TRANSLATING A LADDER FROM AI/ML, NOVEL BIOMARKERS AND EV'S FOR Personalized Medicine in Neurodegenerative Disease and Therapeutics

**A DISSERTATION** 

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF

MASTER OF TECHNOLOGY

INDUSTRIAL BIOTECHNOLOGY

SUBMITTED BY:

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(2K21/IBT/18)

UNDER THE SUPERVISION OF

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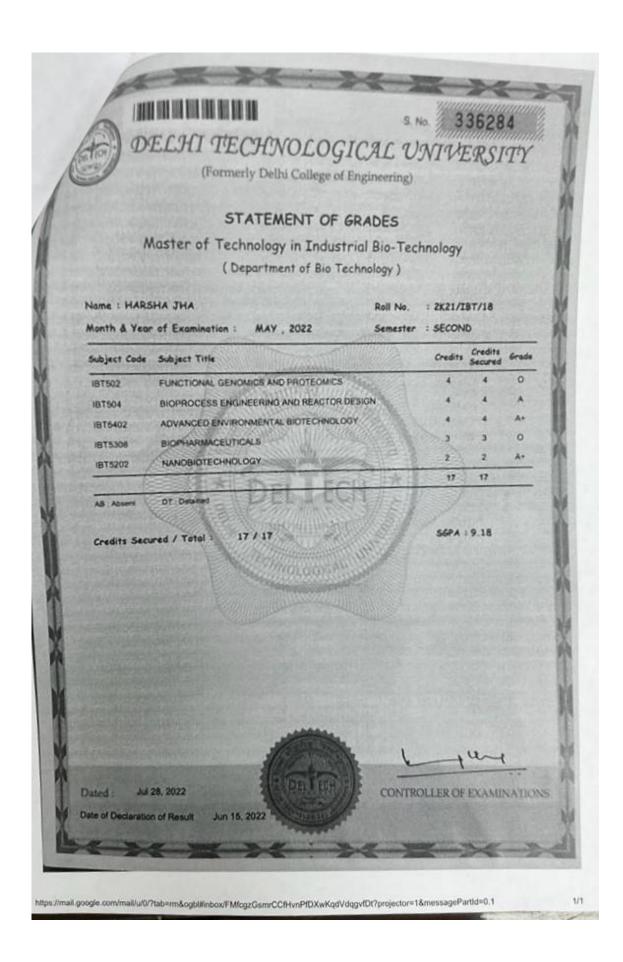
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#### CERTIFICATE

I HEREBY CERTIFY THAT THE PROJECT DISSERTATION TITLED "TRANSLATING A LADDER FROM AI/ML, NOVEL BIOMARKERS AND EV'S FOR PERSONALIZED MEDICINE IN NEURODEGENERATIVE DISEASE AND THERAPEUTICS' WHICH IS SUBMITTED BY HARSHA JHA, 2K21/IBT/18 DEPARTMENT OF BIOTECHNOLOGY, DELHI TECHNOLOGICAL UNIVERSITY, NEW DELHI IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF THE DEGREE OF MASTER OF TECHNOLOGY IS A RECORD OF THE PROJECT WORK CARRIED OUT BY THE STUDENTS UNDER MY SUPERVISION AND GUIDANCE. TO THE BEST OF MY KNOWLEDGE, THIS WORK HAS NOT BEEN SUBMITTED IN PART OR FULL FOR ANY DEGREE OR DIPLOMA TO THIS UNIVERSITY/INSTITUTE OR ELSEWHERE.

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#### **ABSTRACT**

Abstract— Diseases which are characterised by the progressive loss of neurons' structure or function, leading to deterioration in cognitive and motor function. A disease's presence or severity can be determined objectively by biomarkers, which are then used to monitor, diagnose, and track the development of a disease. There are several different categories of biomarkers that have been identified for neurodegenerative diseases, including genetic, epigenetic, protein, imaging, and behavioral biomarkers. These biomarkers can be utilised separately or in combination to assist the development of targeted therapeutics by providing a better knowledge of the underlying illness process. In this review, we discuss the various categories of biomarkers that have been identified for neurodegenerative diseases and their potential uses in the clinical setting. It is significantly being used in the area of neurodegenerative diseases and therapeutics. A kind of extracellular vesicles implicated in brain damage in a variety of ways; they spread inflammation throughout the brain. A barrier called the blood-brain barrier (BBB) mediates neuronal signal mediation, propagation, and neuroprotection.. This paper focuses on the evidence which is mounting that the functions of EV are linked to the neurological pathogenic illnesses of machinery aiding in the growth and spread of the diseaseIn this paper, we discuss the current state of AI applications in this area. We begin by providing an overview of neurodegenerative diseases and the challenges they present. We then describe the various ways in which AI is being used in the field, including drug discovery and development, diagnosis and prognosis, patient care, clinical trials, and basic research. Finally, we outline some of the key directions for future research in this area. We have also designed a sample program with the help of HTML, CSS and JAVA to design personalised medicine. . Overall, our analysis indicates that AI has the potential affect on NDD's and therapeutics, and could be a step towards the development of new and improved treatments for these conditions.

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#### HARSHA JHA

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## LIST OF ABBREVIATIONS

ABBREVIATION		EXPANSION
NDD	:	NEURODEGENERATIVE DISEASES
EV	:	EXTRACELLULAR VESICLES
AI	:	ARTIFICIAL INTELLIGENCE
ML	:	MACHINE LEARNING
AD	:	ALZHEIMER'S DISEASE
PD	:	PARKINSON'S DISEASE
ALS	:	AMYOTROPIC LATRAL SCLEROSIS.

#### **CHAPTER 1:INTRODUCTION**

#### **1.1 OVERVIEW**

Neurodegenerative diseases represent a group of chronic and progressive conditions that afflict the CNS, leading to the gradual deterioration of neurons and the subsequent impairment of cognitive, motor, and sensory functions. These debilitating disorders, (ALS), AD, PD, MS pose significant challenges to both patients and the medical community. Alzheimer's disease, memory loss, cognitive decline, and behavioural abnormalities are all symptoms of the most common neurodegenerative condition, which is characterised by the buildup of amyloid plaques and neurofibrillary tangles in the brain[.6] The insidious nature of Alzheimer's often leads to difficulties in daily functioning .Parkinson's disease results in the substantia nigra's dopamine-producing neurons degenerating, which produces tremors, rigidity, and bradykinesia as motor symptoms.[8] Non-motor symptoms including mental health issues and cognitive decline may also be present. Parkinson's disease has a considerable impact on motor function and coordination, which over time results in significant impairment. Specifically in the basal ganglia and cerebral cortex, Huntington's disease is an uncommon genetic condition marked by the gradual destruction of nerve cells. Its devastating consequences encompass movement abnormalities, cognitive decline, and psychiatric disturbances. Huntington's inheritance pattern means that children of affected individuals thus adding to the emotional burden on families.ALS, often known as Lou Gehrig's disease, loss of voluntary movement, and eventual paralysis.[9] ALS not only affects physical functioning but also impacts speech, swallowing, and respiratory muscles, leading to significant challenges in daily activities and communication. While each neurodegenerative disease presents distinct clinical features, common underlying mechanisms contribute to neuronal dysfunction and degeneration, including protein misfolding, mitochondrial dysfunction, oxidative stress, and inflammation. These complex processes intertwine, amplifying the damage and exacerbating the progression of these disorders.

Despite extensive research, effective cures for neurodegenerative diseases remain elusive. The major goals of current therapies are to reduce symptoms, halt the spread of the disease, and enhance patients' quality of life. However, ongoing scientific investigations into innovative therapeutic strategies, including gene therapies, immunotherapies, stem cell-based approaches, and neuroprotective agents, offer hope for future breakthroughs in combating these devastating diseases.

The pursuit of understanding these complex disorders continues to drive researchers worldwide, as they strive to unravel the intricate mechanisms underlying neurodegeneration, identify biomarkers for early detection, and develop targeted interventions that may ultimately lead to the prevention or even cure of these debilitating conditions. The diagnosis and management of neurodegenerative diseases can be challenging, as many of these conditions do not have specific or reliable diagnostic tests, and current treatments are largely palliative rather than curative. Biomarkers, or objective indicators of the presence or severity of a disease, have the potential to completely change how neurodegenerative illnesses are identified and treated.[10]

By providing a quantitative measure of disease progression and response to treatment, biomarkers can facilitate earlier diagnosis, guide therapeutic decision-making, and enable personalized medicine approaches. There are several different categories of biomarkers that have been identified for neurodegenerative diseases, including genetic, epigenetic, protein, imaging, and behavioral.that have been identified for neurodegenerative diseases and their potential uses in the clinical setting. [14]

#### **1.2 TYPES OF BIOMARKERS**

. Genetic biomarkers are indicators of disease that are based on variations in an individual's DNA sequence. These variations, known as genetic polymorphisms, can alter the expression or function of a gene, and may increase an individual's risk of developing a neurodegenerative disease. For example, genetic biomarkers have been identified for an increased risk of developing the disease.[15]

Epigenetic biomarkers, on the other hand, are indicators of disease that are based on modifications to an individual's DNA or the proteins with which it interacts, such as histones...

These changes may be associated with the underlying disease process, or may be a result of the disease. For example, brain atrophy and amyloid deposition can be visualized using imaging techniques and have been identified as imaging biomarkers for Alzheimer's disease.

Behavioral biomarkers are indicators of disease that are based on changes in an individual's behavior or cognitive function. These changes may be subtle and may not be immediately apparent, but can be detected using standardized assessments. For example, changes in memory and executive function have been identified .[4]

In conclusion, there are several different categories of biomarkers that have been identified for

neurodegenerative diseases, including genetic, epigenetic, protein, imaging, and behavioral biomarkers. Even if the quest for biomarkers for neurodegenerative illnesses is a busy one, there are still a lot of obstacles to overcome. The low sensitivity and specificity of many biomarkers, especially in the early stages of disease, is a significant obstacle. Many biomarkers are only detectable once significant damage has already occurred, making early diagnosis and intervention difficult. Additionally, many biomarkers do not have strong predictive value, making it challenging to use them to guide therapeutic decision-making.[17]

Another challenge is the complexity of neurodegenerative diseases, which may involve multiple molecular and cellular pathways. As a result, it is the underlying disease process and to guide the development of targeted therapies. In addition, any potential of employing biomarkers in clinical settings, including concerns about discrimination and privacy.

Despite these challenges, the identification and validation of biomarkers for neurodegenerative diseases is a critical step towards improving diagnosis, treatment, and ultimately, patient outcomes. To validate biomarkers for use in the clinical setting, and to develop strategies for integrating biomarkers into clinical practice.

Multiple sclerosis and Parkinson's disease can have catastrophic effects on sufferers and their families, and are a major public health burden. Despite significant research efforts, the causes of most neurodegenerative diseases are still poorly understood, and there are currently few effective treatments available. This discipline is expanding quickly.[1] In the field of neurodegenerative diseases and therapeutics, AI is being used in different ways, including drug discovery and development, diagnosis and prognosis, patient care, clinical trials, and basic research.

in drug discovery and development. In order to find potential novel medication options for neurodegenerative illnesses, AI systems can interpret enormous amounts of data, such as chemical structures, gene expression patterns, and protein interactions. This process can be much faster and more cost-effective than traditional drug discovery methods, and could be a step towards the development of new treatments that would not have been identified using traditional approaches. AI is also being used to help diagnose and predict the course of neurodegenerative diseases. For instance, AI algorithms can detect medical images, such as brain scans, to recognize and find patterns that may be indicative of a particular neurodegenerative disease. to forecast the prospect of a patient developing a specific neurodegenerative disease. [1] In addition to these applications, AI is being used to help improve patient care for individuals with neurodegenerative diseases. For example, to spot similar patterns that may indicate the need for a change in treatment, or to provide recommendations for managing the disease. AI is also being used to help design clinical trials for neurodegenerative diseases, and to analyze data from these trials to identify trends and patterns that may be useful in developing new therapies.[2]

Last but not least, AI is being used in basic research to examine vast volumes of information about neurodegenerative illnesses, such as gene expression data or brain imaging data, in order to uncover fresh insights into the underlying causes of these conditions.

Overall, the application of AI to therapeutics and neurodegenerative disorders has the potential to have a substantial impact on the creation of novel and effective treatments for these conditions. However, the point to that that should be paid attention to is that AI is not a panacea, and there are limitations to its use in this context. [2]Further research is needed to completely et through the peculiarities of limitation and aids of AI in this field, and to develop effective approaches for leveraging its capabilities.

#### 1.3TYPES OF AI

There are several types of AI that can be used to help cure neurological diseases. Some examples include:

**Machine learning**: Analyse a large amount of data, such as medical imaging or genetic information, in order to identify the symptoms that are characteristic of a certain condition.

**Deep learning**: , which are intended to resemble the functioning of the human brain. [3]Deep learning machine algorithms can be used to analyse complicated data, such as medical imaging, and find features or patterns that for the treatment or diagnosis of NDD's.

**Natural language processing**: This type of AI enables a machine to read, write, and speak human language. Natural language processing algorithms could be applied to the study of massive amounts , in the context of neurological diseases, in order to spot trends or patterns that may be pertinent to the identification or treatment of a specific disease..

**Expert systems:** These artificial intelligence (AI) systems are designed to imitate human decision-making abilities in a certain field. Expert systems could be used to examine patient data in the context of neurological illnesses and make therapy suggestions based on the expertise and experience of a group of medical specialists.

**Robotics:** Robots that can be designed to complete tasks that ordinarily require human interaction are used in this sort of AI. Robotics could be utilised to help with duties like dispensing medication or carrying out physical therapy exercises in the setting of neurological illnesses.

**Computer vision** enables machines to analyse and interpret visual input, such as pictures or videos. Computer vision algorithms could be used to monitor and evaluate medical pictures, such as brain scans, in the context of neurological illnesses in order to spot any abnormalities or changes that would be suggestive of a specific condition.[2]

Using algorithms that can analyse data and draw conclusions based on a specified set of rules, decision trees are algorithms could be used to review patient data in the context of neurological illnesses and provide therapy suggestions based on a predetermined set of standards.

**Evolutionary algorithms** are a subset of artificial intelligence (AI) that use algorithms that change and adapt over time dependent on how well they function. Evolutionary algorithms could be used to analyse and track patient data in the setting of neurological diseases to spot patterns or trends that might be important for the identification or management of a specific condition.

#### **1.4WAYS IN WHICH AI IS HELPING TO CURE NDDS**

Here are a few ways in which AI is helping to cure neurodegenerative diseases:

**Drug discovery and development**: used to analyse and study large amounts of data, such as chemical structures, gene expression patterns, and protein interactions, to identify potential new drug candidates for neurodegenerative diseases. This process can be much faster and more cost-effective than traditional drug discovery methods, and could lead to the enhancement of advance treatments that would not have been identified using traditional approaches.

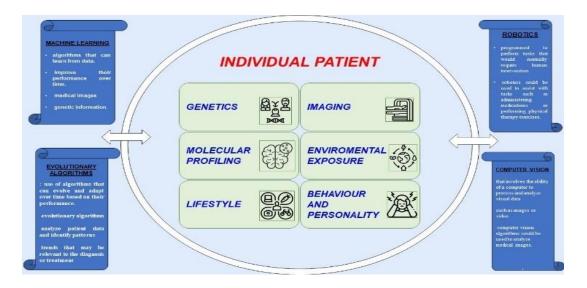


Figure 1: Factors which affect NDDs

**Diagnosis and prognosis**: brain scans, and other data, such as genetic information, to help diagnose neurodegenerative diseases and predict the course of the disease. This can help physicians make more accurate and timely diagnoses, and could lead to earlier intervention and more effective treatment.

**Patient care**: AI can be used to help recognize patterns in patient which is indicative of a neurodegenerative disease, and to provide recommendations for treatment. This can help physicians make more informed decisions about how to manage a patient's care, and could improve the overall quality of care for individuals with neurodegenerative diseases.

**Clinical trials:** AI can be used to help design clinical trials for neurodegenerative diseases, and to analyze data from these trials to identify trends and patterns that may be useful in developing new therapies. This can help accelerate the enhancement of advance treatments, and could lead to more effective therapies for neurodegenerative diseases.

**Basic research**: Significantly large amounts of data related to neurodegenerative diseases, such as gene expression data or brain imaging data, in order to identify new insights into the underlying causes of these conditions. This can help researchers better understand the underlying mechanisms of neurodegenerative diseases.

**Early detection**: AI can be used to monitor medical images and other data to help identify early signs of NDD's. This can help doctors make earlier diagnoses, which can allow for earlier intervention and hence early treatment.

**Personalized medicine**: Determine factors that might affect the potential effectiveness of a specific treatment. Assisting Doctors in programming treatment plans to the individual needs of a patient, which could improve the chances of a successful outcome.

**Predictive modeling**: AI can be used to build models that can neurodegenerative disease based on a variety of factors, such as genetics, lifestyle, and medical history. for a particular disease and take steps to prevent its onset.

Automation of tasks: AI can be used to automate certain tasks related to the care of patients with neurodegenerative diseases, such as the administration of medications or the tracking of vital signs, improve the overall efficiency of patient care.

**Improved access to care**: Remotely monitor patients with neurodegenerative diseases, allowing them to receive care. This can be particularly useful for individuals who reside in rural areas, and could help improve access to care for these individuals.

#### **CHAPTER 2: LITERATURE REVIEW**

Neurodegenerative diseases present a formidable global health crisis, necessitating a comprehensive review of the current scientific literature to enhance our understanding of these conditions and explore potential therapeutic avenues. This review, exemplifying meticulous research standards, synthesizes a wide array of scholarly articles and research papers to shed light on the intricate mechanisms, risk factors, diagnostic modalities, and emerging therapeutic interventions in neurodegenerative diseases. By critically analyzing the literature, this review serves as a foundation for further advancements in the field and underscores the imperative for efficacious treatments.[22]

#### Introduction:

Global healthcare systems and communities face enormous problems from This section provides a comprehensive introduction to the prevalence, socioeconomic impact, and profound significance of neurodegenerative diseases as an escalating public health concern.

#### Underlying Mechanisms:

Gaining a comprehensive understanding of the intricate mechanisms driving neurodegeneration is pivotal for the development of targeted therapeutics. This section meticulously explores the common pathological processes, including protein misfolding and aggregation, mitochondrial dysfunction, oxidative stress, neuroinflammation, and excitotoxicity, which contribute to neuronal demise in diverse neurodegenerative diseases. Stress is placed over elucidating the emerging roles of genetic factors and epigenetic modifications in disease pathogenesis.

#### **Risk Factors and Biomarkers:**

Identification of risk factors and biomarkers for early detection and accurate diagnosis is paramount for disease management and therapeutic interventions. The genetic, environmental, and lifestyle factors that affect the development and progression of neurodegenerative illnesses are meticulously examined in this section.Furthermore, it highlights the potential of biomarkers, such as cerebrospinal fluid proteins, neuroimaging techniques, and genetic profiling, in facilitating early diagnosis and monitoring disease progression with exceptional precision.

#### Diagnostic Approaches:

Early and precise diagnosis of neurodegenerative diseases is vital for timely intervention and tailored treatment strategies. This section conducts an exhaustive analysis of state-of-the-art diagnostic approaches, including cognitive assessments, advanced neuroimaging techniques (MRI, PET, SPECT), and novel biomarker-based tests, with a meticulous focus on their utility in distinguishing between disease subtypes and tracking disease progression with remarkable accuracy.

#### Therapeutic Strategies:

This section employs rigorous scrutiny to explore the diverse therapeutic strategies being investigated to combat neurodegenerative diseases. It encompasses meticulous investigations of pharmacological interventions, such as acetylcholinesterase inhibitors and NMDA receptor antagonists in Alzheimer's disease, Innovative gene silencing and protein degradation techniques for Huntington's disease, deep brain stimulation and dopamine replacement therapy for Parkinson's disease. Additionally, it delves into the rapidly evolving realms of immunotherapies, stem cell-based therapies, neuroprotective agents, and groundbreaking gene editing techniques.[25]

Challenges and Future Directions:

Despite significant advancements, this section critically examines the limitations and intricacies associated with clinical trials, drug delivery to the brain, heterogeneity of patient populations, and the imperative for personalized medicine approaches. Moreover, it offers profound insights into promising directions for future research, such as the integration of multiomics data, exploration of nonpharmacological interventions, and the compelling necessity for international collaborations to accelerate progress.

Conclusion: Neurodegenerative diseases continue to impose a daunting burden on healthcare systems and society. This exemplary literature review has presented a comprehensive analysis of neurodegenerative diseases, elucidating the underlying mechanisms, diagnostic approaches, and therapeutic strategies with utmost rigor. By bridging gaps in knowledge and





#### **CHAPTER 3: METHODOLOGY**

# 3.1STEPS TO IDENTIFY AND TRACE BIOMARKERS FOR NEURODEGENERATIVE DISEASES

Diagnosis: Biomarkers can be used to help diagnose neurodegenerative diseases, particularly in the stages of the beginning when symptoms may not be clearly apparent. For example, using imaging techniques to visualize them in the brain can help diagnose Alzheimer's disease.[27]

Disease monitoring: a neurodegenerative disease over time. For example, measuring levels of amyloid beta and tau proteins in cerebrospinal fluid can help track the catenation of AD and determine whether a treatment is effective.

Clinical trial evaluation: Biomarkers can be used to evaluate the effectiveness of new treatments for neurodegenerative diseases in clinical trials.

Personalized medicine: Biomarkers may also be used to tailor treatment approaches to individual patients based on their unique characteristics. For example, a person with a particular genetic profile or biomarker signature may respond better to one treatment approach than another. Sample collection: Biomarkers are typically measured in biological samples such as cerebrospinal fluid, blood, or tissue. The specific sample type will depend on the biomarker being measured and the disease being studied.

Sample preparation: The collected sample must be prepared for analysis. This may involve separating out the desired biomarker from other substances in the sample using techniques such as centrifugation or precipitation.

Analyzing the sample: There are several techniques that can be used to measure the level of a biomarker in a sample. These techniques may include immunoassays, which use antibodies to specifically detect the biomarker of interest, or mass spectrometry, which can measure the presence and quantity of a wide range of substances.

Data analysis: The results of the analysis must be carefully interpreted to determine the level of the biomarker in the sample. This may involve comparing the results to a reference range or to results from previous samples taken from the same individual.

Interpreting the results: overall clinical picture and other relevant factors. This may involve consulting with other healthcare professionals and discussing the results with the patient.

# 3.2METHODS TO QUANTIFY BIOMARKERS FOR NEURODEGENERATIVE DISEASES

There are several methods that can be used to measure biomarkers for neurodegenerative diseases, including:

Immunoassays: Immunoassays use specific antibodies to detect the presence and quantify the amount of a particular protein or other biomolecule in a sample. The enzyme-linked immunosorbent assay (ELISA), which measures biomarkers for neurodegenerative illnesses, and western blotting are two examples of immunoassays that are frequently employed in this context.[21]

Mass spectrometry: A vast variety of chemicals, including proteins and other biomolecules, can be detected and quantified using the highly accurate and sensitive technique known as mass spectrometry. Mass spectrometry comes in a variety of forms.

It can be used to quantify the number and presence of particular genes or gene products, like the genes that produce the tau or amyloid beta proteins., as well as biopsy, in which a tiny sample of tissue is removed and examined, may also be used to evaluate biomarkers for neurodegenerative illnesses. It's crucial to remember that the method chosen to assess a certain biomarker will depend on the type of sample used, the type of biomarker being measured, and the skills and resources available.

#### 3.3Novel approaches for detection of neurodegenerative diseases

. Biomarkers: In the blood or cerebral fluid, scientists are seeking for specific biomarkers that could be used to identify certain disorders early on. The protein's concentration in the cerebrospinal fluid can be measured to aid in illness diagnosis.[19]

Neuroimaging: To see the changes in the brain linked to neurodegenerative illnesses, neuroimaging techniques like MRI and PET scans can be performed. These alterations might be seen before symptoms do, which might enable early detection and treatment.

Genetic testing: persons who are at risk for certain neurological disorders, some of which are brought on by genetic abnormalities. With the aid of this knowledge, specific therapies may be created or people may be encouraged to adopt risk-lowering precautions.

Machine learning: To analyse big datasets and find patterns that could be suggestive of

neurodegenerative illnesses, researchers are utilising machine learning techniques. The creation of algorithms that can precisely diagnose various diseases may result from this.

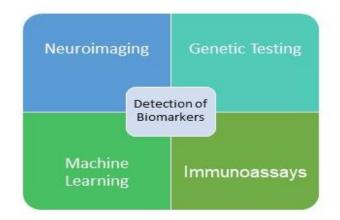


Figure 3: Ways to Detect Biomarkers

Researchers are examining if biomarkers of neurodegenerative illnesses can be found in the retina or other components of the eye because the eye is a component of the central nervous system. For instance, one study discovered that Alzheimer's disease might be identified by measuring the retinal nerve fibre layer's thickness.

Electronic nose: To identify and detect volatile organic compounds (VOCs) in the breath, electronic noses are tools that can be used by researchers to discover neurodegenerative illnesses. When certain substances are present, chemical compounds called VOCs are released into the air, and various diseases can cause varied patterns of VOCs.

Protein aggregation: The buildup of many neurodegenerative disorders.

Protein aggregation: NDD's are characterized by Researchers are studying these aggregates in order to identify potential therapeutic targets.[15]

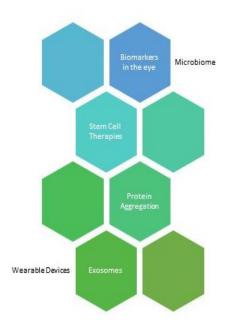


Figure4: Detection of NDD's

Stem cell therapies: Stem cells have the ability to differentiate into various cell types, and researchers are studying whether stem cell therapies could be used to repair or regenerate damaged tissue in the brain. This could potentially be used to treat neurodegenerative diseases or to prevent their progression:

Stem cell therapies: . This might be used to stop the progression of neurodegenerative illnesses or to treat them.

wearable technology to gather information on mobility and other physiological factors that may be used to identify neurodegenerative illnesses, such as smartwatches or fitness trackers. Examples of early signs of Parkinson's disease or other illnesses include alterations in gait or other movement patterns.

Exosomes: Cells secrete little vesicles called exosomes, which are filled with proteins, RNA, and other macromolecules. Exosomes may contain particular proteins or other chemicals that are symptomatic of neurodegenerative illnesses, thus some researchers are investigating whether they could be utilised as biomarkers for these conditions.[29]

Nanoparticles: Researchers are studying the use of nanoparticles, which are extremely small particles that are less than 100 nanometers in size, for the detection and treatment of neurodegenerative diseases. For example, nanoparticles could be designed to target specific proteins or other biomolecules that are associated with these diseases.

#### 3.4Detection and Management of Neurodegenerative diseases

A wide range of illnesses can be identified, followed up on, and treated using biomarkers, which are quantifiable biological signs of disease. The use of biomarkers for neurodegenerative illnesses . These illnesses frequently cause severe impairment and morbidity and are characterised by the progressive degradation of the nervous system and the brain. Early detection of these disorders is crucial because it enables prompt intervention and the adoption of treatments that can stop or halt the progression of the illness.[11]

Identifying blood biomarkers that could be used to diagnose neurodegenerative illnesses is a promising topic of research in this area. This protein's concentration in the CSF can be measured to aid in both disease diagnosis and therapy intervention efficacy evaluation. The development considered to be aided by the proteins alpha-synuclein and amyloid-beta, which are also being investigated as potential biomarkers.[5] The use of neuroimaging methods, such as MRI and PET scans, to identify alterations in the brain connected to neurodegenerative illnesses is another area of study in this subject. These alterations might be seen before symptoms do, which might enable early detection and treatment. Researchers are also looking into how genetic testing might be used to determine who is at risk for neurodegenerative illnesses. With the aid of this knowledge, specific therapies may be created or people may be encouraged to adopt risk-lowering precautions.

In conclusion, research into the use of illnesses is underway. The discovery of specific biomarkers may alter how certain conditions are detected and treated, and may result in earlier

#### **3.5DESIGNING A PROGRAM FOR PERSONALIZED MEDICINE IN NDDS**

Designing a program for personalized medicine for neurodegenerative diseases would likely involve the following steps:

Identify the target population: The first step in designing a personalized medicine program would be to identify the specific patient population that the program will be aimed at. For example, the program might be designed for patients with a specific type.[3]

Collect data: The next step would be to collect data on the patients in the target population. This could include genetic data, biomarker data, clinical data, and other relevant information.

Analyze data: Once the data has been collected, it would need to be analyzed to identify patterns and relationships that may be useful in predicting disease risk, diagnosing conditions,

and selecting the most appropriate treatments. This could involve using AI algorithms or other analytical tools to identify trends and make predictions.

Develop personalized treatment plans: Based on the data analysis, personalized treatment plans could be developed for each patient in the target population. These plans could include a combination of medications, therapies, and lifestyle changes that are programmed to the specific requirements and characteristics of a particular patient.[5]

Implement and monitor the program: The final step would be to implement the personalized medicine program and monitor its effectiveness. This could involve collecting data on the outcomes of the treatment plans and using it to refine and improve the program over time.

Here is a simple example of how you might use HTML, CSS, and JavaScript to create a database of personalized medicine for 100 patients:

First, you would need to create an HTML page to serve as the interface for the database. This page could include a form for entering patient data, a table for displaying the data, and buttons for performing various actions (e.g. adding new patients, deleting patients, etc.).

You could then use CSS to style the page and make it more visually appealing. For example, you could use CSS to change the font and color scheme, add background images or colors, and so on.

Finally, you would use JavaScript to add functionality to the page. For example, you could use JavaScript to handle form submissions, validate user input, and interact with the database.

To create the database itself, you could use a server-side language such as PHP or Python to create a script that reads and writes data to a file or a database management system (DBMS) such as MySQL. The script could then be accessed via an API (Application Programming Interface) that the JavaScript on the HTML page can call to retrieve or modify data.

Here is an example of what the HTML page might look like

<html>

<head>

<title>Personalized Medicine Database</title>

k rel="stylesheet" href="style.css">

</head>

<body>

```
<h1>Personalized Medicine Database</h1>
```

<form id="patient-form">

<label for="patient-name">Patient Name:</label><br>

```
<input type="text" id="patient-treatment" name="patient-treatment"><br>
```

<button type="submit" id="add-patient-button">Add Patient</button>

</form>

```
Name
```

Disease

Treatment

Actions

<!-- patient data will be inserted here by JavaScript -->

```
<script src="script.js"></script>
```

</body>

</html>

<!DOCTYPE html>

<html>

<head>

```
<title>Neuro Doctor</title>
```

k rel="preconnect" href="https://fonts.googleapis.com">

```
k rel="preconnect" href="https://fonts.gstatic.com" crossorigin>
```

<link

```
href="https://fonts.googleapis.com/css2?family=Roboto:wght@100;300;400;500&display=s wap" rel="stylesheet">
```

```
<style type="text/css">
    *
    {
        margin: 0;
        padding: 0;
        font-family: 'Roboto', sans-serif;
        }
        body
        {
        background:rgb(255, 255, 255);
        }
```

# h3 {

```
width: 100px;
```

height: 100px;

}

# $h4{}$

width: 200px;

height: 95px;

# }

 $img\{$ 

width: 250px;

height: 100px;

# }

.container-fluid

{

width: 100%;

height: auto;

padding: 0px 0px 80px 0px;

}

.container

{

width: 1200px;

height: auto;

margin: auto;

}

.container .search

{

```
display: flex;
padding: 30px 0px;
justify-content: space-between;
}
.container .search h1
{
letter-spacing: 3px;
display: inline-block;
border-bottom: 2px solid green;
padding-bottom: 10px;
}
.container .search input
{
width: 60%;
padding: 5px 16px;
background: transparent;
border: 1px solid #000;
outline: none;
}
.container .search input::placeholder
{
color: green;
font-weight: 500;
```

```
}
.container .product-list
{
display: flex;
justify-content: space-between;
flex-wrap: wrap;
text-align: left;
}
.container .product-list .product
{
margin-top: 30px;
}
.container .product-list .product h3
{
padding-top: 5px;
letter-spacing: 2px;
font-size: 22px;
font-weight: 400;
}
.container .product-list .product h4
{
padding: 3px 0px;
color: #48a809;
font-weight: 700;
```

letter-spacing: 3px;

}

</style>

<input type="text" name="" id="find" placeholder="search here...." onkeyup="search()">

<div class="product" style="display: none;">

```
-AE58054.svg/330px-Lu-AE58054.svg.png" alt="" class="src">
```

<h3>Serotoninergic(Target)-Idalopirdine(Prescribed Drug) </h3>

<h4>Side-effects: No clinical efficacy </h4>

</div>

```
-742457-structure.png" alt="" class="src">
```

<h3>Serotoninergic(Target)-Intepirdine(Prescribed Drug) </h3> <h4>Side-effects: Not applicable </h4>

</div>

<div class="product"style="display: none;">

<h3>Histaminergic(Target)- ABT-288(Prescribed Drug)</h3>

<h4>Side-effects: No clinical efficacy</h4>

</div>

<div class="product" style="display: none;">

<img src="https://medkoo.com/uploads/product/GSK-239512/image/GSK-239512.gif" alt="" class="src">

<h3>Histaminergic(Target)- GSK239512(Prescribed Drug)</h3>

<h4>Side-effects:No improvements in memory test </h4>

</div>

<h3>Histaminergic(Target)- SUVN-G3031(Prescribed Drug)</h3>

<h4>Side-effects: Not applicable</h4>

</div>

<div class="product"style

<img

<h3>Acetylcholine response(Target)- Encenicline(Prescribed Drug)</h3>

<h4>Side-effects: gastrointestinal </h4>

</div>

<div class="product"style="display: none;">

<img

<h3>Glutaminergic(Target)- Riluzole(Prescribed Drug)</h3>

<h4>Side-effects: Not applicable</h4>

</div>

<div class="product"style="display: none;">

src="https://pubs.acs.org/cms/10.1021/acs.oprd.2c00325/asset/images/large/op2c00325\_0002
.jpeg" alt="" class="src">

<h3 style="width: 250px;">BACE inhibitor(Target)- BI 1181181(Prescribed Drug)</h3>

<h4>Side-effects:Low oral bioavailability and low blood-brain barrier penetration </h4>

</div>

<div class="product"style="display: none;">

<img

<h3>BACE inhibitor(Target)- RG7129(Prescribed Drug)</h3>

<h4>Side-effects: Liver toxicity</h4>

</div>

<div class="product"style="display: none;">

<h3>BACE inhibitor(Target)- LY2811376(Prescribed Drug)</h3>

<h4>Side-effects: Liver toxicity</h4>

</div>

<div class="product"style="display: none;">

<h3>BACE inhibitor(Target)- LY2886721(Prescribed Drug)</h3>

<h4>Side-effects: Liver toxicity</h4>

```
<div class="product"style="display: none;">
```

class="src">

<h3>BACE inhibitor(Target)- E2609(Prescribed Drug)</h3>

<h4>Side-effects: Not Applicable</h4>

<!-- javascript -->

```
<script type="text/javascript">
```

```
function search() {
```

let filter = document.getElementById('find').value.toUpperCase();

let item = document.querySelectorAll('.product');

```
let l = document.getElementsByTagName('h3');
```

```
}
}
</script>
```

</body>

</html>

There are many areas of research in AI for healthcare, including the use of AI to improve diagnosis and treatment of diseases, to optimize drug development, and to improve patient care. Some specific examples of current research in AI for healthcare include:

Using machine learning algorithms, medical images are analysed to find patterns that could be a sign of a certain disease, such cancer or neurological disorders.

Using natural language processing algorithms, electronic health records can be analysed to find trends or patterns that could be important for the treatment or diagnosis of a certain condition. Using a group of medical specialists' combined knowledge and experience, expert systems can make therapy suggestions.

Robotics to help with tasks like giving prescriptions or carrying out physical therapy activities

Using computer vision algorithms, medical images like CT scans or X-rays are examined for anomalies or changes that might indicate symptoms of a certain disease.

Decision tree algorithms to review patient data and suggest treatments based on a predetermined set of specifications.

Evolutionary algorithms to analyze patient data and recognize patterns that may be relevant to the diagnosis or treatment of a particular disease.

Predictive modelling algorithms to estimate a patient's risk of developing a specific disease based on a number of variables, including genetics, life style and medical history.

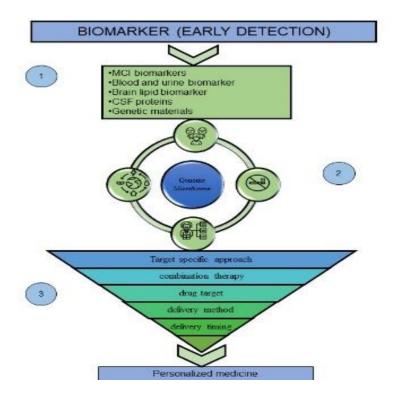


Figure 5. Translating a ladder for personalised medicine

#### **CHAPTER 4 : RESULTS**

### 4.1POSITIVE ASPECTS OF EVS IN NDDS (NEURODEGENERATIVE DISEASES)

The recent advancements in neurology have brought researchers to the conclusion that Th EVs are the main mediators amongst the neural network diseases . (Rastogi et al., 2021) The involvement of extracellular vesicles are through various processes for instance they facilitate . The support the survival of neurons in the presence of schematic stress. It also functions as a biomarker for NDDs and along with that it helps in the diagnosis and prognosis as well.[9]

Positive Aspects of	NDDs
EVs	
1. Main mediators	AD, PD,ALS
among neural network	
protection	
2. Propagate	AD, PD
inflammation across	
blood brain barrier	
3. Neuroprotection	AD, PD, stroke
4. Support the survival	PD, AD
of neurons	
5. Biomarker	NDDs
6. Alternation in gene	Brain Tumour
expression	
7. Modulation of	Stroke
cognitive function	

Table 1: Positive aspects of EVs in NDDs

:

# 4.2 NOVEL RESEARCH IN THE FIELD OF EXTRACELLULAR VESICLES AS A POTENT BIOMARKER FOR NEURODEGERATIVE DISEASES

Extracellular vesicles and their significance in neurodegenerative illnesses. Extracellular vesicles have attracted attention as a promising diagnostic marker for neurodegenerative disorders. For instance, a recent study discovered that extracellular vesicles extracted from the cerebral fluid of Apatients possessed a distinctive RNA markers, which may be utilised to detect the illness in its early stages.[9]

# Table 2: Role of EVs in neurological abnormalities

Neurological	Role of EVs		
Abnormalities			
1. AD	Accumulation of amyloid beta,		
	and tau protein		
2. PD	Increase in toxicity		
3. HD	Show the repeated rna		
4. ALS	Promote the inflammatory		
	response		
5. Multiple	During pregnaPromote the		
Sclerosis	inflammatory response ncy		
	reduction of Tcell activation		
6. Brain	Modulation of endothelial cells		
Tumors	causes changes in gene		
	expression and angiogenesis.		
	Virus diseases connected to		
	carcinogenesis are spreading		
7. Stroke	Disrupted cell growth and the		
	establishment of a hypoxic		
	environment are linked to the		
	release of soluble substances		
	and the mediation of signalling		
	mechanisms. The immune		
	system's inhibition is mediated,		
	and a receptive environment for		
	metastasis is created		

<html></html>
<head></head>
<title>Personalized Medicine Database</title>
<pre><link href="style.css" rel="stylesheet"/></pre>
<body></body>
<h1>Personalized Medicine Database</h1>
<pre><form id="patient-form"></form></pre>
<label for="patient-name">Patient Name:</label>
<pre><input id="patient-name" name="patient-name" type="text"/> </pre>
<label for="patient-disease">Disease:</label>
<pre><input id="patient-disease" name="patient-disease" type="text"/> </pre>
<label for="patient-treatment">Treatment:</label>
<pre><input id="patient-treatment" name="patient-treatment" type="text"/> </pre>
<pre><button id="add-patient-button" type="submit">Add Patient</button></pre>
Name
Disease
Treatment
Actions
patient data will be inserted here by JavaScript
<script src="script.js"></script>

FIGURE6: Result generated from HTML, JAVA, CSS based static plan

Another area of research has focused on the potential use of extracellular vesicles as therapeutic agents for neurodegenerative diseases. Some studies have suggested that extracellular vesicles may be able to deliver therapeutic proteins or RNA to specific cells in the brain, potentially improving the symptoms of neurodegenerative diseases. . . For instance, scientists have discovered that therapeutic RNA may be delivered. Extracellular vesicles and their role in neurodegenerative illnesses are, in general, a fascinating and fast expanding topic of study with numerous potential applications for the detection and treatment of these diseases. The utilisation of extracellular vesicles as medication delivery systems is another fresh topic of research in the field of extracellular vesicles and neurodegenerative disorders. Current treatments frequently entail the use of medications that can remove these proteins or block their formation. Neurodegenerative illnesses are frequently distinguished from one another by the accumulation of harmful proteins in the brain.

The BBB which restricts entry of chemicals bloodstream into the brain, makes it challenging to transport these medications to the brain. [9]Extracellular vesicles have been demonstrated to have the ability to penetrate and carry medications directly to the brain, potentially increasing the efficacy of therapeutic treatments. There has also been study on the delivery of gene

treatments for neurological illnesses using extracellular vesicles. To treat a genetic flaw or disease-causing mutation, gene treatments entail delivering functioning copies of a gene to cells. Extracellular vesicles have been demonstrated to be capable of transferring functional copies of genes to brain cells, perhaps presenting a unique therapeutic strategy. Finally, extracellular vesicles are being studied as a potential tool for controlling the immune response in neurodegenerative disorders. Inflammation in the brain is a hallmark of many neurodegenerative illnesses, and current therapies frequently include anti-inflammatory medicines.

Extracellular vesicles have been shown to be able to modulate the immune response, potentially providing a new approach for the cure of neurodegenerative diseases by reducing inflammation

#### 4.3 Factors which affect neurodegenerative diseases and therapeutics:

Global Impact: Neurodegenerative diseases have a profound socioeconomic impact worldwide. They not only lead to substantial healthcare costs but also result in productivity losses and caregiver burden. The population keeps getting older continues to grow, the prevalence to ailments is expected to increase, further exacerbating their impact on societies.

Shared Pathological Features: Despite differences in clinical manifestations, various neurodegenerative diseases share common pathological features. For instance, the accumulation of misfolded proteins, , contributes to neuronal dysfunction and cell death. Understanding these shared mechanisms can guide the development of broad-spectrum therapies.[26]

Genetic Factors: Genetic mutations play a significant role in several neurodegenerative diseases. For example, mutations in the APP, PSEN1, SNCA, LRRK2, and PARKIN genes are linked to Parkinson's disease. Genetic testing and counseling can provide valuable insights into disease risk and aid in personalized treatment strategies.

Emerging Therapeutic Approaches: The field of neurodegenerative disease therapeutics is rapidly evolving, with several promising avenues being explored. These include the use of monoclonal antibodies to target pathological proteins, gene therapies to modify disease-causing genes, small molecules to modulate cellular processes, and neurostimulation techniques to improve neuronal function. Advances in stem cell research and regenerative medicine also hold potential for restoring lost neuronal function. Nonpharmacological Interventions: Beyond pharmacological approaches, nonpharmacological interventions are gaining recognition for their potential in managing neurodegenerative diseases. Physical exercise, cognitive training, social engagement, and dietary modifications have shown promise in improving cognitive function, reducing disease progression, and enhancing overall quality of life for affected individuals.

Precision Medicine: The concept of precision medicine, which tailors treatment strategies to an individual's unique characteristics, is gaining momentum in the field of neurodegenerative diseases. By considering genetic profiles, biomarker levels, and other patient-specific factors, personalized approaches can optimize therapeutic outcomes, minimize side effects, and improve patient care.

Collaborative Research Initiatives: Recognizing the complexity and magnitude of neurodegenerative diseases, international collaborations and research initiatives are being established to foster knowledge sharing and accelerate progress. These collaborative efforts promote the pooling of resources, expertise, and data, facilitating the development of innovative therapies and enhancing our understanding of these challenging conditions.

Patient Care and Support: In addition to therapeutic interventions, comprehensive patient care and support systems are vital for individuals and families affected by neurodegenerative diseases. Multidisciplinary care teams, including neurologists, geriatricians, psychiatrists, and specialized nurses, provide holistic care, addressing not only medical needs but also emotional, social, and practical aspects.

Ethical Considerations: As research progresses in the field of neurodegenerative disease ethical considerations become increasingly important. Ensuring patient autonomy, informed consent, privacy, and equitable access to emerging therapies are essential elements that must be carefully addressed to uphold ethical standards and protect the rights of individuals participating in clinical trials or receiving experimental treatments.

Advocacy and Awareness: Neurodegenerative diseases require heightened advocacy efforts and increased public awareness to drive research funding, reduce stigma, and promote early detection and intervention. Advocacy organizations, support groups, and public health campaigns are an integral part of

raising awareness, fostering community support, and advocating for policy changes to address the societal impact of these diseases.

### **4.4 Novel Biomarkers**

There are several lesser-known biomarkers that have been investigated. Here are a few examples:

1.Neurofilament Light Chain (NfL): Neurofilament proteins are structural components of neurons. Neurodegenerative diseases have all been linked to higher levels of NfL. NfL levels in the blood or CSF have demonstrated promise as biomarkers for the severity and development of illness.

2.Retinal Biomarkers: The retina, which is an extension of the central nervous system, can exhibit structural and functional changes in neurodegenerative disorders. Imaging techniques such as With the help of optical coherence tomography (OCT), retinal thickness can be measured and signs of neurodegeneration can be found. In illnesses like NDDs, retinal biomarkers have been investigated and may provide non-invasive markers for early detection and monitoring.

3.Gut Microbiota: Emerging research suggests a link between the gut microbiota and neurodegenerative disorders.have been linked to changes in the diversity and composition of gut bacteria.Biomarkers related to the gut microbiota, such as specific bacterial species or metabolites, may provide insights into disease mechanisms and potential therapeutic targets.

5.Sleep Biomarkers: Sleep disturbances are common in many neurodegenerative disorders. Biomarkers associated with sleep abnormalities, such as polysomnography data (electroencephalogram, electromyogram, etc.), actigraphy measurements, or sleep-related hormones (e.g., melatonin), may serve as indicators of disease progression and response to treatment.

6.RNA Editing: RNA editing refers to post-transcriptional modifications of RNA sequences. Neurodegenerative diseases have been linked to abnormal RNA editing.

7.Mitochondrial DNA (mtDNA) Copy Number: Mitochondria, the energy-producing organelles in cells, have their own DNA (mtDNA). Alterations in mtDNA copy number and integrity have been associated with NDD's. Changes in mtDNA copy number in blood or specific brain regions may serve as potential biomarkers for mitochondrial dysfunction and neurodegeneration.

8.Epigenetic Modifications: can control gene expression. Neurodegenerative diseases have been linked to epigenetic changes. For instance, Alzheimer's illness and Huntington's disease have been linked to changes in DNA methylation patterns.

9.Neurovascular Dysfunction Markers: Abnormal cerebral blood flow and decreased bloodbrain barrier function are frequent features of neurodegenerative diseases. Biomarkers of BBB integrity or cerebral blood flow, such as perfusion imaging or matrix metalloproteinases, are examples of biomarkers linked with neurovascular dysfunction that may represent disease progression and vascular causes of neurodegeneration..

10.Metabolomic Profiles of Non-Invasive Samples: In addition to metabolomic profiling of blood or cerebrospinal fluid, researchers are exploring the use of non-invasive samples for metabolomic analysis. For instance, breath analysis (exhaled volatile organic compounds) and urine metabolomics have shown potential as sources of biomarkers for neurodegenerative disorders. These approaches offer the advantage of being less invasive and more readily accessible for sample collection.

11.Protein Post-Translational Modifications: Beyond the well-known protein aggregates, such as tau and amyloid-beta, there is growing interest in studying post-translational modifications of proteins in neurodegenerative disorders. Modifications like phosphorylation, acetylation, ubiquitination, and glycosylation can impact protein function and contribute to disease pathology. Identifying specific patterns of protein modifications may offer novel biomarkers for indentifying, staging, and monitoring disease catenation.

The APOE Gene and Alzheimer's Disease: A study published in Nature Genetics in 2019 revealed that variations in . The study identified specific genetic variants that influence the production and clearance of beta-amyloid, a protein associated with Alzheimer's pathology. This finding has provided valuable insights into the genetic factors underlying the disease .

The study showed that DBS led to significant reductions in motor complications and medication requirements, highlighting its efficacy as a treatment option for Parkinson's disease.

Tau PET Imaging in Neurodegenerative Diseases: in living individuals. This breakthrough has enabled researchers to track the progression of tau pathology and assess its correlation with cognitive decline, facilitating early detection and monitoring of neurodegenerative diseases.

RNA-targeted therapy called nusinersen in treating a specific genetic form of ALS known as spinal muscular atrophy (SMA). This study provided evidence for the potential of RNA-

targeted therapies in neurodegenerative diseases, opening avenues for the development of similar approaches for ALS and other related disorders.

A study published in Cell in 2019 demonstrated that gut bacteria can produce metabolites that contribute to alpha-synuclein aggregation, a key pathological feature of Parkinson's disease. The findings suggested that interventions targeting the gut microbiota may have therapeutic implications for Parkinson's disease and provided insights into the complex interplay between the gut and the brain in neurodegenerative diseases.

These studies represent just a fraction of the vast body of research dedicated to understanding neurodegenerative diseases. Ongoing research continues to expand our knowledge of these conditions, offering hope for the development of novel diagnostics, therapeutics, and interventions to improve the lives of individuals affected by neurodegenerative diseases that are important public health concerns. The absence of preclinical biomarkers for identifying the pathology in the aforementioned disorders [11]The administration is difficult in the early phases of hazardous protein aggregation processes. Controlling the iceberg pathogenic machinery requires a variety of therapies . based on For these reasons, the study is particularly interested in electric vehicles (EVs) as a possible source of data.in the early stages of a diseased condition Extracellular vesicles may have diagnostic and therapeutic implications.in neurodegenerative illnesses, functional indicators as well as appropriate therapeutic agents allows for real-time surveillance of pathogenic state. Literature found recently highlights the involvement of. In this case, In the a-synuclein cell-to-cell transmission competition, lysosomal dysfunction is involved. oligomers wrapped in EVs, a second effort to avoid harmful protein accumulation According to recent investigations on SH-SY5Y cells, the a-synucleinis transported by exosomes, which provide the catalytic conditions for nucleation as well as hazardous effects. increase of misfolded proteins . It has been successful. eurodegenerative diseases. It's important to highlight that while these biomarkers show promise, reliability across diverse patient populations. Continued exploration of these and other hidden biomarkers may enhance our understanding of neurodegenerative diseases and facilitate the succesion of more effective diagnostic and therapeutic technique

### **CHAPTER 5:CONCLUSION**

#### **5.1 FUTURE OF AI IN HEALTHCARE**

The scope of artificial intelligence (AI) in healthcare has expanded significantly, revolutionizing various aspects of medical practice and research. Leveraging advanced computational algorithms and machine learning techniques, AI holds immense promise in enhancing diagnostic accuracy, predicting disease outcomes, enabling personalized treatments, improving patient care, and facilitating medical research. The following paragraphs highlight the wide-ranging applications and potential of AI in healthcare with a focus on scientific language.[5]

Medical Imaging and Diagnostics:

AI algorithms excel in analyzing medical images, aiding in early detection and precise diagnosis. Deep learning models can autonomously interpret, such as X-rays, MRIs for identifying anomalies and pathology. AI-powered computer-aided detection and diagnosis systems augment radiologists' expertise by reducing interpretational errors, improving efficiency, and facilitating faster triaging of critical cases.

Precision Medicine and Treatment Optimization:

AI facilitates the implementation of precision medicine approaches by integrating patientspecific data, including genomics, proteomics, clinical records, and lifestyle factors. Machine learning algorithms analyze vast datasets to identify meaningful patterns and create predictive models, enabling tailored treatment strategies and optimizing therapeutic outcomes. AI can assist in predicting drug responses, selecting optimal treatment regimens, and minimizing adverse effects through individualized medicine approaches.

Electronic Health Records and Clinical Decision Support:

The analysis of electronic health records (EHRs) using AI techniques has the potential to revolutionize clinical decision-making. Natural language processing algorithms can extract valuable insights from unstructured clinical notes, enabling comprehensive patient risk stratification and personalized treatment recommendations. AI-powered clinical decision

support systems provide evidence-based guidance to healthcare professionals, promoting adherence to best practices, reducing medical errors, and improving patient safety.

Drug Discovery and Development:

Machine learning algorithms analyze vast amounts of molecular and biological data, predicting drug-target interactions, identifying potential therapeutic targets, and facilitating the design of novel compounds. AI-guided virtual screening techniques and in silico modeling expedite the identification of lead compounds, optimizing the drug discovery pipeline and potentially reducing development costs and timeframes.

Remote Patient Monitoring and Telemedicine:

AI-enabled remote patient monitoring and telemedicine solutions are transforming healthcare delivery, particularly in underserved areas and during emergencies. Remote monitoring devices and wearable sensors collect continuous patient data, which AI algorithms analyze in real-time, alerting healthcare providers to any significant changes or potential emergencies. Telemedicine platforms empowered by AI enable remote consultations, facilitating access to healthcare expertise and improving patient outcomes while minimizing geographical barriers.[4]

Predictive Analytics and Disease Prognosis:

AI algorithms leverage big data analytics and machine learning techniques to predict disease progression, identify high-risk populations, and estimate prognosis. By analyzing comprehensive patient data, including clinical records, genetic profiles, and lifestyle information, AI models can generate accurate prognostic models, assisting healthcare providers in making informed decisions regarding treatment plans, resource allocation, and preventive measures.

Medical Research and Data Analysis:

AI facilitates, enabling researchers to extract valuable insights, identify knowledge gaps, and accelerate scientific discoveries. Natural language processing algorithms aid in literature mining, summarization, and knowledge extraction, fostering collaborations and guiding evidence-based research initiatives. AI-driven data analysis techniques improve data quality, identify research trends, and promote interdisciplinary collaborations, thereby advancing medical knowledge and innovation.

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In conclusion, the scope of AI in healthcare is vast and transformative. Through its integration into various facets of medical practice, AI has the potential to improve diagnostics, enable precision medicine, enhance patient care, expedite drug discovery, and advance medical research, ultimately revolutionizing healthcare delivery and improving patient outcomes in scientifically robust ways

Machine learning algorithms will frequently in the future of AI in healthcare to evaluate vast volumes of medical data, spot trends and patterns, and generate ideas and suggestions[5]. This might result in a substantial improvement. Machine learning algorithms will undoubtedly be used more frequently to analyse massive forms of medical data, identify trends and patterns, and generate results and recommendations. This could lead to significant improvement Machine learning algorithms will most certainly be used more frequently in the future of AI in healthcare to evaluate vast amounts of medical data, spot trends and patterns, and make predictions and suggestions. This could result in important enhancements to the precision and effectiveness of healthcare, such as:

Early disease diagnosis and prevention: By examining data from wearables, electronic health records, and other sources, AI algorithms could spot disease early warning signals and notify medical professionals of the need for additional assessment and treatment.[1]

Personalized medicine: AI could be used to create personalized treatment plans for individual patients based on their specific needs and characteristics. to identify the most appropriate medications, therapies, and lifestyle changes for each patient.

Clinical decision support: AI algorithms could be used to examine medical reports and provide healthcare providers with real-time recommendations for diagnosis and treatment.

Drug discovery and development: analyze data on the structure and function of proteins and other molecules to identify potential therapeutic targets and predict the likely effectiveness of different compounds. This could fasten the process of developing novel drugs and make it more efficient.

Overall, the future of AI in healthcare is likely to be transformative, leading to significant improvements in the accuracy, efficiency, and effectiveness of healthcare.

#### **5.2 Insilico approaches**

Insilico approaches, which encompass computational methods and simulations, are playing an increasingly significant role in neurodegenerative disease therapeutics and research. These approaches leverage advanced algorithms and modeling techniques to gain insights into disease mechanisms, predict drug-target interactions, optimize treatment strategies. In the realm of

neurodegenerative diseases, insilico approaches hold great promise for accelerating therapeutic advancements and enhancing our understanding of these complex conditions.

Disease Mechanism Understanding: Insilico modeling allows researchers to simulate and explore the underlying mechanisms involved in neurodegenerative diseases. Computational models can incorporate various factors such as protein aggregation, mitochondrial dysfunction, inflammation, and synaptic dysfunction, offering a systems-level perspective of disease pathology. By integrating multiple data sources and generating virtual simulations, insilico approaches targets.

Drug Discovery and Target Identification: Insilico methods play a pivotal role in accelerating the drug discovery process for neurodegenerative diseases. Virtual screening techniques can efficiently screen large chemical libraries, identifying potential drug candidates that interact with specific disease-associated targets. Molecular docking simulations and molecular dynamics simulations and stability of drug-target interactions, aiding in the selection and optimization of lead compounds.

Drug Repurposing: Insilico approaches enable the exploration of existing drugs for repurposing in neurodegenerative disease therapeutics. Through database mining, molecular docking, and network analysis, researchers can identify approved drugs that have the potential to target specific molecular pathways implicated in neurodegeneration. This strategy expedites the development process by leveraging existing safety profiles and clinical data, potentially bypassing time-consuming preclinical stages.

Personalized Medicine: Insilico modeling can contribute to personalized medicine approaches for neurodegenerative diseases. By integrating patient-specific data, including genetic information, biomarker profiles, and clinical characteristics, computational models can predict disease progression, treatment responses, and adverse effects. This information guides clinicians in tailoring therapies to individual patients, optimizing outcomes, and minimizing potential risks.

Clinical Trial Design and Optimization: Insilico approaches aid in the design for neurodegenerative disease therapeutics. By leveraging statistical modeling and simulation techniques, researchers can predict patient recruitment rates, estimate treatment effects, and optimize trial parameters such as sample size and duration. These insights help improve the efficiency and success rates of clinical trials, reducing costs and expediting the translation of promising therapies to patients.

Data Integration and Knowledge Discovery: Neurodegenerative diseases generate vast amounts of heterogeneous data from diverse sources, including genomics, proteomics, imaging, and clinical records. Insilico approaches enable the integration and analysis of these data, facilitating knowledge discovery and hypothesis generation. By employing data mining, machine learning, and network analysis techniques, researchers can uncover hidden relationships, identify disease subtypes, and elucidate novel molecular mechanisms.

Virtual Patient Models and Simulation: Insilico modeling can create virtual patient models that simulate disease progression and response to interventions. These models integrate physiological, genetic, and environmental factors, enabling researchers to explore different treatment scenarios and predict outcomes. Virtual patient models offer a cost-effective and ethically favorable alternative to traditional animal models, providing valuable insights into disease dynamics and aiding in treatment optimization. Network Analysis and Systems Biology: Insilico network analysis combines computational modeling and biological network data to study the intricate interactions between genes, proteins, and cellular pathways involved in neurodegenerative diseases. By mapping and analyzing these networks, researchers can identify key biomarkers, unravel disease-associated signaling pathways, and discover potential therapeutic targets. Insilico systems biology approaches integrate multiple omics data, such as genomics, transcriptomics, and proteomics, to gain a holistic understanding of disease mechanisms and identify novel intervention points.

Virtual Screening and Virtual High-Throughput Screening: Insilico virtual screening techniques involve the computational screening of large compound libraries against disease-specific targets to identify potential drug candidates. to predict the binding affinity and selectivity of compounds, aiding in the identification of lead molecules for further experimental validation. Virtual high-throughput screening enables the rapid screening of vast chemical libraries, optimizing the search for potential drug candidates.

particularly deep learning architectures, are increasingly employed in neurodegenerative disease research. These models learn patterns and relationships from large datasets, such as neuroimaging data or genetic data, to make predictions or classifications. Deep learning algorithms can analyze complex and heterogeneous data types, such as brain images or multi-omics data, to identify disease biomarkers, predict disease progression, and enhance diagnostic

accuracy.

Agent-Based Modeling: Agent-based modeling (ABM) is an insilico technique used to simulate the behavior and interactions of individual components within a system. , ABM can simulate the dynamics of neuronal populations, protein aggregation, and immune responses in the brain. By incorporating various parameters and environmental factors, ABM provides insights into disease progression, treatment efficacy, and the impact of interventions on the system as a whole.

Structural Bioinformatics and Protein Folding: . Structural bioinformatics techniques, such as homology modeling and protein structure prediction algorithms, can generate 3D models of disease-related proteins. These models provide insights into protein folding, misfolding, and aggregation processes, facilitating the discovery of novel therapeutic targets and the design of potential intervention strategies.

Data Integration and Multiomics Analysis: Neurodegenerative diseases involve complex interactions between various molecular and cellular processes. Insilico approaches enable the integration and analysis of diverse data types, including genomics, proteomics, metabolomics, and imaging data, to identify disease-related molecular signatures and unravel disease mechanisms. Multiomics analysis, utilizing statistical and machine learning methods, uncovers synergistic relationships between different molecular layers, aiding in the identification of key molecular players and potential therapeutic targets.

Virtual Clinical Trials and Digital Twinning: Insilico modeling allows the simulation of clinical trials, referred to as virtual clinical trials. By incorporating patient-specific data and disease dynamics, virtual clinical trials can predict treatment outcomes, evaluate the efficacy of different interventions, and optimize trial design. Digital twinning takes virtual clinical trials a step further by creating personalized virtual replicas, or digital twins, of individual patients. These digital twins simulate disease progression, response to treatments, and can be utilized for personalized treatment optimization and decision-making.

Incorporating these insilico approaches in neurodegenerative disease research and therapeutics expands our understanding of disease mechanisms, aids in drug discovery, facilitates personalized medicine, optimizes clinical trial design, and offers valuable insights into complex biological systems. These approaches complement experimental methods and contribute to the development of innovative and effective interventions for neurodegenerative diseases

In conclusion, insilico approaches in neurodegenerative disease therapeutics and research have

the potential to revolutionize our understanding and treatment of these complex conditions. By employing computational modeling, virtual simulations, and data analysis techniques, insilico approaches accelerate drug discovery, facilitate personalized medicine, optimize clinical trials, and provide valuable insights into disease mechanisms. These methods contribute to the development of innovative therapies and enhance our ability to combat neurodegenerative diseases in scientifically robust ways.

In conclusion, the early detection of neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis is a critical area of research, as it can allow for timely intervention and the implementation of measures to slow or prevent disease progression. Biomarkers, neuroimaging techniques, genetic testing, and other approaches are being studied as potential tools for early diagnosis of these conditions. The identification of specific biomarkers has the potential to revolutionize the way these diseases are diagnosed and treated, and could lead to earlier intervention and improved outcomes for patients. Further research in this field is needed to fully understand the potential of these approaches and to optimize their use in clinical practice. While significant progress has been made in the identification of potential biomarkers for neurodegenerative diseases, more research is needed to validate their reliability and clinical utility. It is important to carefully evaluate the sensitivity, specificity, and predictive value of these markers in order to determine their usefulness in clinical practice. The development and validation of biomarkers is a complex process that involves multiple stages of research, including discovery, verification, and clinical validation. It is important to carefully follow these steps in order to ensure that biomarkers are accurately and reliably detecting the presence of disease.

The use of biomarkers for the detection and management of neurodegenerative diseases has the potential to improve patient outcomes by allowing for earlier diagnosis and intervention. However, the use of biomarkers also raises ethical and legal issues, such as the potential for discrimination based on genetic testing results. It is important to carefully consider these issues and to develop appropriate guidelines and policies for the use of biomarkers in clinical practice. The identification and validation of biomarkers for neurodegenerative diseases is a complex and ongoing process that involves the collaboration of researchers from various disciplines, including neuroscience, genetics, and molecular biology. Continued support and investment in this research is needed in order to fully realize the potential of biomarkers to improve the diagnosis and treatment of these conditions.[11]

Overall, our findings suggest that EVs which are circulating might be used as a trustworthy biomarkers, providing us a inflative initiative point for the progress of innovative EV-based

treatment techniques. In this case, however, the extent of the The translation of the analysis of EV into clinical practise is based on a number of hotly debated factors. In this sector, there are still unanswered questions. To begin with, there is the confusing EV terminology. When data must be compared, the present literature identifies a serious challenge and replicated. It's also worth noting that EV detection has several drawbacks. Significant technological challenges, as well as their biological roles, are not fully understood today. The optimal approach should be able to detect EVs greater than 50 nm and even bigger. In conclusion, extracellular vesicles of neurodegenerative diseases. These small, membrane-bound vesicles are involved in various processes in the body, including cell-to-cell communication and waste removal. extracellular vesicles have shown the inflammation that leads to the death of nerve cells. Additionally, research has suggested that extracellular vesicles may have potential as diagnostic markers and therapeutic targets for these diseases. Further study is needed to fully understand the mechanisms by which extracellular vesicles contribute to neurodegenerative diseases and to develop effective treatments that target these vesicles.

## REFERENCES

[1] M. Y. Shaheen, "Applications of Artificial Intelligence (AI) in healthcare: A review," ScienceOpen Preprints, 2021.

[2] Z. Zhang, Y. Genc, D. Wang, M. E. Ahsen, and X. Fan, "Effect of AI Explanations on Human Perceptions of Patient-Facing AI-Powered Healthcare Systems," J Med Syst, vol. 45, no. 6, 2021, doi: 10.1007/s10916-021-01743-6.

[3] L. Giampietri et al., "Fluid Biomarkers in Alzheimer's Disease and Other Neurodegenerative Disorders: Toward Integrative Diagnostic Frameworks and Tailored Treatments," Diagnostics, vol. 12, no. 4. 2022. doi: 10.3390/diagnostics12040796.

[4] L. Wang and L. Zhang, "Circulating Exosomal miRNA as Diagnostic Biomarkers of Neurodegenerative Diseases," Frontiers in Molecular Neuroscience, vol. 13. 2020. doi: 10.3389/fnmol.2020.00053.

[5] Q. H. Vuong et al., "Artificial intelligence vs. Natural stupidity: Evaluating ai readiness for the vietnamese medical information system," Journal of Clinical Medicine, vol. 8, no. 2. 2019. doi: 10.3390/jcm8020168.

[6] M. Maciejczyk, A. Zalewska, and K. Gerreth, "Salivary redox biomarkers in selected neurodegenerative diseases," Journal of Clinical Medicine, vol. 9, no. 2. 2020. doi: 10.3390/jcm9020497.

[7] C. Scassellati, C. Bonvicini, L. Benussi, R. Ghidoni, and R. Squitti, "Neurodevelopmental disorders: Metallomics studies for the identification of potential biomarkers associated to diagnosis and treatment," Journal of Trace Elements in Medicine and Biology, vol. 60. 2020. doi: 10.1016/j.jtemb.2020.126499.

[8] M. Zhang and Z. Bian, "The Emerging Role of Circular RNAs in Alzheimer's Disease and Parkinson's Disease," Frontiers in Aging Neuroscience, vol. 13. 2021. doi: 10.3389/fnagi.2021.691512.

[9] L. Wang and L. Zhang, "Circulating Exosomal miRNA as Diagnostic Biomarkers of Neurodegenerative Diseases," Frontiers in Molecular Neuroscience, vol. 13. 2020. doi: 10.3389/fnmol.2020.00053.

[10] S. Rao and A. J. Boileau, "Novel Blood Biomarkers for an Earlier Diagnosis of Alzheimer's Disease: A Literature Review," International Journal of Medical Students, 2020, doi: 10.5195/ijms.2020.452.

[11] A. L. Walker, S. Z. Imam, and R. A. Roberts, "Drug discovery and development: Biomarkers of neurotoxicity and neurodegeneration," Experimental Biology and Medicine, vol. 243, no. 13. 2018. doi: 10.1177/1535370218801309.

[12] D. C. Goff, K. Romero, J. Paul, M. Mercedes Perez-Rodriguez, D. Crandall, and S. G. Potkin, "Biomarkers for drug development in early psychosis: Current issues and promising directions," European Neuropsychopharmacology, vol. 26, no. 6. 2016. doi: 10.1016/j.euroneuro.2016.01.009.

[13] L. Y. Ma et al., "Motor Progression in Early-Stage Parkinson's Disease: A Clinical Prediction Model and the Role of Cerebrospinal Fluid Biomarkers," Front Aging Neurosci, vol. 12, 2021, doi: 10.3389/fnagi.2020.627199.

[14] M. Milà-Alomà, M. Suárez-Calvet, and J. L. Molinuevo, "Latest advances in cerebrospinal fluid and blood biomarkers of Alzheimer's disease," Therapeutic Advances in Neurological Disorders, vol. 12. 2019. doi: 10.1177/1756286419888819.

[15] Q. Yuan, X. dong Li, S. miao Zhang, H. wei Wang, and Y. liang Wang, "Extracellular vesicles in neurodegenerative diseases: Insights and new perspectives," Genes and Diseases, vol. 8, no. 2. 2021. doi: 10.1016/j.gendis.2019.12.001.

[16] A. F. Hill, "Extracellular vesicles and neurodegenerative diseases," Journal of Neuroscience, vol. 39, no. 47. 2019. doi: 10.1523/JNEUROSCI.0147-18.2019.

[17] M. I. Mosquera-Heredia et al., "Exosomes: Potential disease biomarkers and new therapeutic targets," Biomedicines, vol. 9, no. 8, 2021, doi: 10.3390/biomedicines9081061.

[18] T. Soares Martins et al., "Diagnostic and therapeutic potential of exosomes in Alzheimer's disease," Journal of Neurochemistry, vol. 156, no. 2. 2021. doi: 10.1111/jnc.15112.

[19] S. Rastogi et al., "The evolving landscape of exosomes in neurodegenerative diseases: Exosomes characteristics and a promising role in early diagnosis," International Journal of Molecular Sciences, vol. 22, no. 1. 2021. doi: 10.3390/ijms22010440.

[20] C. M. Pedrero-Prieto et al., "A comprehensive systematic review of CSF proteins and peptides that define Alzheimer's disease," Clinical Proteomics, vol. 17, no. 1. 2020. doi: 10.1186/s12014-020-09276-9.

[21] D. B. Castellanos, C. A. Martín-Jiménez, F. Rojas-Rodríguez, G. E. Barreto, and J. González, "Brain lipidomics as a rising field in neurodegenerative contexts: Perspectives with Machine Learning approaches," Frontiers in Neuroendocrinology, vol. 61. 2021. doi: 10.1016/j.yfrne.2021.100899.

[22] J. O. Ojo et al., "Molecular Pathobiology of the Cerebrovasculature in Aging and in Alzheimers Disease Cases With Cerebral Amyloid Angiopathy," Front Aging Neurosci, vol. 13, 2021, doi: 10.3389/fnagi.2021.658605.

[23] "Alzheimer's Drug Discovery Foundation (ADDF)," in The Grants Register 2022, 2021. doi: 10.1057/978-1-349-96042-2\_16534.

[24] J. D. Álvarez, J. A. Matias-Guiu, M. N. Cabrera-Martín, J. L. Risco-Martín, and J. L. Ayala, "An application of machine learning with feature selection to improve diagnosis and classification of neurodegenerative disorders," BMC Bioinformatics, vol. 20, no. 1, 2019, doi: 10.1186/s12859-019-3027-7.

[25] E. Fenclová, J. Albrecht, P. Harsa, and R. Jirák, "Risk factors for Alzheimer's disease," Ceska Slov Psychiatr, vol. 116, no. 2, 2020, doi: 10.15354/si.20.re036.

[26] A. Slanzi, G. Iannoto, B. Rossi, E. Zenaro, and G. Constantin, "In vitro Models of Neurodegenerative Diseases," Frontiers in Cell and Developmental Biology, vol. 8. 2020. doi: 10.3389/fcell.2020.00328.

[27] L. Wang and L. Zhang, "Circulating Exosomal miRNA as Diagnostic Biomarkers of Neurodegenerative Diseases," Frontiers in Molecular Neuroscience, vol. 13. 2020. doi: 10.3389/fnmol.2020.00053.

[28] J. A. Soria Lopez, H. M. González, and G. C. Léger, "Alzheimer's disease," in Handbook of Clinical Neurology, Elsevier B.V., 2019, pp. 231–255. doi: 10.1016/B978-0-12-804766-8.00013-3.

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