BIOMARKERS

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ABSTRACT

Biomarkers have gained immense scientific and clinical value and interest in medical practice. Biomarkers can be used throughout the disease process. The markers can be used for screening and risk assessment prior to diagnosis. At diagnosis, symptoms can determine the degree, level, and choice of initial treatment. They can be used during treatment to monitor therapy, select additional treatments, or monitor disease recurrence.Advances in genomics, proteomics, and molecular pathology have led to many candidate biomarkers of clinical value. In the future, biomarkers identified using new technologies will be incorporated into clinical practice to help "personalize" treatment and prevent disease. The application and identification of biomarkers in clinical and clinical settings has a major impact on clinical and clinical practice. people. In this section, we discuss the history, various definitions, classification, properties, and discovery of biomarkers. In addition, the potential use of biomarkers in the diagnosis, diagnosis and treatment of various diseases has been reviewed over the past decade.

Keywords: Biomarkers, epidemiology, medicine, monitoring, pharmacology/toxicology

I. INTRODUCTION

In recent years, biomarkers have become important in drug discovery, determining drug action mechanisms, examining early performance indicators of toxicity and development, and identifying patients who will respond to treatment. In addition, many tools capable of determining this complexity have emerged throughout science and the use of such information in personalized medicine is increasing [1]. Biomarkers are currently used in personal drug or therapy treatment and to evaluate the safety of drugs. [2,3]. Chapter of the National Academy of Sciences Report (USA NRC, 1989b) uses the term "biomarker" broadly to include virtually any measure that indicates that it may be biological and potentially hazardous, chemical or toxic.The measured response can be functional, physical, biochemical or molecular interactions at the cellular level. [4] Biomarkers produced by diseased organs (such as tumors) or the body's response to disease. Biomarkers can be used throughout the disease process.The markers can be used for screening and risk assessment prior to diagnosis. Once diagnosed, symptoms can determine the level, degree, and choice of initial treatment. They can then be used to monitor treatment, select additional treatments, or monitor disease recurrence [5]. Therefore, identification of biomarkers includes all diagnostic tests, imaging procedures, and other objective measurements of the patient. Biomarkers can also change clinical endpoints, reducing the time and cost of Phase I and II clinical trials.Biomarkers cover a wide spectrum of human health and have been used since the dawn of understanding of human biology and diseases. So why are biomarkers getting so much attention today? Genetics, genomics, proteomics, modern imaging techniques and other high-throughput technologies allow us to measure more markers than ever before. In addition, we gain a better understanding of the disease, the goals of intervention, and the impact of pharmacological agents. [6]

II. HISTORY OF BIOMARKERS

The term "biomarker" was first used in 1973 by Rho et al. With or without special biological properties. However, the term is older, being used by Mundcourt in 1949 for "biochemical marker" and Porter in 1957 for "biomarker". The term "surrogate" has been used as a synonym for biomarker since the early 1980s. The concept of “representative” means “without a doubt” [7,8,9]. Representative endpoints or surrogate markers are defined as biomarkers of disease progression [10]. Studies have shown that the importance of using a "biomarker" increases over other concepts [11]. The term "biomarker" is an abbreviation for "biomarker". Biomarkers, or biomarkers, were defined by the National Institutes of Health Biomarker Definition Working Group in 2000 [12]. According to this definition, biomarkers are indicators of biological processes and pathogenic organisms or responses to drugs that are frequently measured and measured.This definition is widely accepted as the universal definition of clinical pharmacology biomarkers. Also, as the US Food and Drug Administration (FDA) states, a biomarker, or a biomarker, is a measurable indicator that can play a role throughout disease; research and development of treatment; disease, diagnosis and provision of care; or disease progression or response to treatment [13]. Thus, biomarkers can be defined as specific substances associated with normal biological processes, pathogenic processes, or biological responses to external influences or chemicals or group of drug agents, but do not include drugs or their metabolites present in the body. Tissue (inner needle) [6,14]. The idea of using biomarkers to diagnose disease and improve treatment dates back to the early days of medicine. The practice of urethroscopy - examining a patient's urine for signs of infection - dates back to the 14th century or earlier, when doctors routinely examined patients' urine for color and deposits [15].In the 1960s, researchers discovered that some patients with chronic myeloid leukemia (CML), a type of leukemia in which adult myeloid cells multiply in the bone marrow, had a cancer-related genetic mutation, a short version of chromosome 22. is is. It is called the Philadelphia Chromosome, which is caused by a mutation between chromosomes 9 and 22. Researchers used Philadelphia chromosome as a biomarker to show which patients would benefit from drugs (tyrosine kinase inhibitor) that target abnormal proteins [16]. In the late 1980s, researchers discovered that HIV could be used as a marker of infection and subsequently to measure the effectiveness of antiretroviral therapy. Viral load indicates that patients receiving the combination therapy have a lower viral load than those receiving immunosuppressive therapy, thus again having a positive effect in slowing the disease.Finally, viral load biomarkers are used to design and evaluate highly active antiretroviral drugs (HAART), which are among the many drugs used by many people living with HIV today. Perhaps the most famous biomarker in recent drug development history is the discovery of the HER-2 gene and its receptor in the mid-1980s. The HER-2 receptor is overexpressed on cancer cells in 20-30% of cancer patients. The anticancer drug trastuzumab (Heretic) was developed to target the HER-2 receptor in overexpressing patients and has been successful in reducing the risk of breast cancer in many women [5]. People with diabetes can check their blood sugar levels with a glycated hemoglobin (HbA1c) test, which shows blood sugar levels over the past two weeks. Liver function tests (LFT) to evaluate liver toxicity and prostate specific antigen (PSA) to assess cancer and disease risk. These historical biomarkers have been used as part of clinical practice for decades. [17,18]

III. CHARACTERISTICS OF AN IDEAL BIOMARKER [4, 6, 19]

- An ideal biomarker should be accurate, reproducible and superior
- Easy to sample
- Should be safe and easy to measure.
- Clinical trials should be cost-effective and a good treatment should be found to update biomarkers.
- Biomarkers should provide evidence supporting a reasonable basis for their use. Evidence indicates that some measure or change occurs in a physiological or pathological process within a short period of time.
- Reliable, capable analysis for measuring biomarkers. Changes in biomarkers should be detected with accuracy, precision, robustness, and reproducibility;
- Energy efficiency means no interference or adverse effects to avoid inconvenience or inconvenience to healthy people or patients
- Simplicity means easy to use and low cost of equipment. The simplicity makes it widely accepted in medicine and medicine.

IV.CLASSIFICATION OF BIOMARKERS

Biomarkers have been classified based on different parameters, including their characteristics, clinical applications, and genetic and molecular biology methods

A. Based on genetic biology: Type 0 - Natural history markers**,** Type 1 - Drug activity markers**,** Type 2 - Surrogate markers.

B. Based on characteristics: Imaging biomarker, Cellular biomarker, Molecular biomarker

C. Based on Clinical applications:, Diagnostic biomarker, Prognostic biomarker, Therapeutic biomarker [15,19]

A. **Based on genetic biology (Genetic Biomarker)**:[15,20,21,22]
Biomarkers with biophysical properties that allow measurement in biological samples (such as plasma, serum, cerebrospinal fluid, bronchoalveolar dissection and biopsies), nucleic acid-based biomarkers such as gene changes or polymorphisms, and many gene expression molecules. Over the years, genetic (DNA mutations, DNA single nucleotide polymorphisms, karyotype) changes have been widely used as diagnostic biomarkers. The MarkerDB database contains 26374 genetic biomarkers and 154 karyotype biomarkers. DNA biomarkers are the largest collection of biomarkers associated with more than 319 diseases or conditions. Genetic biomarkers can be measured in the DNA of all nucleated cells extracted from biological samples, especially cancer cells, because most cancer cells are capable of altering the change.

(Type 0) - Natural history markers:
A marker of natural history of a disease and correlates longitudinally with known clinical indices.

(Type 1) - Drug activity markers:
A marker that captures the effect of a therapeutic intervention in accordance with its mechanism of action.

Type 2) - Surrogate markers:
A marker intended to substitute for a clinical end point; a surrogate end point is expected to predict clinical benefit or lack of benefit on the basis of epidemiology, therapeutic, Patho physiological or other scientific evidence.

B. **Based on Characteristics**

a. Imaging Biomarkers:[23]
Biomarkers are indicators that measure biological processes in the body, pathological processes, or the body's response to treatment. Imaging-based biomarkers use a variety of techniques to capture images of anatomical and physiological changes in the body. They are generally non-invasive and produce intuitive, multidimensional results. They can produce good and valuable information and are generally good for patients.

X-Ray: X -ray technology has been in use for over 100 years and almost in biomedicine to identify markers.

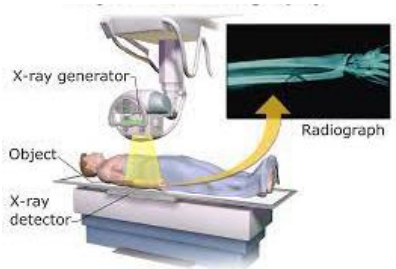

Figure 1: X-ray Machine

Computed Tomography (CT): Sometimes also called computed axial tomography. The 2D image is then converted to a 3D image. Introduced in the 1970s, CT expanded its use.

Figure 2: CT Scanner

Magnetic Resonance Imaging (MRI): MRI can distinguish soft tissues better than tomography.The first MR image was released in 1973. Additionally, optical imaging is often used more and more in drug discovery and preclinical animal research, and in human clinical applications such as treating CT scans.

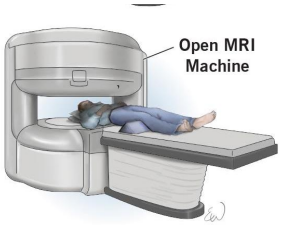

Figure 3: MRI Scanner

Positron Emission Tomography (PET): Computed Tomography provides 3D images of the region of interest. The first PET machine for humans was introduced in the early 1970s

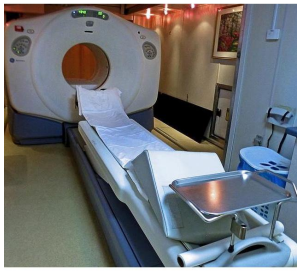

Figure 4: PET Scanner

b. Cellular Biomarkers

Cellular biomarkers are biological and measurable markers that can be used in clinical and laboratory tests. Cellular biomarkers are often measured and evaluated in blood, body fluid, or soft tissue for prognosis or probability to respond to a specific treatment. This type of biomarkers allows for the isolation, sorting, quantification, and characterization of cells by their morphology and physiology properties [24, 25].

c. Molecular Biomarkers [26,27,28,29]

Molecular biomarkers are indicators based on proteomic and genomic methods.They are important for diagnosis and have applications in epidemiological screening, randomized clinical trials, disease prevention, surveillance and control. These biomarkers have biophysical properties and can be measured in biological samples such as plasma, plasma, cerebrospinal fluid, bronchoalveolar lavage fluid, and biopsies. They include molecules ranging from small to large, such as peptides, proteins, lipid metabolites, nucleic acids (DNA and RNA), and others. Molecular biomarkers are divided into three subtypes: chemical and protein biomarkers.

Chemical biomarkers: Chemical biomarkers contain information about birth through metabolic or genetic diseases such as cancer, disability and metabolic diseases, infectious diseases, nutritional foods, drugs, chemicals, and pollution.In total, 1089 drug biomarkers were associated with 448 disease/diseases and 106 outcomes in the Molecular Biomarkers Online Database (MarkerDB). Many biomarkers can be measured quantitatively and accurately with high efficacy and reliability [30,32].

Protein biomarkers: Protein biomarkers are useful for detecting many biological changes. They can be used as indicators of changes in inflammation, immunity and stress or other diseases such as cancer, diabetes, heart disease, neurological disease and other conditions. The MarkerDB database represents 142 protein biomarkers covering more than 160 diseases [30,31,33]

C. **Based on Clinical Applications:**

Disease-related biomarkers may indicate whether the disease is already present, whether there is a threat of disease, or how the disease arose in a patient.

a. **Diagnostic biomarker:**

Diagnostic biomarkers provide a way to identify a population with a disease. (I.For example, cardiac troponin for the diagnosis of myocardial infarction). These biomarkers are used to identify diseases such as cardiac troponin for diagnosis of myocardial damage, 3-hydroxy fatty acid profile for Planctomyces, glycans as cancer biomarkers, visceral fat and altered metabolism Glutamate, catechin challenge. mortality in patients with heart disease, cystatin-C for glomerular filtration, liver-type fatty acid-binding protein (L-FABP) as a diagnostic biomarker to predict the severity of kidney injury or oxidative stress [31, 34, 35, 36, 37].

b. **Prognostic biomarker:**

Prognostic biomarkers are associated with outcomes.For example, overexpression of Her-2/neu in breast cancer or EGFR in cancer indicates a poor prognosis. Such markers are often the basis for designing clinical trials to include or identify patients. Prognostic biomarkers provide information about the disease by screening and monitoring the disease and measuring the increase or decrease in the internal precursors that the disease may reach. For example, blood pressure and cholesterol (for heart disease), N-acetyl-beta-D-glucosaminidase (for heart failure and kidney failure), D-serine (for ketamine for antidepressants), and osteocalcin (for bone and healthy bone metastases). have been used as prognostic biomarkers [31,38,39,40,41].

c. **Therapeutic biomarker:**

These biomarkers are useful in the treatment of illness and play an important role in monitoring the response and treatment of stress or illness. Clinical biomarkers are proteins such as miRNAs and exosomes that can be used for therapy. Takamura et al. using malondialdehyde-modified LDL.As a good indicator of clinical outcome in patients after endovascular intervention for peripheral arterial disease. Clinical studies of D-serine demonstrate its effectiveness as a clinical biomarker in patients with schizophrenia and depression. As a tumor biomarker, Ca15-3 can be used to monitor breast cancer therapy. Use of HBA1C (glycosylated hemoglobin A1C) to monitor the progress of diabetes treatment. [39, 42-48]

V.APPLICATIONS OF BIOMARKER

The potential applications of biomarkers for disease diagnosis, diagnosis, diagnosis and treatment in medicine have been greatly expanded. Biomarkers can be of different types, such as physical, physiological, and histological (tissue biopsy). Perhaps the type most relevant to early clinical research are biochemical biomarkers derived from bodily fluids, suitable for early investigators. Molecular biomarkers of safety have been used in preclinical and clinical research for many years. [51]. Accurate diagnosis is important in chronic diseases, the treatment of which may require the use of drugs for many years, especially in cases where treatment has serious side effects. In these cases, biomarkers have become important as they can confirm difficult diagnoses and also make them possible. Many diseases, such as Alzheimer's disease or rheumatoid arthritis, often begin early asymptomatically. In these asymptomatic patients, actual symptoms may be more or less severe. In these cases, biomarkers help identify high-risk individuals in a timely and reliable manner so that they can be treated as soon as possible before or after the illness. This may be a blood sample taken by a doctor, a urine or saliva sample, or a drop of blood like those diabetes patients extract from their own fingertips for regular blood-sugar monitoring.[49, 50]

A. Covid-19 [51 - 63]

The novel coronavirus disease (SARS-CoV-2 or COVID-19) first emerged in Wuhan city, China in December 2019. COVID-19.Unfortunately, this new virus has caused more than a million infections and deaths worldwide. In the study reported by Pu et al., deep learning techniques and high-resolution tomography images were used as biomarkers to examine the parameters associated with COVID-19. The findings suggest that certain biomarkers may not be able to distinguish all cases of COVID-19 in the filter from community-acquired pneumonia. However, image analysis can identify a small fraction of COVID-19 patients because certain images can distinguish more than non-COVID-19 patients. Biomarkers of myocardial injury or heart disease, particularly cTnI, cardiac troponin T (cTnT) and D-dimer, have demonstrated their potential in the prediction, diagnosis and treatment of COVID-19.High serum amyloid A, C-reactive protein, urea and creatinine (kidney biomarkers), ferritin and lactate dehydrogenase levels have been used as biomarkers in the diagnosis of COVID-19.

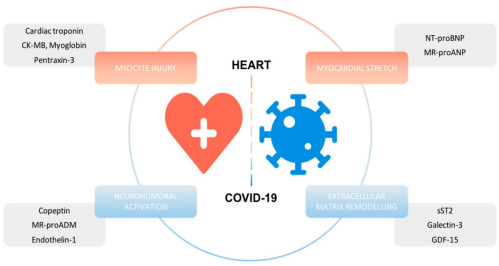

Figure 5: biomarkers of COVID-19

B. **Cancer [10, 64 -77]**

Cancer is the leading cause of death worldwide and is a contagious disease that occurs when it metastasizes to the remaining organs.fear of the body. Cancer biomarkers play an important role in improving our understanding and knowledge of cancer processes in clinical practice, enabling the development of better diagnoses and reducing the number of acute toxicity lines. They were designed to assess cancer risk, examine interactions between tumors, and influence tumor and cell viability. Proteins, metabolites, nucleic acids and extracellular vesicles can be identified in the urine, which is an important part of the biopsy fluid.

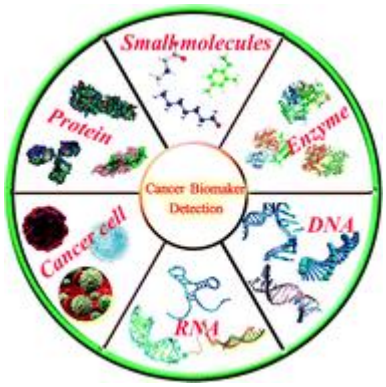

Figure 6 : Cancer Biomarkers

C. **Disorders of Skeletal Muscles and Bone [78 - 84]**

Skeletal muscles can be damaged throughout life by exercise, contracture, chemical injury, immunodeficiency, or muscle degeneration. MRI and proton magnetic resonance spectroscopy have been used to characterize and evaluate GNE myopathy, a rare degenerative skeletal muscle disease. In addition, MRI is a diagnostic tool and biomarker to evaluate changes in adipose tissue and fibrous tissue. Measurement of pyridinoline, deoxypyridinoline and osteocalcin to predict future bone disease with clinical outcomes. Plasma interleukin-6 has been identified as a marker of inflammation and can be used to predict long-term changes in growth retardation, joint pain, and hip dysplasia.Fourier transforms infrared spectroscopy as a biomarker for primary mitochondrial myopathy and other mitochondrial diseases. This device is a rapid, non-invasive, non-destructive, sensitive and specific biomarker test that requires small samples. The use of amino acids, especially cysteine, methionine, taurine and glutathione, which are important components of skeletal muscle, can be used for the prevention and diagnosis of skeletal muscle. Research objective may identify how to use MRI technology to evaluate osteoarthritis and outcomes of cartilage and cartilage treatment in osteoarthritis. In this context, MRI has proven promising in diagnosing soft tissue swelling and cartilage damage in rheumatoid arthritis.If found to be a reproducible biomarker, MRI can be used to help identify the potential of new treatments, determine dosage, and stratify patients for risk with early assessment.

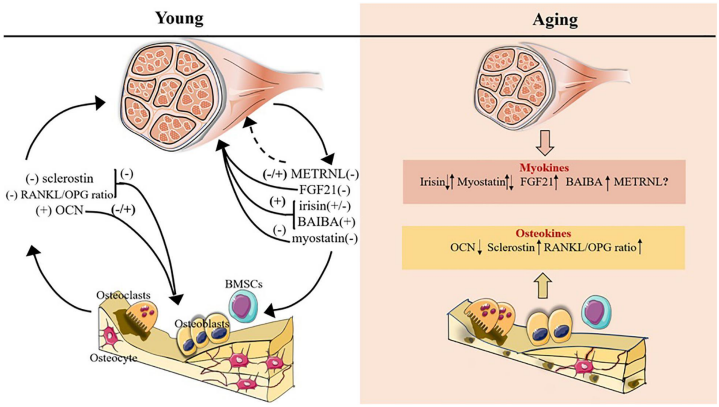

Figure 7: Biomarkers of arthritis

D. Heart failure [23, 85 - 99]

New ideas for evaluating heart disease and its treatment are needed to facilitate the development of new treatments. Intravenous ultrasound (IVUS), MRI, or multislice CT can be used to assess central function parameters to assess the progression of atherosclerosis and prevent heart failure. The development of these strategies to measure progress will require a thorough assessment of the current state of knowledge about measurement methods, standard measures, and appropriate testing to measure association with treatment response. Heart failure (HF) is a complex disease with multiple phenotypes caused by multiple cardiac and extracardiac pathophysiological mechanisms. Emergency and specialized testing in the emergency room can be important to quickly "diagnose" heart failure. Image biomarkers provide important information about the function and abnormal functioning of the heart, but reading these biomarkers does not identify subclinical and early stages of heart failure. Protein biomarkers currently used to predict heart failure prognosis are released from the heart, indicating the heart's value as tissue-specific damage or other brain-based responses to heart failure. Natriuretic peptide (NP), For example, measurements of brain natriuretic peptide (BNP) and BNP N-terminal prohormone and cardiac troponin are included in the American Heart Association and European Society of Cardiology guidelines for the management and diagnosis of heart disease. The predictive utility of NT-proBNP and BNP biomarkers in various heart failures (such as congestive heart failure or congestive heart failure) has been investigated in several studies, given the strong evidence for their increasing value. Other diagnostic biomarkers, such as biomarkers of oxidative stress (eg, oxidative stress), growth factor-15), cardiovascular (eg, galectin-3) and inflammation (eg, soluble ST2 receptor) may be added to the treatment of heart disease.Recent advances in genetic analysis have opened new avenues to study the pathophysiology of cardiovascular diseases and paved the way for the development of gene-based biomarkers. A new approach to identify DNA/RNA-based biomarkers using omics technology that can identify genome-wide (GW) and transcriptome-wide (TW) genetic variants. Omics analysis can understand the molecular mechanisms behind the disease and identify genes that could help identify patients with heart failure. New biomarkers of heart failure may promote widespread use of biomarkers, improving diagnosis and prognosis, and therefore patient care. There is interest in various methods because they are more useful than single biomarkers for improving risk stratification and increasing the accuracy of cardiovascular disease.

E. **Chronic Obstructive Pulmonary Diseases** [15]

High resolution computed tomography of the thorax may be useful in the evaluation of disease in COPD, in which emphysema is an important component, particularly emphysema. Complications associated with alpha 1 antitrypsin deficiency. While data to date indicate that high-resolution CT (HRCT) can provide reliable assessment of lung structures in fewer patients than it would take time to tell the difference between a diagnosis of pneumonia or death, it still remains uncertain.

F. **Neurocognitive Diseases: [100, 101]**

Currently, the treatment of chronic neurological diseases such as Parkinson's and Alzheimer's is based on recent symptoms, whose progression may require years of monitoring. Functional imaging such as FDG-PET as a measure of glucose metabolism may provide biomarkers to quantify early, subtle changes in disease. Focusing on the use of new techniques to evaluate and respond to measures for neurocognitive diseases and depression may also lead to new ways to monitor treatment for these problems. For example, evaluation of amyloid content from PET scans alongside MRI measurements

may be the best methods to demonstrate the effects of Alzheimer's treatment.Markers that provide early disease information can make prevention efforts more effective.

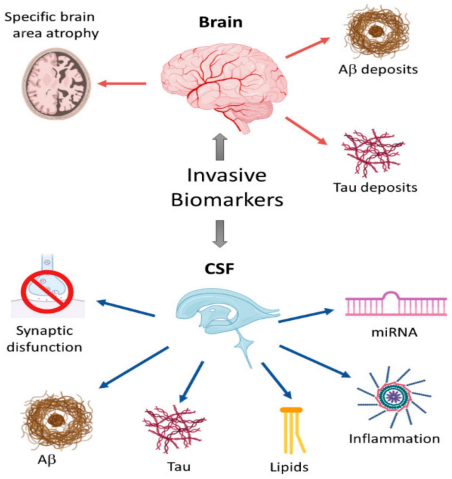

Figure 8: Biomarkers of Alzheimer's Disease

G. **Kidney Disease [102 - 106]**

The role of the kidney is to filter the blood, produce urine, remove toxins and maintain the volume of different fluids in the body. Microalbumin, N-acetyl-β-glucosaminidase, fatty acid binding protein, and cysteine-rich protein have been used successfully as biomarkers of kidney disease. Hepcidin-25, an iron-binding protein associated with acute kidney injury, can be used as a new kidney biomarker in blood and urine in the diagnosis of renal dysfunction after cardiac surgery.Novel Synthetic Antibodies Against Polypyrrole/Multiwalled Carbon Nanotubes on Carbon Screen Printed Electrodes Designed to Detect the Renal Biomarker Cystatin C in Clinical Practice. Recently, the FDA approved a panel of 6 standard biomarkers for the detection of preclinical ASO, including clusterin for urinary creatinine, cystatin C, kidney injury molecule 1, N-acetyl-β-D-glucosaminidase, intermediate Granulocyte gelatinase-associated lipocalin and osteopontin. Confirmed. induced kidney pathology. D-serine levels in blood and urine are often used as dual biomarkers to indicate kidney function and disease.

H. Liver disease [107 - 112]

The liver is an essential part of the body that performs many important functions such as digestion, distribution of food, conversion and storage of food into energy, helping to filter toxins and removing toxins from the blood. There are many liver diseases such as hepatitis, hepatitis, cancer, cirrhosis, hemochromatosis, Wilson's disease, fascioliasis, liver failure and autoimmune diseases. Liver disease can be caused by many factors and conditions, including diseases, medications, alcohol, and toxins. Symptoms of hepatitis vary according to the occurrence and severity of the infection and can be easily confused with other conditions, but usually include yellowing of the skin and pores, soft, dark urine, swelling of the stomach and legs, easy bruising and vomiting.Liver disease is often difficult to diagnose; however, the use of biomarkers facilitates the diagnosis and follow-up of liver disease. Liver damage can be confirmed by liver tests, including albumin, alanine aminotransferase, lactate dehydrogenase, aspartate aminotransferase, alkaline phosphatase, and gamma-glutamyltransferase. Section Alanine aminotransferase is a surrogate biomarker that is highly specific for liver disease and can be detected in blood. Hyaluronic acid, bilirubin, cytokines, laminin and fibroblast growth can be used as biomarkers of the liver.

I. **Gastrointestinal Disorders [113 - 121]**

Gastrointestinal Disorders are diseases of the entire human digestive system, from the mouth to the anus. Metabolic intermediates are useful biomarkers for the diagnosis of intestinal diseases using non-invasive methods. Organic compounds such as acetone, ammonia, ethanol, indole, carbon disulfide, 2,3-butanedione and acetic acid can be used as biomarkers. These low molecular weight drugs are produced in the digestive tract, pass through the bloodstream, reach the lungs and appear in the respiratory tract, and are finally analyzed by GC-MS techniques. Calprotectin is used as a non-invasive biomarker in the treatment of active inflammatory bowel disease (IBD) and digestive system diseases.Lactoferrin is a laboratory biomarker used to diagnose Clostridium difficile. MicroRNA, surface acoustic waves, carbon black polymer composites, carbon black polymer composites, metal

oxide semiconductors, etc. such as electronic noses have been used to identify intestinal diseases. Fatty acid-binding proteins have also been evaluated as diagnostic biomarkers for inflammatory bowel disease. Urine metabolomics, such as tricarboxylic acids and amino acids, are different in IBD patients and healthy people and may serve as non-invasive biomarkers of gastrointestinal disease. Most of the potential biomarkers currently studied have not yet been validated and approved for real-world clinical use to screen or diagnose certain gastrointestinal diseases; however, the future of biomarkers looks risky.While some studies have shown positive results for different biomarkers, the heterogeneity of the findings raises our questions. Therefore, extensive research and clinical trials using methods developed by multicenter consortia are needed.

Specific Organ Biomarkers Tests [51]
Liver Function: Transaminases , bilirubin, alkaline phosphates.
Kidney Function Serumcreatinine, creatinine clearence, cystatinC.
Skeletal Muscle Marker: Myoglobin.
Cardiac Muscle Injury: CK-MB, teroponinI (or) T.
Bone markers: Bone specific alkaline phosphates.

VI. BIOMARKER AS AN EMERGING TOOL [122 - 125]

Biomarkers are useful throughout drug discovery and development. In the past, biomarkers tended to appear in drug development projects as a time-consuming process—using leftover samples and remaining budgets—often resulting in incomplete or insufficient data

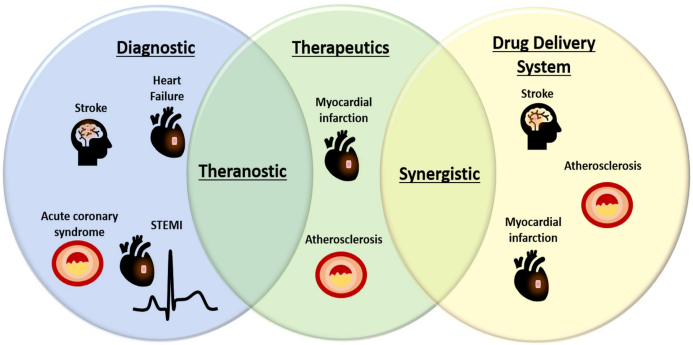

Figure 9: Biomarkers in Drug Research

However, they are now becoming more and more integrated into all stages of the development process, ranging from:

- Target discovery
- Evaluation of drug activity
- Understanding mechanisms of action
- Toxicity and safety evaluation
- Internal decision making
- Clinical study design
- Diagnostic tools
- Understanding disease processes

Biomarker research will eventually become an integral part of the drug development process. The ultimate goal is to create more effective drugs at lower cost. Although it is still early days and there are many questions to be answered, the promise of biomarkers is bright. The clinical development of gefitinib, an oral epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI), is a challenging example of biomarker development. During the performance of large randomized trials, changes in biomarkers will become the rule rather than the exception.Although the initial candidate biomarker is evaluated early in the development phase, knowledge grows exponentially as research and clinical information is widely published and clinical information is linked to action. Translation work increases. Biomarkers that identify prodromal manifestations can lead to early diagnosis or enable determination of the outcome of interest in the early stages of the disease. Biomarkers are used as biomarkers that represent subclinical symptoms, disease stages, or disease surrogate outcomes.

Biomarkers used for screening or diagnosis also often represent the outcome of the disease. Identification of individuals who should be affected or who are in the early stages of the disease, possible use of biomarkers such as reducing disease heterogeneity in clinical trials or infection studies, and influence the history of the disease, including the following stages: induction, incubation. and discovery, the purpose of clinical trials.Its efficiency and accuracy outweigh the difficulty of obtaining tissue from patients. In research and practice, diagnostic tests for diseases are used with increasing frequency. In diagnostic work, the collection of information from various sources, some of which includes the results of the diagnosis, leads to the main goal of increasing the risk of diagnosis. Diagnostic tests may be performed less frequently for other reasons (such as assessing disease severity, predicting disease onset, or monitoring response to certain treatments): severe disease predicts disease severity. Another advantage of this diagnosis is that it reduces the heterogeneity of the disease in clinical trials or epidemiological studies, leading to a better understanding of the history of the disease involved, which includes the induction, incubation, and detection phase.

VII. BIOMARKER DEVELOPMENT PROCESS [19]

The biomarker development process involves several iterative steps that begin with the discovery of biomarkers in healthy and diseased samples. To ensure that effective, evidence-based biomarker development for clinical and research is still required, a development process that includes many different aspects of regulatory integration Acts is needed. The field is rapidly changing due to continued and recent growth in computing, analytics and measurement. The biomarker development process includes the following stages: preanalytical and analytical validation, clinical validation, regulatory approval, and clinical demonstration. In the pre-evaluation phase, indicators are standardized and quality indicators such as procedures, storage and collection are reviewed.Analytical validation for a biomarker to ensure that the test is reproducible, reliable, and has an appropriate level of specificity and sensitivity enhancement. Biomarkers have been associated with clinical and biological products through relevance (level of evidence). However, there are some difficulties in the development of biomarkers, for example:

- The scientific basis of some biomarkers is not always investigated, making it difficult to identify and accept biomarkers in the future. In addition, it is important not to misinterpret biomarker measurements and not to associate biomarkers with disease.
- Due to longer clinical trials or more testing, the cost of biomarker development will increase.
- The development and characterization of biomarkers often requires significant time and resources. More evidence for benefit-risk analysis is often required for appropriate purposes rather than as part of the regulatory approval process for medicinal products.
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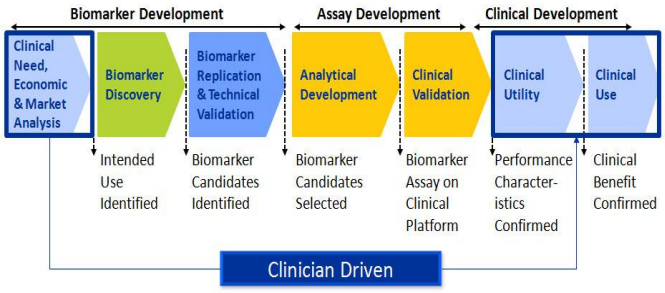

Figure 10. Biomarker Development Process

VIII. CONCLUSION

Biomarkers are part of new medical tools and are essential for the diagnosis, diagnosis and treatment of various diseases. There are benefits to using biomarkers to study many aspects of disease, develop drugs, and monitor the effects of treatment. Biomarkers promise to provide more sensitive and specific testing than existing measurements, improve decision making, and contribute to the development of treatment. Further efforts are being made to explore the biomarker frontier to discover new and/or better biomarkers to improve health and develop better treatments. However, because the mechanisms leading to disease pathogenesis are often complex, it is easier to identify useful biomarkers for assessing drug response, diagnosis, and follow-up of diseases to better understand disease-associated abnormalities and chemical processes.Gathering this information is a challenge for physicians and

primary health care professionals and others involved in biomarker analysis. The distinction between potential biomarkers and reliable biomarkers that can be used worldwide to guide important clinical and commercial decisions is one of the biggest challenges in the biomarker field. Biomarkers, which are changes in tissues or body fluids, provide a powerful way to understand chronic diseases with their use in at least 5 areas such as screening, diagnosis, follow-up, predicting disease recurrence and clinical care. Biomarkers that identify prodromal manifestations can lead to early diagnosis or enable determination of the outcome of interest in the early stages of the disease. Biomarkers are used as biomarkers to represent subclinical symptoms, disease stages, or surrogate disease outcomes. Biomarkers are specific only to a particular drug or disease, so development costs should be carefully considered. Good biomarkers should influence clinical assessment to improve patient care. Treatment decisions based on accurate test results should be more valuable than those based on false positive or negative results. Biomarkers should reduce costs and adverse effects while preventing mortality in a risk management environment. The validity of a biomarker is determined by comparing it with an ideal biomarker and investigating its properties.

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