking presents exciting opportunities for the discovery of novel therapeutics. It requires careful consideration of both, advantages and challenges associated with natural product-based drug discovery.

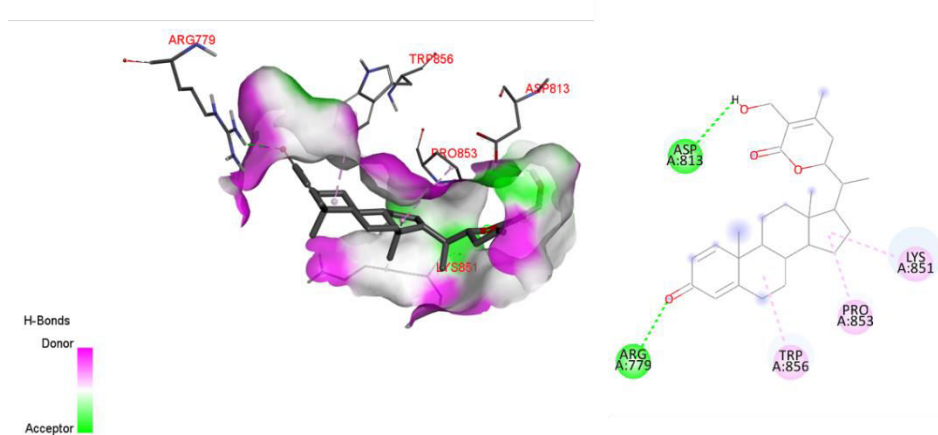


Figure 1: A docked complex and interaction plot between EGFR with Withasomidienone showing H-bond interaction.

Table 1: Swiss-ADME analysis of selected compounds showing Lipinski's rule violations and Boiled egg presentations.

Plants	Phytochemicals	IMPPAT ID	Binding Energy	Lipinski's rule violation	GI absorption	BBB permeation	Molecular weight (g/mol)
<i>Ziziphus nummularia</i>	Manogenin	IMPHY011402	-9.6	0	High	Yes	446.62
	Taxifolin	IMPHY011967	-9.0	0	High	No	304.25
<i>Curcuma longa</i>	Cyclocurcumin	IMPHY006549	-9.3	0	High	No	368.38
<i>Phyllanthus amarus</i>	Quercetin	IMPHY004619	-8.9	0	High	No	302.24
<i>Withania somnifera</i>	Withanone	IMPHY005214	-9.6	0	High	No	470.60
	Withasomidienone	IMPHY000630	-9.7	1	High	Yes	438.60
	Withanolide A	IMPHY000090	-9.0	0	High	No	470.60
	Viscosalactone B	IMPHY005904	-9.5	0	High	No	488.61
<i>Cedrus deodara</i>		IMPHY003355 Cedeodarin	-9.5	0	High	No	318.28
Erlotinib		CID: 176870	-8.3	0	High	Yes	393.40

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RESEARCH HIGHLIGHTS

ELUCIDATING THE ROLE OF NUCLEAR FACTOR-Y (NF-Y) TRANSCRIPTION FACTORS IN STRESS TOLERANCE USING GENOMICS AND BIOINFORMATICS APPROACH

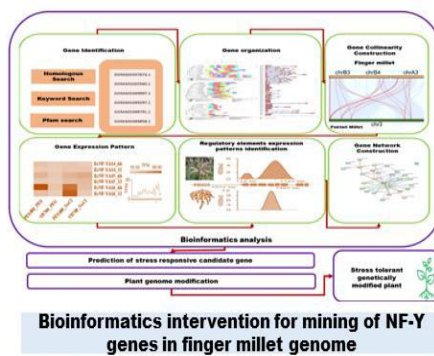
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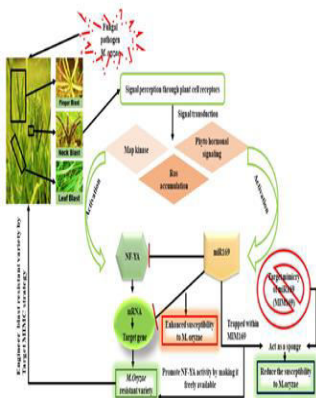
Finger millet



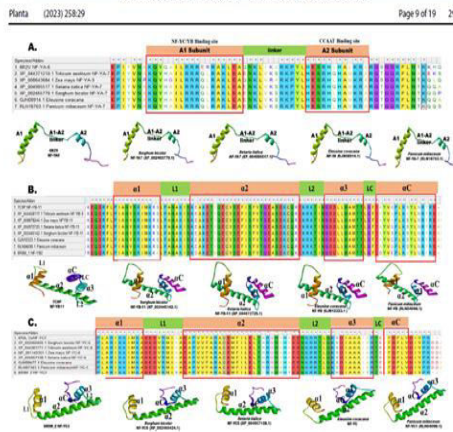
Bioinformatics intervention for mining of NF-Y genes in finger millet genome



Finger millet cultivation



Hypothetical mechanism proposed for developing finger millet resistance against Biotic stress



Homology modelling for prediction of conserved amino acid residue in millets

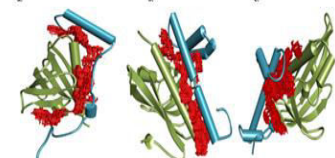
Table 5
Statistical report of best PYL-NF-Y dimeric complex through HADDOCK Server.

P-Y dimeric complex	Binding Energy (kcal/mol) by Prodigal server	RMSD (Å) from the overall lowest energy structure	Van der Waals energy	Electrostatics	Z-score
RPFL3-ANP100	-102	-43.9 ± 3.2	1.9 ± 3.7	-79.1 ± 6.7	-34.0 ± 37.1
RPFL3-ANP105	-125	-79.1 ± 11.5	1.9 ± 1.1	-88.4 ± 4.6	-104.1 ± 24.5
RPFL3-ANP102	-164	-88.4 ± 4.6	1.7 ± 1.3	-104.1 ± 5.4	-104.1 ± 24.5

Table 6
Dimeric production by HADDOCK server and interface analysis by using PyMol server.

PP Complex	Class	HADDOCK predicted dimeric residues	No. of interfaces residues	Interface area (Å ²)	No. of salt bridge	No. of hydrogen bond	No. of base stacked contact
RPFL3-ANP	A	Pro ¹⁰⁰ , Phe ¹⁰¹ , Leu ¹⁰² , Ser ¹⁰³ , Thr ¹⁰⁴ , Asp ¹⁰⁵ , Asp ¹⁰⁶ , Asp ¹⁰⁷ , Asp ¹⁰⁸ , Asp ¹⁰⁹ , Asp ¹¹⁰ , Asp ¹¹¹ , Asp ¹¹² , Asp ¹¹³ , Asp ¹¹⁴ , Asp ¹¹⁵ , Asp ¹¹⁶ , Asp ¹¹⁷ , Asp ¹¹⁸ , Asp ¹¹⁹ , Asp ¹²⁰ , Asp ¹²¹ , Asp ¹²² , Asp ¹²³ , Asp ¹²⁴ , Asp ¹²⁵ , Asp ¹²⁶ , Asp ¹²⁷ , Asp ¹²⁸ , Asp ¹²⁹ , Asp ¹³⁰ , Asp ¹³¹ , Asp ¹³² , Asp ¹³³ , Asp ¹³⁴ , Asp ¹³⁵ , Asp ¹³⁶ , Asp ¹³⁷ , Asp ¹³⁸ , Asp ¹³⁹ , Asp ¹⁴⁰ , Asp ¹⁴¹ , Asp ¹⁴² , Asp ¹⁴³ , Asp ¹⁴⁴ , Asp ¹⁴⁵ , Asp ¹⁴⁶ , Asp ¹⁴⁷ , Asp ¹⁴⁸ , Asp ¹⁴⁹ , Asp ¹⁵⁰ , Asp ¹⁵¹ , Asp ¹⁵² , Asp ¹⁵³ , Asp ¹⁵⁴ , Asp ¹⁵⁵ , Asp ¹⁵⁶ , Asp ¹⁵⁷ , Asp ¹⁵⁸ , Asp ¹⁵⁹ , Asp ¹⁶⁰ , Asp ¹⁶¹ , Asp ¹⁶² , Asp ¹⁶³ , Asp ¹⁶⁴ , Asp ¹⁶⁵ , Asp ¹⁶⁶ , Asp ¹⁶⁷ , Asp ¹⁶⁸ , Asp ¹⁶⁹ , Asp ¹⁷⁰ , Asp ¹⁷¹ , Asp ¹⁷² , Asp ¹⁷³ , Asp ¹⁷⁴ , Asp ¹⁷⁵ , Asp ¹⁷⁶ , Asp ¹⁷⁷ , Asp ¹⁷⁸ , Asp ¹⁷⁹ , Asp ¹⁸⁰ , Asp ¹⁸¹ , Asp ¹⁸² , Asp ¹⁸³ , Asp ¹⁸⁴ , Asp ¹⁸⁵ , Asp ¹⁸⁶ , Asp ¹⁸⁷ , Asp ¹⁸⁸ , Asp ¹⁸⁹ , Asp ¹⁹⁰ , Asp ¹⁹¹ , Asp ¹⁹² , Asp ¹⁹³ , Asp ¹⁹⁴ , Asp ¹⁹⁵ , Asp ¹⁹⁶ , Asp ¹⁹⁷ , Asp ¹⁹⁸ , Asp ¹⁹⁹ , Asp ²⁰⁰	22	1177	4	18	127
Y52	B	Asp ¹⁰¹ , Thr ¹⁰² , Ser ¹⁰³ , Thr ¹⁰⁴ , Asp ¹⁰⁵ , Asp ¹⁰⁶ , Asp ¹⁰⁷ , Asp ¹⁰⁸ , Asp ¹⁰⁹ , Asp ¹¹⁰ , Asp ¹¹¹ , Asp ¹¹² , Asp ¹¹³ , Asp ¹¹⁴ , Asp ¹¹⁵ , Asp ¹¹⁶ , Asp ¹¹⁷ , Asp ¹¹⁸ , Asp ¹¹⁹ , Asp ¹²⁰ , Asp ¹²¹ , Asp ¹²² , Asp ¹²³ , Asp ¹²⁴ , Asp ¹²⁵ , Asp ¹²⁶ , Asp ¹²⁷ , Asp ¹²⁸ , Asp ¹²⁹ , Asp ¹³⁰ , Asp ¹³¹ , Asp ¹³² , Asp ¹³³ , Asp ¹³⁴ , Asp ¹³⁵ , Asp ¹³⁶ , Asp ¹³⁷ , Asp ¹³⁸ , Asp ¹³⁹ , Asp ¹⁴⁰ , Asp ¹⁴¹ , Asp ¹⁴² , Asp ¹⁴³ , Asp ¹⁴⁴ , Asp ¹⁴⁵ , Asp ¹⁴⁶ , Asp ¹⁴⁷ , Asp ¹⁴⁸ , Asp ¹⁴⁹ , Asp ¹⁵⁰ , Asp ¹⁵¹ , Asp ¹⁵² , Asp ¹⁵³ , Asp ¹⁵⁴ , Asp ¹⁵⁵ , Asp ¹⁵⁶ , Asp ¹⁵⁷ , Asp ¹⁵⁸ , Asp ¹⁵⁹ , Asp ¹⁶⁰ , Asp ¹⁶¹ , Asp ¹⁶² , Asp ¹⁶³ , Asp ¹⁶⁴ , Asp ¹⁶⁵ , Asp ¹⁶⁶ , Asp ¹⁶⁷ , Asp ¹⁶⁸ , Asp ¹⁶⁹ , Asp ¹⁷⁰ , Asp ¹⁷¹ , Asp ¹⁷² , Asp ¹⁷³ , Asp ¹⁷⁴ , Asp ¹⁷⁵ , Asp ¹⁷⁶ , Asp ¹⁷⁷ , Asp ¹⁷⁸ , Asp ¹⁷⁹ , Asp ¹⁸⁰ , Asp ¹⁸¹ , Asp ¹⁸² , Asp ¹⁸³ , Asp ¹⁸⁴ , Asp ¹⁸⁵ , Asp ¹⁸⁶ , Asp ¹⁸⁷ , Asp ¹⁸⁸ , Asp ¹⁸⁹ , Asp ¹⁹⁰ , Asp ¹⁹¹ , Asp ¹⁹² , Asp ¹⁹³ , Asp ¹⁹⁴ , Asp ¹⁹⁵ , Asp ¹⁹⁶ , Asp ¹⁹⁷ , Asp ¹⁹⁸ , Asp ¹⁹⁹ , Asp ²⁰⁰	24	1099	3	14	142
RPFL3-ANP	B	Pro ¹⁰⁰ , Phe ¹⁰¹ , Leu ¹⁰² , Ser ¹⁰³ , Thr ¹⁰⁴ , Asp ¹⁰⁵ , Asp ¹⁰⁶ , Asp ¹⁰⁷ , Asp ¹⁰⁸ , Asp ¹⁰⁹ , Asp ¹¹⁰ , Asp ¹¹¹ , Asp ¹¹² , Asp ¹¹³ , Asp ¹¹⁴ , Asp ¹¹⁵ , Asp ¹¹⁶ , Asp ¹¹⁷ , Asp ¹¹⁸ , Asp ¹¹⁹ , Asp ¹²⁰ , Asp ¹²¹ , Asp ¹²² , Asp ¹²³ , Asp ¹²⁴ , Asp ¹²⁵ , Asp ¹²⁶ , Asp ¹²⁷ , Asp ¹²⁸ , Asp ¹²⁹ , Asp ¹³⁰ , Asp ¹³¹ , Asp ¹³² , Asp ¹³³ , Asp ¹³⁴ , Asp ¹³⁵ , Asp ¹³⁶ , Asp ¹³⁷ , Asp ¹³⁸ , Asp ¹³⁹ , Asp ¹⁴⁰ , Asp ¹⁴¹ , Asp ¹⁴² , Asp ¹⁴³ , Asp ¹⁴⁴ , Asp ¹⁴⁵ , Asp ¹⁴⁶ , Asp ¹⁴⁷ , Asp ¹⁴⁸ , Asp ¹⁴⁹ , Asp ¹⁵⁰ , Asp ¹⁵¹ , Asp ¹⁵² , Asp ¹⁵³ , Asp ¹⁵⁴ , Asp ¹⁵⁵ , Asp ¹⁵⁶ , Asp ¹⁵⁷ , Asp ¹⁵⁸ , Asp ¹⁵⁹ , Asp ¹⁶⁰ , Asp ¹⁶¹ , Asp ¹⁶² , Asp ¹⁶³ , Asp ¹⁶⁴ , Asp ¹⁶⁵ , Asp ¹⁶⁶ , Asp ¹⁶⁷ , Asp ¹⁶⁸ , Asp ¹⁶⁹ , Asp ¹⁷⁰ , Asp ¹⁷¹ , Asp ¹⁷² , Asp ¹⁷³ , Asp ¹⁷⁴ , Asp ¹⁷⁵ , Asp ¹⁷⁶ , Asp ¹⁷⁷ , Asp ¹⁷⁸ , Asp ¹⁷⁹ , Asp ¹⁸⁰ , Asp ¹⁸¹ , Asp ¹⁸² , Asp ¹⁸³ , Asp ¹⁸⁴ , Asp ¹⁸⁵ , Asp ¹⁸⁶ , Asp ¹⁸⁷ , Asp ¹⁸⁸ , Asp ¹⁸⁹ , Asp ¹⁹⁰ , Asp ¹⁹¹ , Asp ¹⁹² , Asp ¹⁹³ , Asp ¹⁹⁴ , Asp ¹⁹⁵ , Asp ¹⁹⁶ , Asp ¹⁹⁷ , Asp ¹⁹⁸ , Asp ¹⁹⁹ , Asp ²⁰⁰	26	1226	3	14	142
RPFL3-ANP	A	Pro ¹⁰⁰ , Phe ¹⁰¹ , Leu ¹⁰² , Ser ¹⁰³ , Thr ¹⁰⁴ , Asp ¹⁰⁵ , Asp ¹⁰⁶ , Asp ¹⁰⁷ , Asp ¹⁰⁸ , Asp ¹⁰⁹ , Asp ¹¹⁰ , Asp ¹¹¹ , Asp ¹¹² , Asp ¹¹³ , Asp ¹¹⁴ , Asp ¹¹⁵ , Asp ¹¹⁶ , Asp ¹¹⁷ , Asp ¹¹⁸ , Asp ¹¹⁹ , Asp ¹²⁰ , Asp ¹²¹ , Asp ¹²² , Asp ¹²³ , Asp ¹²⁴ , Asp ¹²⁵ , Asp ¹²⁶ , Asp ¹²⁷ , Asp ¹²⁸ , Asp ¹²⁹ , Asp ¹³⁰ , Asp ¹³¹ , Asp ¹³² , Asp ¹³³ , Asp ¹³⁴ , Asp ¹³⁵ , Asp ¹³⁶ , Asp ¹³⁷ , Asp ¹³⁸ , Asp ¹³⁹ , Asp ¹⁴⁰ , Asp ¹⁴¹ , Asp ¹⁴² , Asp ¹⁴³ , Asp ¹⁴⁴ , Asp ¹⁴⁵ , Asp ¹⁴⁶ , Asp ¹⁴⁷ , Asp ¹⁴⁸ , Asp ¹⁴⁹ , Asp ¹⁵⁰ , Asp ¹⁵¹ , Asp ¹⁵² , Asp ¹⁵³ , Asp ¹⁵⁴ , Asp ¹⁵⁵ , Asp ¹⁵⁶ , Asp ¹⁵⁷ , Asp ¹⁵⁸ , Asp ¹⁵⁹ , Asp ¹⁶⁰ , Asp ¹⁶¹ , Asp ¹⁶² , Asp ¹⁶³ , Asp ¹⁶⁴ , Asp ¹⁶⁵ , Asp ¹⁶⁶ , Asp ¹⁶⁷ , Asp ¹⁶⁸ , Asp ¹⁶⁹ , Asp ¹⁷⁰ , Asp ¹⁷¹ , Asp ¹⁷² , Asp ¹⁷³ , Asp ¹⁷⁴ , Asp ¹⁷⁵ , Asp ¹⁷⁶ , Asp ¹⁷⁷ , Asp ¹⁷⁸ , Asp ¹⁷⁹ , Asp ¹⁸⁰ , Asp ¹⁸¹ , Asp ¹⁸² , Asp ¹⁸³ , Asp ¹⁸⁴ , Asp ¹⁸⁵ , Asp ¹⁸⁶ , Asp ¹⁸⁷ , Asp ¹⁸⁸ , Asp ¹⁸⁹ , Asp ¹⁹⁰ , Asp ¹⁹¹ , Asp ¹⁹² , Asp ¹⁹³ , Asp ¹⁹⁴ , Asp ¹⁹⁵ , Asp ¹⁹⁶ , Asp ¹⁹⁷ , Asp ¹⁹⁸ , Asp ¹⁹⁹ , Asp ²⁰⁰	21	1111	6	7	105
Y52	B	Pro ¹⁰⁰ , Phe ¹⁰¹ , Leu ¹⁰² , Ser ¹⁰³ , Thr ¹⁰⁴ , Asp ¹⁰⁵ , Asp ¹⁰⁶ , Asp ¹⁰⁷ , Asp ¹⁰⁸ , Asp ¹⁰⁹ , Asp ¹¹⁰ , Asp ¹¹¹ , Asp ¹¹² , Asp ¹¹³ , Asp ¹¹⁴ , Asp ¹¹⁵ , Asp ¹¹⁶ , Asp ¹¹⁷ , Asp ¹¹⁸ , Asp ¹¹⁹ , Asp ¹²⁰ , Asp ¹²¹ , Asp ¹²² , Asp ¹²³ , Asp ¹²⁴ , Asp ¹²⁵ , Asp ¹²⁶ , Asp ¹²⁷ , Asp ¹²⁸ , Asp ¹²⁹ , Asp ¹³⁰ , Asp ¹³¹ , Asp ¹³² , Asp ¹³³ , Asp ¹³⁴ , Asp ¹³⁵ , Asp ¹³⁶ , Asp ¹³⁷ , Asp ¹³⁸ , Asp ¹³⁹ , Asp ¹⁴⁰ , Asp ¹⁴¹ , Asp ¹⁴² , Asp ¹⁴³ , Asp ¹⁴⁴ , Asp ¹⁴⁵ , Asp ¹⁴⁶ , Asp ¹⁴⁷ , Asp ¹⁴⁸ , Asp ¹⁴⁹ , Asp ¹⁵⁰ , Asp ¹⁵¹ , Asp ¹⁵² , Asp ¹⁵³ , Asp ¹⁵⁴ , Asp ¹⁵⁵ , Asp ¹⁵⁶ , Asp ¹⁵⁷ , Asp ¹⁵⁸ , Asp ¹⁵⁹ , Asp ¹⁶⁰ , Asp ¹⁶¹ , Asp ¹⁶² , Asp ¹⁶³ , Asp ¹⁶⁴ , Asp ¹⁶⁵ , Asp ¹⁶⁶ , Asp ¹⁶⁷ , Asp ¹⁶⁸ , Asp ¹⁶⁹ , Asp ¹⁷⁰ , Asp ¹⁷¹ , Asp ¹⁷² , Asp ¹⁷³ , Asp ¹⁷⁴ , Asp ¹⁷⁵ , Asp ¹⁷⁶ , Asp ¹⁷⁷ , Asp ¹⁷⁸ , Asp ¹⁷⁹ , Asp ¹⁸⁰ , Asp ¹⁸¹ , Asp ¹⁸² , Asp ¹⁸³ , Asp ¹⁸⁴ , Asp ¹⁸⁵ , Asp ¹⁸⁶ , Asp ¹⁸⁷ , Asp ¹⁸⁸ , Asp ¹⁸⁹ , Asp ¹⁹⁰ , Asp ¹⁹¹ , Asp ¹⁹² , Asp ¹⁹³ , Asp ¹⁹⁴ , Asp ¹⁹⁵ , Asp ¹⁹⁶ , Asp ¹⁹⁷ , Asp ¹⁹⁸ , Asp ¹⁹⁹ , Asp ²⁰⁰	22	1179	3	7	105

Note: Black bold highlighted residues also appeared as active site residue for PPY in CD search for PVL receptor protein of finger millet.



Finger millet NF-Y and Pyl interaction for abiotic stress signalling

Ensuring food and nutritional security for a population of approximately 10 billion by 2050 is the foremost important challenge, given that crop production is under changing climates with severity in facing several abiotic and biotic constraints with limited agricultural land. It was estimated that approximately 690 million people were hungry in 2019 and the number had sharply elevated to 720–811 million in 2020 under the obscurity of the COVID-19 pandemic (FAO 2021). It also projects that if the situation remains the same, it will be difficult to achieve zero hunger by 2030. Most of the underutilized crops, i.e., millets are sometimes referred to as “Orphan Crops,” or even “Lost Crops.” These crops are not actually lost but the term indicates their abundance by the developed countries and also their world production statistics indicate

significantly low volumes compared to the other more popular food crops. However, these neglected crops are important because of their contribution to biodiversity their immense nutritional value for eradicating hidden hunger, and their high tolerance potential against drought and salt, which is a major threat to the sustainable development of agriculture. Altogether, it is realized that millet crops are nutritionally superior as compared to regular crops which demonstrates their potential to attain United Nation's Sustainable Development Goal (SDG) 2, which is zero hunger. Wider applications of emerging genomics and biotechnological tools regarding preservation, genetic diversity analysis, identification and elimination of pests and diseases; and mining of novel genes to enhance the productivity and further improvement of millet crops may provide an avenue to enhance the genetic gains of yield and mainstreaming their cultivation.

Millets comprised of six major small-grained cereal crops, namely finger millet (*Eleusine coracana*), foxtail millet (*Setaria italica*), kodo millet (*Paspalum scrobiculatum*), proso millet (*Panicum miliaceum*), barnyard millet (*Echinochloa spp.*), and little millet (*Panicum sumatrense*), and all of them are known for their unique traits and nutritional values. The generic name *Eleusine* is derived from the Greek goddess of cereals, "*Eleusine*" while the common name finger millet indicates "finger-like" branching of the panicle. It is a highly productive crop with the richest source of calcium and polyphenolic compound, that can thrive under a variety of harsh environmental conditions and is also organic by default. It can be grown on low-fertility soils and is not dependent on the use of chemical fertilizers, hence, is a boon for the vast arid and semi-arid regions. Due to this plant's natural adaptation to adverse geographical conditions, it is also the source of many important genes and proteins. However very little research has been done around the world to identify these important genes, proteins, and transcription factors that govern the regulation of several genes associated with different pathways.

Keeping these important facts in mind, Prof. Dinesh Yadav, Professor, Department of Biotechnology and Director, Research and Development Cell, DDU Gorakhpur University, together with her Ph.D. scholar Ms. Varsha Rani in Gene Cloning and expression lab (GCEL) and collaborator from Dept. of Botany, DDU Gorakhpur University, Dr. Ramwant Gupta, Dr. D.C. Joshi from ICAR VPKAS Almora, and Dr. M Muthamilarasan, from the University of Hyderabad, Dr. Vinay Kumar Singh from BHU, substantially worked on Genome-wide study of Nuclear Factor -Y (NF-Y) Transcription Factor of Finger Millet (*Eleusine coracana*).

The Nuclear Factor Y (NF-Y) transcription factors are known for imparting abiotic stress tolerance in different plant species. However, there is no information on the role of this transcription factor family in naturally drought-tolerant crop finger millet (*Eleusine coracana L.*). Therefore, after 3 years of extensive research and interpretation of expression profiles against drought and salinity stress, we can provide valuable insights into specific and/or overlapping expression patterns of finger millet Nuclear Factor -Y (*EcNF-Y*) genes. For the first time, we reported 59 NF-Y genes in finger millet by Bioinformatics intervention. Then we performed its Expression profiling by qRT-PCR. The expression profiling of these genes was performed in two finger millet genotypes, PES400 and VR708, subjected to dehydration and

salt stresses. The expression analysis reveals that the six *NF-Y* genes of finger millet are associated with tolerance to both dehydration and salinity stress. In contrast, the transcript abundance of one gene of finger millet was also observed in the sensitive genotype VR708 for both dehydration and salinity stress. Therefore, this gene might be important for adaptation to salinity and dehydration stress in sensitive finger millet genotypes. Therefore, this gene could be considered as a susceptibility determinant, which can be edited to impart tolerance. This is the first report of *NF-Y* genes from the finger millet genome which, reveals potential candidates for enhancing dehydration and salt tolerance. Therefore, this research allows us to provide insight into some novel stress-responsive genes in finger millet, which may serve as possible candidates for engineering improved adaptability to crops of agronomic importance by the research community and helps us to attain United Nation's Sustainable Development Goal (SDG) 2, that is zero hunger. The output of the research was published in highly reputed international journals like PLANTA (SCIE/Q1) and Crop Design.

Finger millet grains are used as flour in the preparation of cakes, bread, and other pastry products, and malted and used as a beneficial food for infants. The germinated seeds are also nutritious and easily digestible. Finger millet grains contain a higher content of minerals, such as calcium (Ca), phosphorus (P), iron (Fe), and manganese (Mn), compared to other major cereals. Notably, it has 10-fold higher Ca in seeds compared to other major cereals and possesses higher therapeutic values for type II diabetic patients. So, our research group is also working on its nutraceutical properties to decode its important target toward diabetes which will be a boon to attaining Sustainable Development Goal (SDG) 3, i.e., good health and well-being.

Moreover, the U.P Council of Agricultural Research (UPCAR), Lucknow has recently sanctioned a project entitled "Improving photosynthetic electron transport and CO₂ flow in the leaves of finger millet to enhance yield" with a grant of 73.14 lakhs for a period of three years. The main objective of this project is to evaluate the structural and functional integrity of photosynthetic apparatus in leaves for improving electron transport and to improve the flow of carbon dioxide (CO₂) through the internal layers of the leaf, which allocate resources among organs to optimize whole-plant fitness and we are also working on the development of value-added products of finger millet. which will be one of the significant steps towards the promotion of such an underutilized minor crop and to meet (SDG) 2, which is zero hunger.

HARNESSING THE POTENTIAL OF INDIGENOUSLY ISOLATED FUNGAL STRAINS FROM THE SOIL OF GORAKHPUR FOR INDUSTRIALLY IMPORTANT ENZYME-PECTINASES

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Pectinases represent an important group of enzymes comprising mainly polygalacturonase, pectin lyases, pectin methyl esterases, and pectate lyases. With more than 25% share in industries, they are chiefly used in textile, beverage, food processing, and paper-pulp industries. Soil acts as a natural habitat for diverse microorganisms that have been extensively studied for the isolation of novel microbial strains to produce several industrially important enzymes. The study has been carried out in the Gene Cloning and Expression Lab, Department of Biotechnology by Ph.D. Scholar Ms. Shruti Dwivedi under the supervision of Prof. Dinesh Yadav. In the present study, the soil of different fruit orchards of the Gorakhpur region representing the North Eastern Terai region was collected for the isolation of indigenous fungus showing immense potential to produce an industrially important enzyme-pectinases. A total of 22 fungal strains were isolated and 13 strains were further selected for study based on their potential for pectinase production using solid-state and submerged state fermentation technology.

These strains were identified primarily in lab and was finally confirmed by molecular tools from MTCC (Microbial Type Culture Collection), Chandigarh and were deposited in the culture collection centre. These fungal strains represented four genera and 10 different species. Among them, two fungi are being reported for the very first time to produce pectinases from Indian soil. Pectinases produced by these fungal strains showed great variability in the pH optima, temperature optima, and tolerance towards metal ions, revealing the possibility for diverse applications. These fungal pectinases were studied for retting of hemp and Sunnhemp stem fibers and showed retting within 24 hours in comparison with untreated stems.

The fruit juice clarification of apple and malta using these fungal pectinases showed efficient clarification to eliminate chemical usage. These fungal pectinases were also used to make calcium-pectate gel sheets that can make sustainable food-packaging materials. carried out Based on the efficiency of these fungal pectinases three patent applications based on their application studies are also filed. These soil fungal pectinases can act as green agents for sustainable industrial use. The significant findings have been published in Scopus-indexed International Journal of Repute- World Journal of Microbiology and Biotechnology and Ecological Genetics and Genomics. A total of three patents have been filed recently reflecting the diverse application of pectinases produced by these fungal strains isolated from soil.

DEPARTMENTAL ACHIEVEMENTS/ACTIVITIES (Jan-June 2024)**PATENTS**

Sl. No.	Title of patent filed	Application no.	Date	Name of inventor(s)
1	A process of bioremediation and plant growth promotion using bacterium strain having resistance to arsenic	202411028451	06/04/2024	Ms. Priyanka Bharti Prof. Sarad Kumar Mishra
2	A method of enhanced bio-retting of natural fibers using pectinases	202411031591	20/04/2024	Ms. Shruti Dwivedi Prof. Dinesh Yadav
3	An enhanced method of retting and clarification of fruit juice using pectinase from an indigenous soil fungi	202411031592	20/04/2024	Ms. Shruti Dwivedi Prof. Dinesh Yadav
4	An enzyme cocktail and an enzyme cocktail based deinking method for tinted sheets	202411031593	20/04/2024	Dr. Aiman Tanveer Supriya Gupta Prof. Dinesh Yadav
5	A multi-enzyme cocktail mediated preparation of handmade seed paper using agricultural waste	202411033369	26/04/2024	Dr. Aiman Tanveer Supriya Gupta Prof. Dinesh Yadav
6	A method for calcium pectate gel sheets formation using pectinase	202411033370	26/04/2024	Ms. Shruti Dwivedi Prof. Dinesh Yadav
7	Detection of begomovirus (plant virus) by using a silicon wafer	202411034404	30/04/2024	Prof. Rajarshi Kumar Gaur Mr. Rakesh Kumar Verma
8	A method of isolating rhizospheric bacterial strains	202411039115	18/05/2024	Prof. Rajarshi Kumar Gaur Neetu Singh Yadav
9	Multiple enzyme production by aspergillus flavus isolated from enrichment culture using vegetable waste	202411039116	18/05/2024	Dr. Aiman Tanveer Supriya Gupta Prof. Dinesh Yadav
10	A radial chromatographic cum molecule fractionator that can be fitted on rotor	202411039803	22/05/2024	Prof. Rajarshi Kumar Gaur Sandeep Mishra
11	A method of production of pectinase using co-culture based solid-state fermentation for fruit juice clarification	202411043742	06/06/2024	Ms. Shruti Dwivedi Km Arti Prof. Dinesh Yadav
12	A Process to Formulate Syrup from Indigenous Plant Species Fruit Pods Post Ripening	202411046287	14/06/2024	Dr. Poornima Saraswat Prof. Rajarshi Kumar Gaur

PUBLICATIONS**RESEARCH/REVIEW PAPERS**

1. *In-silico* prediction and validation of Carica papaya protein domains interaction with the Papaya leaf curl virus and associated betasatellite encoded protein. Aarshi Srivastava, Vineeta Pandey, Avinash Marwal, Akhtar Ali, R. K. Gaur. (2024) *Discover Applied Sciences*, 6:287 | <https://doi.org/10.1007/s42452-024-05961-8>
2. *In silico* identification of papaya genome-encoded microRNAs to target begomovirus genes in papaya leaf curl disease Aarshi Srivastava, Vineeta Pandey, Nupur Singh, Avinash Marwal, MS Shahid and RK Gaur (2024) *Front. Microbiol.* 15:1340275. doi: 10.3389/fmicb.2024.1340275
3. Molecular characterization of a bipartite begomovirus associated with leaf crinkle and curling symptoms of *Duranta erecta* in India. Anurag Sahu, Vineeta Pandey, Aarshi Srivastava. *et al.* (2024) *Indian Phytopathology* 77, 191–201. <https://doi.org/10.1007/s42360-024-00718-0>
4. CRISPR/Cas9 Protection System for Chilli Leaf Curl Virus. Rakesh Kumar Verma, Megha Mishra, Avinash Marwal, Ali Akhtar³, Nikolay Manchev Petrov, R. K. Gaur (2024) *Acta Microbiologica Bulgarica* Volume 40 / 1.
5. Biochemical characterization of bacteria isolated from Rhizosphere soils of sugarcane grown in Uttar Pradesh Yadav N.S., Issar Sakshi and Gaur R.K. (2024). *Res. J. Biotech.*; Vol. 19(3); 70-75; doi: <https://doi.org/10.25303/1903rjbt070075>;
6. Recycling of printed Xerographic paper using *Aspergillus assiutensis* enzyme cocktail: an integrated approach to sustainable development. Tanveer, A., Gupta, S., Dwivedi, S. *et al.* (2024). *Environ Sci Pollut Res* <https://doi.org/10.1007/s11356-024-33780-2>
7. Expression profiling of Nuclear Factor-Y (NF-Y) transcription factors during dehydration and salt stress in finger millet reveals potential candidate genes for multiple stress tolerance. Rani, V., Rana, S., Muthamilarasan, M. *et al.* (2024). *Planta* 259, 136 <https://doi.org/10.1007/s00425-024-04417-y>
8. Molecular docking insights into nuclear factor Y (NF-Y) transcription factor and pyrabactin resistance 1 (PYL) receptor proteins reveal abiotic stress regulation in finger millet, Varsha Rani, Vinay Kumar Singh, D.C. Joshi, Rajesh Singh, Dinesh Yadav (2024) *Crop Design*, Volume 3, Issue 1,100051, ISSN 2772-8994,
9. Exploring the correlation between environmental pesticide exposure and anti-oxidant level in recently diagnosed cancer patients A. Ojha, P. Sahani, S. Shekhar, S.K. Mishra (2024) *Journal of Environmental Biology*; Volume 45, Number 2, pp 139-144.

ABSTRACTS

1. Study on Mercury Exposure and Different Approaches for the Management of Mercury Toxicity” PK Maddheshiya, P Bharti, SK Mishra, K Gupta (2024). Proceedings (MDPI), 3rd International Conference on Biomolecules, 103, 29, 202 (Abstract)
2. Molecular Docking Studies of Cell Wall Degrading Enzymes of *Fusarium Graminearum* and Bioactive Compounds of *Trichoderma* Species, Kanchan Yadav and Dinesh Yadav (2024), International Conference on Bio-Technological Interventions for Health, Agriculture and Circular Economy organized by Department of Biotechnology, Motilal Nehru Institute of Technology, Allahabad, Prayagraj (Abstract)

3. Fungal Pectinases mediated retting of *Sesbania aculeata* for extraction of sustainable natural fibers. Shruti Dwivedi, Ankur Singh and Dinesh Yadav (2024) Biosangam-2024; 6th International Conference on Bio-Technological Intervention for Health, Agriculture and Circular Economy, Prayagraj, February 23-25. (Abstract)
4. Bioinformatics intervention for the identification of novel therapeutic candidates for type II diabetes in Finger millet. Varsha Rani, Mukesh K Singh and Dinesh Yadav (2024) Biosangam-2024; 6th International Conference on Bio-Technological Intervention for Health, Agriculture and Circular Economy, Prayagraj, February 23-25. (Abstract)

Book Chapter

1. Genetic Diversity Assessment in Cereal Crops. V. Rani, M.K. Yadav, R. Singh, D. Yadav (2024). In: Al-Khayri, J.M., Jain, S.M., Penna, S. (eds) Sustainable Utilization and Conservation of Plant Genetic Diversity. Sustainable Development and Biodiversity, vol 35. Springer, Singapore. https://doi.org/10.1007/978-981-99-5245-8_11
2. The Intervention of Microbial Enzymes in Wastewater Management. Kanchan Yadav, Shruti Dwivedi, Supriya Gupta, Aiman Tanveer, Dinesh Yadav (2024). In: Vineet Kumar, Sunil Kumar, Pradeep Verma, Sartaj Ahmad Bhat (eds) Microbial Nexus for Sustainable Wastewater Treatment. Pages 19. CRC Press. <http://dx.doi.org/10.1201/9781003441069-8>

Edited Book

1. Pepper Virome Molecular Biology, Diagnostics and Management Editors: Akhtar Ali, R.K. Gaur April 25, 2024 ISBN: 9780443155765. Academic Press. <https://doi.org/10.1016/C2022-0-01404-5>
2. Molecular Dynamics of Plant Stress and its Management. Editors: Muhammad Shahid, Rajarshi Gaur. 26 June 2024 ISBN 978-981-97-1698-2. Springer Nature Singapore Pte Ltd. <https://doi.org/10.1007/978-981-97-1699-9>

Lecture Delivered/Participation in conferences/workshops by Faculty Members

1. Prof. Dinesh Yadav delivered a talk entitled “*Intellectual Property Rights and its Relevance: An Overview*” in the Faculty Induction Program (06/01/24 to 04/02/24) organized by UGC-Malaviya Mission Teacher Training Centre, DDU Gorakhpur University on 18th Jan. 2024.
2. Prof. Dinesh Yadav delivered an invited talk entitled “*Fungal Pectinases: A Recent Insights into Genomics and Bioinformatics Driven Research*” at the International Conference on Fungal Biology and Plant-Microbe Interactions (ICFBPMI)-2024” (Feb 16-18, 2024) organized by Department of Botany, BHU, Varanasi on 16th Feb. 2024.
3. Prof. Dinesh Yadav delivered an invited talk entitled “*Investigating Diverse Roles of Nuclear Factor-Y (NF-Y) Transcription Factors in Finger Millet: A Genomics and Bioinformatics Approach*” at International conference on Bio-Technological Interventions for Health, Agriculture and Circular Economy (BIOSANGAM-2024) organized by Department of Biotechnology, Motilal Nehru Institute of Technology, Allahabad, Prayagraj (23-25th Feb. 2024) on 24th Feb. 2024.

4. Prof. Dinesh Yadav delivered a talk entitled “*Genomics and Bioinformatics Interventions in Microbial Enzyme Research: An Overview*” in the Department of Microbiology, Dr. R. M L Awadh University, Ayodhya on National Science Day on 28th Feb. 2024.
5. Prof. Rajarshi Kumar Gaur delivered an invited talk entitled “*Technology Use and its Integration in NEP 2020*” in a Faculty Development Program (FDP) organized by UGC-Malaviya Mission Teacher Training Centre, DDU Gorakhpur University on 5th March 2024.
6. Prof. Sarad Kumar Mishra gave a Talk on “*Cyber Security*” to NSS students on 09.03.2024 at DDU Gorakhpur University.
7. Prof. Sarad Kumar Mishra gave a Talk on “*Role of Biotechnology in water conservation*” in a workshop on “Water Conservation” organized at DDU Gorakhpur University on 12.03.2024 by YPA, Gorakhpur.
8. Prof. Sarad Kumar Mishra gave a Talk on “*Relevance of Jagadguru Shankaracharya*” on 18.03,2024 organized at DDU Gorakhpur University sponsored by Bharatiya Rajbhasha Samiti, Ministry of Education, Govt. of India.
9. Prof. Sarad Kumar Mishra delivered a special lecture on “*Nanobiotechnology and its Scope*” on 20.04.2024 at DAV P.G. College, Gorakhpur.
10. Prof. Sarad Kumar Mishra gave a talk on “*Personality Development*” on 21.03.2024 in Government P.G. College, Kushinagar.
11. Prof. Rajarshi Kumar Gaur delivered an invited talk entitled “*Advancement in Plant Virus Characterization*” in a Seminar organized by the Botanical Society, Department of Botany, Mahatma Gandhi (PG) College, Gorakhpur on 14th May 2024.
12. Dr. Gaurav Singh participated in Six Weeks International Online Faculty Development Programme on "BIOANALYTICAL TECHNIQUES organized by the Department of Microbiology, Sacred Heart College (Autonomous), Tirupattur, Tamil Nadu, India in association with Biotechnology Society of Nepal (BSN) and Laboratory of Chemical and Biological Analysis (LAQB), Western Rio Janeiro State University (UEZO), Rio de Janeiro, Brazil from 26th April to 25th May 2024.
13. Dr. Gaurav Singh delivered a lecture as a Keynote Speaker in the One Day National Webinar on the Importance and Possibilities of Technology in Education, on 30 May 2024.

Conferences/workshops/seminars attended by students

1. Kanchan Yadav Ph.D. Scholar participated and presented a paper entitled “*Molecular Docking Studies of Cell Wall Degrading Enzymes of Fusarium Graminearum and Bioactive Compounds of Trichoderma Species*” at International conference on Bio-Technological Interventions for Health, Agriculture and Circular Economy organized by Department of Biotechnology, Motilal Nehru Institute of Technology, Allahabad, Prayagraj on 23rd to 25th February 2024 (**Oral Presentation**).

2. Kanchan Yadav, participated in the 6th NEP 2020 Orientation and Sensitization Programme under the Malaviya Mission Teacher Training Programme of University Grants Commission (UGC) organized by UGC-Malaviya Mission Teacher Training Centre, DDU Gorakhpur University, Gorakhpur from 27.5.2024 to 05.06.2024.
3. Supriya Gupta, participated in the 6th NEP 2020 Orientation and Sensitization Programme under the Malaviya Mission Teacher Training Programme of University Grants Commission (UGC) organized by UGC-Malaviya Mission Teacher Training Centre, DDU Gorakhpur University, Gorakhpur from 27.5.2024 to 05.06.2024.
4. Shruti Dwivedi, Ph.D. Scholar participated and presented a paper entitled “*Fungal Pectinases mediated retting of Sesbania aculeata for extraction of sustainable natural fibers*” at the International Conference on Bio-Technological Interventions for Health, Agriculture and Circular Economy organized by the Department of Biotechnology, Motilal Nehru Institute of Technology, Allahabad, Prayagraj on 23rd to 25th February 2024 (**Oral Presentation**).

PhD Awarded /PhD Submission

Sl.No.	Name of Students	Thesis Title	Supervisor/Co-Supervisor	Date of Award
1	Vineeta Pandey	Molecular Computing of Begomovirus Population Associated with Chilli Leaf Curl Disease Across India	Prof. Rajarshi K Gaur	15/04/2024
2	Aarshi Srivastava	Genomics Of Leaf Curl Disease (LCuD) Associated with <i>Carica Papaya</i> Across India	Prof. Rajarshi K Gaur	27/06/2024

Sl.No.	Name of Students	Thesis Title	Supervisor/Co-Supervisor	Date of Submission
3	Sonali Jaiswal	Isolation of endophytes from <i>Argemone mexicana</i> L., <i>Calotropis procera</i> A. and <i>Lycopersicon esculentum</i> M, for the study of their potential in plant growth promotion and bioactive compound production	Prof. Sarad K Mishra	26/01/2024
4	Supriya Gupta	Isolation and characterization of indigenously isolated microbial strains for enzymatic intervention in paper and pulp industries	Prof. Dinesh Yadav	15/06/2024
5	Shruti Dwivedi	Mining of soil fungal wealth for pectinolytic activity and elucidating its potential application	Prof. Dinesh Yadav	15/06/2024
6	Kanchan Yadav	Genome-wide identification, structural and functional characterization of pectin lyase genes of <i>Fusarium</i> species	Prof. Dinesh Yadav	15/06/2024

7	Varsha Rani	Genome-wide study of Nuclear Factor -Y (NF-Y) Transcription Factor of Finger Millet (<i>Eleusine coracana</i>)	Prof. Dinesh Yadav/ Prof. Rajesh Singh	15/06/2024
8	Neetu Singh Yadav	Isolation and characterization of soil bacteria collected from different regions of sugarcane growing field.	Prof. Rajarshi K Gaur	10/07/2024

CONFERENCES/SYMPOSIUM/WORKSHOP/ GUEST LECTURES ORGANIZED

1. Prof. Rajesh Kumar Yadav, Department of Chemistry & Environmental Science, Madan Mohan Malaviya University of Technology, Gorakhpur delivered an invited talk entitled “*A Photocatalyst/Enzyme couple that uses solar energy in the reduction of CO₂ and synthesis of fine chemicals via artificial photosynthesis*” on the occasion of “**Foundation Day Celebration**” of the Department of Biotechnology on 31st Jan. 2024.
2. Dr. Hirawati Devel, Scientist-E, Head, Molecular Biology, ICMR- Regional Medical Research Centre (RMRC), Gorakhpur delivered an invited talk entitled “*Global emerging and Re-emerging infectious diseases*” on the occasion of “**Foundation Day Celebration**” of the Department of Biotechnology on 31st Jan. 2024
3. Research and Development Cell, Deen Dayal Upadhyaya Gorakhpur University organized a One-day Awareness Workshop on “**Intellectual Property Rights (IPR)**” sponsored by the Council of Science and Technology, Uttar Pradesh on 2nd March 2024 in the Department of Biotechnology.
4. Dr. Sripathi Rao Kulkarni, Principal Scientist and Coordinator (IPRs and International Relations) at CSIR- Central Drug Research Institute (CDRI) Lucknow delivered an invited lecture entitled “**Protection and Management of IPR**” on 2nd March 2024.
5. Dr. Shaleena Raizada, MD and CEO of Sanshadow Consultants Pvt. Ltd, New Delhi delivered an invited lecture entitled “**Introduction to Intellectual Property-Value of IP for teachers and students**” on 2nd March 2024.
6. Prof. R.C. Chaudhary, Padma Shree and Chairman, PRDF, Gorakhpur Delhi delivered an invited lecture entitled “**Geographical Indication and its Significance in Uttar Pradesh**” on 2nd March 2024.
7. Dr. Girijesh Kumar Patel, Assistant Professor & Ramalingaswami Fellow, Department of Biotechnology, MNNIT, Allahabad (Prayagraj) delivered a special lecture entitled “**Role of TBX2 in prostate cancer advancements and therapy resistance**” on 28th March 2024.
8. Dr. Badri Nath Dubey, Staff Scientist/ Project Leader, Centre For Structural Systems Biology, German Electron Synchrotron, Hamburg, Germany delivered a special lecture entitled “**Education, Research and Collaboration in Germany**” on 29th March 2024.
9. The Department of Biotechnology organized a Value-Added Course (30hrs) on “**Biotechnology and its role in sustainable development**” from 15-30 June 2024 (online mode). Prof. Sunil Kumar Khare, Director, IISER, Kolkata was the chief guest for the inaugural function on 15th June 2024 and Prof. Nagendra K Singh, President, The Genomics Foundation and J.C. Bose National Fellow, ICAR-National Institute for Plant Biotechnology, IARI, New Delhi was the chief guest for valedictory function on 30th June 2024.

10. Dr. Subash Chandra Gupta, Professor & Head, Department of Biochemistry & Associate Dean (Research), AIIMS, Guwahati, Assam delivered an invited talk entitled “***Applications of Biotechnology in Cancer Management***” on 16th June 2024 (Online)
11. Dr. Dinesh Chandra Joshi, Senior Scientist (Plant Breeding), Division of Crop Improvement, ICAR-Vivekananda Institute of Hill Agriculture (Vivekananda Parvatiya Krishi Anusandhan Sansthan), Almora, Uttarakhand delivered an invited talk entitled “***Trait Mining and Genetic Enhancement of Small Millets and Potential Crops- Modern Prospects of The Ancient Grains***” on 17th June 2024 (Online)
12. Dr. Pradeep Kumar, Associate Professor, Department of Botany, University of Lucknow, Lucknow delivered an invited talk entitled “***Microbial Bioformulations for Sustainable Agriculture***” on 18th June 2024 (Online)
13. Dr. Amresh Kumar Singh, Head, Department of Microbiology, BRD Medical College, Gorakhpur delivered an invited talk entitled “***Role of Biotechnology in Human Health***” on 19th June 2024 (Online)
14. Dr. Swati Tripathi, Associate Professor, Amity University, Noida delivered an invited talk entitled “***Unlocking the Potential: The Role of Plant Growth-Promoting Rhizobacteria (PGPR) In Sustainable Agriculture and Environmental Conservation***” on 20th June 2024 (Online)
15. Dr. Ramwant Gupta, Associate Professor, Department of Botany, DDU Gorakhpur University, Gorakhpur delivered an invited talk entitled “***Remodelling Photosynthetic Apparatus in Plants: An Innovative Approach to Food Security***” on 21st June 2024. (Online)
16. Dr. Naveen Chandra Bisht, Staff Scientist VI, National Institute of Plant Genome Research (NIPGR), New Delhi delivered an invited talk entitled “***Genomics and Gene Editing for Engineering Glucosinolates in Indian Oilseed Mustard***” on 22nd June 2024. (Online)
17. Dr. Ashutosh Mani, Associate Professor, Department of Biotechnology, Motilal Nehru National Institute of Technology, Allahabad delivered an invited talk entitled “***Application of Bioinformatics in Post-Genomic Era***” on 22nd June 2024 (Online)
18. Dr. Vivek Kumar Morya, Research Professor, Department of Orthopedic Surgery, Dongtan Sacred Heart Hospital, School of Medicine, Hallym University, South Korea delivered an invited talk entitled “***Beyond Boundaries: The Future of Regenerative Medicine-Exploring Cell-Based and Cell-Free Innovations***” on 23rd June 2024 (Online)
19. Dr. Rajeev Singh, Scientist, ICMR-RMRC, Gorakhpur, delivered an invited talk entitled “***Point-of-Care Diagnostics in Achieving Sustainable Development Goals***” on 24th Jun2 2024 (Online)
20. Dr. Kapil Gupta, Assistant Professor, Department of Biotechnology, Siddharth University, Kapilvastu Siddharth Nagar delivered an invited talk entitled “***Biotech Crops: An Overview***” on 25th June 2024 (Online)

21. Dr. Gautam Anand, Post-Doctoral Fellow, Department of Plant Pathology and Weed Research, Agricultural Research Organization, Volcani Institute, Rishon LeZion, Israel delivered an invited talk entitled “ *Decoding The Role of Cytokinin in Fungal Biology*” on 26th June 2024 (Online)
22. Dr. Vivek Kumar Hada, Associate Professor, Department of Microbiology, AIIMS, Gorakhpur delivered an invited talk entitled “ *A Primer on Applications of Biotechnology In Medical Sciences*” on 27th June 2024 (Online)
23. Dr. Amit Kumar Srivastava Scientist, CSIR- Indian Institute of Chemical Biology (IICB), Kolkata delivered an invited talk entitled “ *CAR-T Cell Therapy: An Emerging Technology for Cancer Treatment*” on 28th June 2024 (Online)
24. Dr. Pramod Kumar Yadav, Associate Professor & Ramalingaswamy Fellow, Department of Life Sciences and Biotechnology, Chhatrapati Shahu Ji Maharaj University, Kanpur delivered an invited talk entitled “ *Understanding The Biomolecular Assembly by Using Cryoelectronic Microscopy*” on 29th June 2024 (Online)
25. Dr. Manish Kumar Tripathi, Post-Doctoral Scientist, Department of Biomedical Sciences, Cedars Sinai Medical Centre, Los Angeles, California, USA delivered an invited talk entitled “ *Tools And Techniques in Biotechnology*” on 30th June 2024 (Online)
26. Dr. Rupali Gupta, Post-Doctoral Fellow, Department of Plant Pathology and Weed Research, Agricultural Research Organization, Volcani Institute, Rishon LeZion, Israel delivered an invited talk entitled “ *Cytokinin Driven Microbiome Dynamics: Enhancing Plant Growth and Stress Adaptation*” on 30th June 2024 (Online)

INSTRUCTIONS TO AUTHORS

Biotech Innovators is a six-monthly magazine initiated by the Department of Biotechnology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur (Uttar Pradesh), with the first issue released in January 2024. The sole purpose of this magazine is to highlight the recent developments in Biotechnology through the contributions from the experts and summarize the significant achievements of the Department, at a regular interval of six months. To start with, the magazine has the following sections (i) Featured article, (ii) Review articles, (iii) Research Communications, (iv) Research highlights, and (v) Departmental Achievements.

All articles should be submitted to the Chief Editor, Biotech Innovators, Department of Biotechnology, Deen Dayal Upadhyaya Gorakhpur University, Gorakhpur (U.P) 273009. Some important guidelines for the submission include

1. **Featured articles:** relevant to state-of-the-art technology relevant to biotechnology. It will be invitation-based contributions and experts will be invited to contribute under this section. It is expected to have figures and Tables for easy understanding and there is no word limitation. Relevant references should be cited. Each issue will have one featured article.
2. **Review articles:** It will have a word limitation of not more than 5000 words and not more than 50 references. References will be as per according to **Harvard referencing style**. It is expected to have figures and tables. Figures and tables will be labeled as **“Figure. and Table”** Each issue will have a maximum of 5 review articles.
3. **Research Communications:** It will have a word limitation of around 3000 words with not more than 20 references (**Harvard referencing style**). The article should not have been communicated elsewhere and authors are requested to check the plagiarism before submission.
4. **Research highlights:** this will provide an insight into the research activities of the Department. It will be of 1-2 pages with few figures and will be supported by publications as references. The authenticity of this research highlights will be solely borne by the authors.
5. **Departmental Achievements:** This section is exclusively meant to highlight the achievements of the Department in terms of patents, publications, organizing conferences/symposiums/ guest lectures/workshops, etc.

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