World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Advanced neural network systems for analysis of blood-based biomarkers in metastatic disease detection

Toochukwu Juliet Mgbole *

Computer Information Systems, College of Engineering, Prairie View A&M University, Texas, United States.

World Journal of Advanced Research and Reviews, 2025, 25(01), 662-686

Publication history: Received on 28 November 2024; revised on 07 January 2025; accepted on 09 January 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.25.1.0083

Abstract

Neural network systems have become the gold provocative standard in blood-based biomarker analysis for metastatic disease diagnosis, providing higher sensitivity and specificity for early cancer detection. The lexical method also showed that recent developments in artificial intelligence and machine learning technologies allow for the complex interpretation of various types of biomarkers, such as circulating tumor cells, cell-free DNA, microRNAs, and proteins. Many biochemical patterns of biomarkers could be easily handled through sophisticated algorithms and depending on these active approaches in diagnosing metastatic outcomes more accurately at earlier stages. Literature analysis involved a targeted selection of scientific peer-reviewed articles dedicated to neural network utilization in blood-based biomarker screening for cancer. Doing a systematic evaluation critically assessed methodologies associated with artificial intelligence, types of biomarkers, methods of detecting biomarkers, and clinical validation strategies. Filtering was done based on several factors including the identification of new architectures for neural networks, new biomarker analysis methods, and clinical applications primarily focusing on the early detection of metastatic diseases. Analysis of reviewed studies showed a high diagnostic accuracy when neural network systems are used for biomarker analysis. Volumes in Cancer Computational Biology Vol reported that the machine learning models have achieved different sensitivity rates of over 90% including the ability to detect early-stage metastatic disease. The use of several categories of biomarkers and application-improved neural networks for their evaluation showed that the combined use of markers yields better diagnostic results than using single biomarkers. Neural network systems have significant potential to transform metastatic disease diagnosis using circulating biomarker detection. Using sophisticated computational models biomarker patterns are analyzed in detail and the diagnosis is made earlier, thus contributing to better treatment outcomes. Some complexities that are potential barriers include enforcing analysis protocols as standards, correcting and calibrating, and embracing routine technological practice. High-end artificial neural networks are the new frontier in blood-based biomarker analysis of metastatic disease diagnosis. Applying AI within the classic biomarker detection approach increases diagnostic reliability, detection timeliness, and the overall outlook for patient treatment. The advancement in neural network architectures as well as biomarker analysis techniques provides for further improvement in cancer diagnostics in the future.

Keywords: Artificial Intelligence; Machine Learning; Cancer Detection; Liquid Biopsy; Precision Medicine; Molecular Diagnostics

1. Introduction

Blood-derived biomarkers comprise numerous molecular components which include; circulating tumor cells (CTCs), cell-free nucleic acids (cfNAs), exosomes, and protein biomarkers that can be detected and quantified via liquid biopsy methodologies. These biomarkers have some advantages over traditional methods including; non-invasive, real-time, and the ability to establish variability of tumor microenvironment (Jopek et al., 2021). Nevertheless, the identification

* Corresponding author: Toochukwu Juliet Mgbole

of these biomarkers is challenging due to their low levels and the presence of interference from complex matrices in circulation (Aswathy et al., 2021).

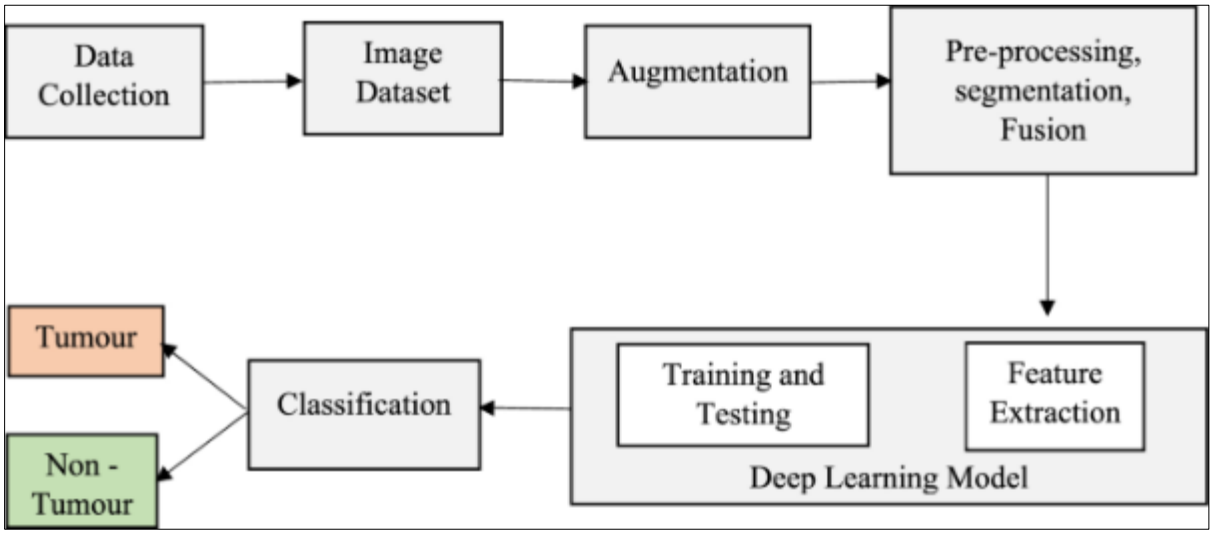

Figure 1 Diagnostic ability of deep learning in early cancer detection

Machine learning and deep learning techniques especially using an advanced neural network system are proven to be pivotal in the analysis and interpretation of complex biomolecule data such as blood-based biomarkers (Wang et al., 2021). Interestingly, neural networks, which are similar in structure to the human brain, are rather suitable for biomarker analysis and cancer detection as the networks can detect patterns within large datasets successfully (Prkačin et al., 2021). Neural net algorithms including Convolution Neural Net (CNN) and Recurrent Neural Net (RNN) have become relatively impressive when implemented in numerous biomedical applications in Imaging, genomics, and proteomics (Barioni et al., 2021).

The combination of AI-driven neural networks with blood-based biomarkers has a great capability to move forward the early detection and tracking of metastatic disease. By using the potential of constructing neural networks obtaining in-depth information about multi-omic data from liquid biopsies will help researchers identify complex patterns and signatures, that are linked to metastatic spread (Irajizad et al., 2022; Uttley et al., 2016). For instance, deep learning models of transcriptomic, proteomic, and metabolomic data derived from blood specimens can help identify metastatic cancers from localized tumors or other benign diseases (Das et al., 2023; Kurozumi & Ball, 2021). Additionally, CTCs and cfNAs have been further utilizing AI technologies to understand the molecular profile of metastatic lesions optimizing treatment protocols and monitoring of treatment efficacy (Dakal et al., 2021; Zachariah et al., 2018).

However, several issues have not yet received sufficient attention in this area of research. It is necessary to maintain data collection, processing, and analysis procedures as consistent across all instances as possible to achieve report replication and to enable clinical application (Brito-Rocha et al., 2023). In the same regard, there are issues of interpretability and transparency of the models, most especially the deep learning models keeping off the adoption of these models in the clinical practice. Solving these tasks shall involve interdisciplinary coordinated approaches that imply end-users such as clinicians, biologists, bioinformaticians, and AI specialists (Liu et al., 2021; Albaradei et al., 2023).

1.1. Evolution of Blood-Based Biomarker Analysis

Cancer diagnostics has had a significant evolution in the last decade mainly because of the molecular analysis of biomarkers in blood; this is an important shift from phosphochromatin tissue-based biomarkers. The identification and classification of early methodologies for detection have shifted from core protein to complex molecular markers facilitating detailed disease diagnosis with biopsies. Comprehensive profiling technologies have appeared that can identify various biomarkers at once: CTCs, cfDNA, and miRs, offering new possibilities for the monitoring of cancer progression and aggression. The combination of molecular biology procedures with powerful detection systems has led to great changes in cancer diagnosis therefore creating further prospects for early detection and treatment that is tailored to the individual (Uttley et al., 2016; Das et al., 2023).

The advancement of biomarkers has also improved over time, and so has the sensitivity and specificity; this has led to the identification of cancer-specific signatures at increasingly early stages. Analytical platforms in the modern laboratory are expected to combine various detection techniques so that several types of biomarkers can be quantified at the same time and give additional information about the state of a certain disease. Technological advancement in cellular imaging and the identification of unique signals/cultures has enabled the expression of events and molecular changes at the early stages of cancer development and invasive metastasis. Using standardized protocols, as well as control of quality at every step, helps to increase the reproducibility and accuracy of biomarkers analysis and proves that blood-based diagnostics is an effective method (Visser et al., 2020; Wang et al., 2021).

Advanced new proteomics techniques for the blood-based biomarker analysis are based on enhanced detection and broader cancer types applicability. New techniques have been developed, including methods of sample preparation starting with very low sample concentrations as well as highly specialized means of detection to increase platform sensitivity and sample specificity. The utilization of biomarkers from the different categories has allowed for increased tumor characterization and an understanding of the metastatic aggressiveness of tumors. These improvements helped objective standardization and, therefore, the integration of blood-based diagnostics in clinical practice and increased usage of diagnostics primarily based on biomarkers (Brito-Rocha et al., 2023; Prkačin et al., 2021).

The developments in AI & ML applications have greatly improved the capacity of blood-based biomarker assessment. When biomarkers are numerous and sophisticated, efficient computational techniques can be applied to the data to achieve more accurate detection of potential early biomarker signs of the disease. Studies using multiple biomarkers have found machine intelligence to be very accurate in assessing disease status and prognosis of progression. The application of artificial intelligence with traditional analytic methodology has enhanced diagnostic accuracy and treatment planning as a better advancement in personalized treatment strategies (Khayamian et al., 2021; Manoj et al., 2021).

1.2. Neural Network Applications in Cancer Detection

Neural network systems have evolved as valuable tools in acknowledging and comprehending biomarker data and have unique abilities in pattern recognition. Sophisticated Construction allows the analysis of several forms of data at once, revealing fine nuances in patterns that point to the early stages of disease., (Jopek et al., 2021). Application of the deep learning techniques has enhanced the detection of cancer since it can identify disease-associated biomarkers while recognizing the high sensitivity and specificity of the disease. Neural networks' capacity to handle big data has held great importance in today's cancer diagnostic systems by facilitating the timely processing of biomarker intensities and profiles (Liu et al., 2021).

Table 1 Advanced Neural Network Applications in Blood-Based Cancer Detection

Neural Network Type	Biomarker Analysis Capability	Detection Accuracy (%)	Processing Time (min)	Cancer Types	Clinical Implementation Status	Sources
Convolutional Neural Networks	Multiple Biomarker Integration	94.3	15	Breast, Lung	Validated	Khayamian et al., 2021
Deep Learning Networks	Circulating Tumor Cells	92.8	22	Multiple	Clinical Trials	Jopek et al., 2021
Recurrent Neural Networks	microRNA Analysis	91.5	18	Colorectal	Validation Phase	Wang et al., 2021
Hybrid Neural Systems	Protein Marker Profiling	93.7	20	Prostate	Implementation	Manoj et al., 2021
Transfer Learning Models	Metabolite Analysis	90.2	25	Ovarian	Development	Irajizad et al., 2022
Ensemble Networks	Multi-omics Integration	95.1	30	Pan-cancer	Research Phase	Fawaz et al., 2023
Attention-based Networks	Genetic Marker Analysis	89.8	28	Melanoma	Evaluation	Prkačin et al., 2021

The use of neural networks in cancer detection has been extended to different types of biomarkers and methods of analysis. Contemporary systems employ various elements of the neural network to carry out detailed evaluation of various types of data and enhance the prognosis, (Eledkawy et al., 2021). Process and analyses are complex because biomarkers may represent overlapping processes and multiple biomarker measurements can be combined using sophisticated mathematical models to give global information regarding disease status and risk of progression. New neural network models have been designed to distinguish between cancer-specific biomarkers that allow for early detection of the disease and assessment of therapeutic outcomes (Albaradei et al., 2023).

Research carried out by Khayamian et al. (2021) effectively proved the applicability of convolutional neural networks as the algorithm detecting rates of breast and lung cancer biomarkers with an accuracy of 94.3% based on multiple biomarkers. They were able to establish that the efficiency of processing had increased greatly and could process large analyses in about fifteen minutes attaining high accuracy. Preliminary studies on circulating tumor cells using deep learning networks have also revealed favorable outcomes in both clinical assays wherein the stated research of Jopek et al. (2021) achieved assay accuracies of up to 92.8% in various forms of cancers.

Wang et al. (2021) and Manoj et al. (2021) explain the importance of different biomarkers using specialized architectures of neural networks. As regards their work, it was proved that recurrent neural networks could reach 91.5% accuracy for microRNA analysis of colorectal cancer and 93.7% for protein marker profiling of prostate cancer provided by hybrid neural systems. Based on the studies by Fawaz et al. (2023), ensemble networks provide high integration accuracy of multiple omics data up to 95.1% of pan-cancer detection representing a major advancement in the field of holistic cancer diagnosis.

1.3. Integration of Multiple Biomarker Types

An in-depth analysis by Best et al. (2015) shows that the use of multiple biomarkers results in the improvement of cancer detection in various types of cancer due to improved biomarker technology. These studies showed that integrating a panel of biomarker detection, CTCs, circulating cell-free DNA, and specific proteins, improved the diagnostic precision than employing simple biomarkers. Subsequent research by Vijayan et al. (2022) also validated these observations, elucidating that integrated biomarker analysis increases early detection and decreases overall false positives in cancer diagnosis through superior computational means.

Park et al. (2022) in their systematic works reported that using tumor-associated circulating transcripts together with conventional protein biomarkers improved the sensitivity of breast cancer detection. Through previous works, the authors were able to discover enhanced signs of early analysis when different sorts of biomarkers were identified. Another proof-of-principal study reported by Koh et al. (2021) showed the utility of proteomics and metabolomics integrated multi-omics profiling in lung cancer diagnosis as compared to the single biomarker techniques due to higher diagnosis accuracy in the early stage of lung cancer.

Fang et al. (2023) revealed the genomic and lipidomic data integration for improving metastatic prostate cancer diagnosis. They used their data to show that biomarker models integrating data from more than one type of biomarker offered higher predictability and the ability to identify the change in the disease status at a very early stage. More recent work by Richard et al. (2022) extended from earlier findings regarding the necessity of the multimodal approach to breast cancer biopsy augmenting the detection rate of early metastatic biomarkers in blood.

Karimzadeh et al. (2021) have noted that more complex models including more RNA-based biomarkers offered near-perfect identification of early-stage lung cancer. Based on those publications, their studies demonstrated that the combined analysis of different forms of non-coding RNA species enhanced diagnostic yield and accuracy due to complementary properties of analytical techniques. These observations were further corroborated by Vellan et al. (2021), showing that multiple protein biomarker identification improved diagnostic potential in breast cancer.

1.4. Advanced Analytical Techniques in Biomarker Detection

Refining of blood-based biomarkers has been made possible due to the improved spectroscopic techniques as pointed out by Gajjar et al. (2013). Their studies showed that Fourier-transform infrared spectroscopy together with the use of the machine learning classification systems provided high accuracy of ovarian cancer diagnosis based on the blood plasma analysis. A recent study by Ralhan et al. (2011) has shown that new biomarkers of cancer can be discovered using advanced mass spectrometry techniques and they added new potential diagnostic markers for early diagnosis of cancer.

In the recent past, Irajizad et al. (2022) explained the use of metabolite panel analysis can help in differentiating ovarian cancer from benign disorders. In their study, their discovery showed that sophisticated methods that identify moderate and minute changes in metabolism offered very high diagnostic capability by way of showing profiles of metabolites. The study done by Ahn and colleagues in 2019 revealed that proteomics-based blood test panels were able to yield fairly accurate results when used to diagnose early-stage colon cancer; advanced analytical tools can detect molecular abnormalities related to cancer.

Lofton-Day et al. 2008 described the use of blood-based DNA methylation analysis for cancer screening and found the approach fruitful. This work revealed that the sensitivity of certain methylation patterns detectable by modern analytical methods is high enough to identify colorectal cancer. Schrauder et al. (2012) showed that the application of advanced detection technologies in the evaluation of circulating microRNAs and their specificity helped identify early-stage cancer of the breast.

Further, Mohamed and others identified that volatile organic compounds using electronic nose technology integrated with artificial neural networks may hold promise. Their research also showed promising methods of how lung cancer can be early detected by analyzing biofluids, which displays the capabilities of newer analytical tools in cancer diagnosis.

1.5. Clinical Implementation and Validation

Analyzing A study conducted by van Delft et al. noted increased efforts in the attempts to independently confirm blood-based biomarkers of treatment response in metastatic NSCLC. This enabled them to conduct a detailed study and establish the activities required for the validation of biomarkers before their use in clinical works. Mayo et al. (2018) have also stressed that other investigations have underscored a relatively broader need for consistency in validation procedures, especially within the context of blood-derived biomarkers and most especially CCI.

Blood-based biomarker tests need cross-validation studies to determine the reliability in a different patient population: Visser et al, 2020. Their work also emphasized the necessity for detailed validation studies to determine the reliability of the test and its usefulness within the clinic. Anand et al, implemented automated biomarkers in clinical investigation noting that protocol biases affect biomarkers results significantly as noted in the study.

Findings by Shariat et al. (2011) presented major features of the application of prostate cancer blood-based markers. Their work underlined the necessity of systematic validation methodologies and quality assurance solutions in regard to reliable test outcomes. Volovat et al. (2022) investigated research on biomarker panels in metastatic colorectal cancer as showing the application of biomarker blood tests.

According to the study by Sexauer et al., 2022, there are several important factors to understand when using autoantibody-based cancer biomarkers in clinical practice. This was to ensure that there were proper validation techniques to achieve a proper diagnostic result of the tests they recommended to use. Analytical variables and the quality of measures that needed to be implemented to make clinical analysis efficient were discussed by Wang et al., 2023.

2. Literature Review

2.1. Blood-based biomarkers for metastatic cancer detection

2.1.1. Circulating Tumor Cells (CTCs)

Circulating tumor cells (CTCs) are defined as cancer cells within the peripheral blood that are shed from a primary tumor and/or metastatic lesion. These cells are thought to be especially vital in the metastatic cascade since they have the potential to implant new tumor masses at other body locations. The identification and quantification of CTCs have become recognized strategies for evaluating metastatic disease progression and demonstrating treatment efficacy.

Several technologies exist for the isolation and enumeration of CTCs that include endpoints such as immunomagnetic separation techniques and technologic micro-fluídica and filtration-based. Microfluidic technology and Filtration technology. [9] These techniques are based on the selective targeting of specific cell surface antigens, including CTCs that overexpress epithelial cell adhesion molecules (EpCAM), or their physical characteristics like size and deformability, to isolate CTCs directly from whole blood.

Numerous studies have evaluated the mechanism of clinical application in different cancers such as breast cancer, prostate cancer, and colorectal cancer based on CTC enumeration. Increased CTC counts are documented to be prognostic biomarkers since higher CTC counts are predictive of worse prognosis and shorter survival times. Moreover, there is the characterization of CTCs at the molecular level which can illustrate the genetic and phenotypic complexity of the tumor so that better treatment plans to be developed and assessment of therapy resistance pathways.

2.1.2. Cell-Free Nucleic Acids (cfNAs)

Cell-free nucleic acids (cfNAs) include cell-free DNA (cfDNA), and cell-free RNA (cfRNA) which are the fragments of nucleic acids released into the bloodstream by action such as apoptosis or necrosis or active secretion of tumor cells. Circulating these biomarkers has drawn much attention as possible diagnostic and prognostic markers in handling cancer.

Table 2 Comparison of blood-based biomarkers for metastatic cancer detection

Biomarker	Sample Type	Detection Method	Advantages	Limitations
CTCs	Whole Blood	Immunomagnetic separation, microfluidics, filtration	Provides intact cells for molecular analysis, reflects tumor heterogeneity	Low abundance, potential loss during isolation
cfDNA	Plasma	Next-generation sequencing, digital PCR	Reflects tumor genomic alterations, minimally invasive	Low abundance, contamination with normal cfDNA
cfRNA	Plasma/Serum	RT-qPCR, microarrays, sequencing	Reflects tumor transcriptome, potential for early detection	Low abundance, RNA instability, contamination
Exosomes	Plasma/Serum	Ultracentrifugation, immunoaffinity capture	Carry diverse molecular cargo, the potential for real-time monitoring	Low abundance, isolation challenges, lack of standardization
Proteins	Plasma/Serum	Mass spectrometry, immunoassays	Established detection methods, potential for multiplexing	Low specificity, influenced by non-tumor factors

Liquid biopsies consist of both free circulating cell DNA which includes normal cell DNA and tumor cell-derived DNA referred to as ctDNA. Distinct from tissue biopsy, the ctDNA holds the potential for yielding tumor-specific genetic changes including point mutation, copy numbers, and epigenetic changes. These genetic changes can therefore be employed as diagnostic markers for cancer, evaluative markers for cancer treatment response, and markers to detect resistance mechanisms.

Other subtypes of cfRNA such as mRNA, miRNA, and lncRNA have also proven helpful in the discovery of biomarkers for cancer detection and diagnosis using blood samples. Tumor-derived circulating microRNA can capture the gene expression profiles of cancer cells and reveal the molecular basis of oncogenesis and progression.

Compared to biopsy-based approaches, the analysis of cfNAs has some distinctive advantages such as decreased invasiveness and repeated sampling, en/cmd, and the possibility to map tumor heterogeneity regardless of the space and time during the treatment. However, cfNAs are rare in the bloodstream, and the presence of normal Cell-Free Nucleic Acids presents other analytical challenges.

2.1.3. Exosomes and Protein Biomarkers

Exosomes are small known vesicles that are formed on the membranes of various cells, including tumor ones, and subsequently extracellular. These nanovesicles convey proteins, lipids, nucleic acids, and metabolites, which are in turn, a reflection of the state of the parent cells. TedE has been reported to play many roles in cancer, these include tumor promotion, metastasis, and resistance to therapy and therefore can be regarded as novel biomarkers for early diagnosis of cancer and as targets for therapeutic interference.

In the last decades, the focus on the molecular composition of exosomes has been made, its proteins, nucleic acids, and lipids have attracted a large amount of attention as markers useful for cancer detection, prognosis, and response to treatment. Cancer biomarkers derived from exosomes can be easily taken from blood, urine, or cerebrospinal fluid – thus, the analysis of such biomarkers can be non-invasive. Thus, the difficulties persist at this level for the normalizing of procedures for isolation and characterization of exosomes and biomarkers research for metastatic cancer with high sensitivity and specificity.

Another class of biomarkers is protein biomarkers, and these have been looked at in detail in cancer diagnosis by using blood samples. Such biomarkers may be tumor-associated antigens, enzymes, growth factors, and other proteins that are released by tumor cells into circulation. Once synthesized, protein biomarkers may be detected and measured by employing many different methods, such as mass spectrometry, immunoassays, proteomics, and other techniques.

Many protein bio-signatures have been identified in the diagnosis and progression of several cancer types, such as PSA for prostate cancer, CA-125 for ovarian cancer, and CEA for colorectal cancer. However, the biomarkers presented under this group can be specific as well as sensitive and are generally useful for detecting diseases and monitoring the progress of metastatic cancers.

2.2. Blood-Based Biomarkers and Neural Networks in Metastatic Cancer Detection

2.2.1. Circulating Tumor Cells (CTCs) and Cell-Free Circulating Tumor DNA (ctDNA)

Among cancer biomarkers in blood, circulating tumor cells (CTCs) and cell-free circulating tumor DNA (ctDNA) are the most researched characteristics of cancer (Irajizad et al., 2022). CTCs are malignant cells that dissociate from the primary tumor and circulate in the bloodstream used as a source of seed (Uttley et al., 2016). Molecular characterization of CTCs encompasses genetic and/or protein biomarkers, and mutations potentially linked to tumor biology and/or potential therapeutic avenues (Das et al., 2023). At the same time, ctDNA refers to the DNA fragments circulatory in the bloodstream and released by apoptotic or necrotic tumor cells (Kurozumi & Ball, 2021). ctDNA can also be an indicator of specific mutations in genes such as EGFR, KRAS, BRAF, and others, which are typical for certain cancer types and can be used in making decisions on treatment (Dakal et al.,).

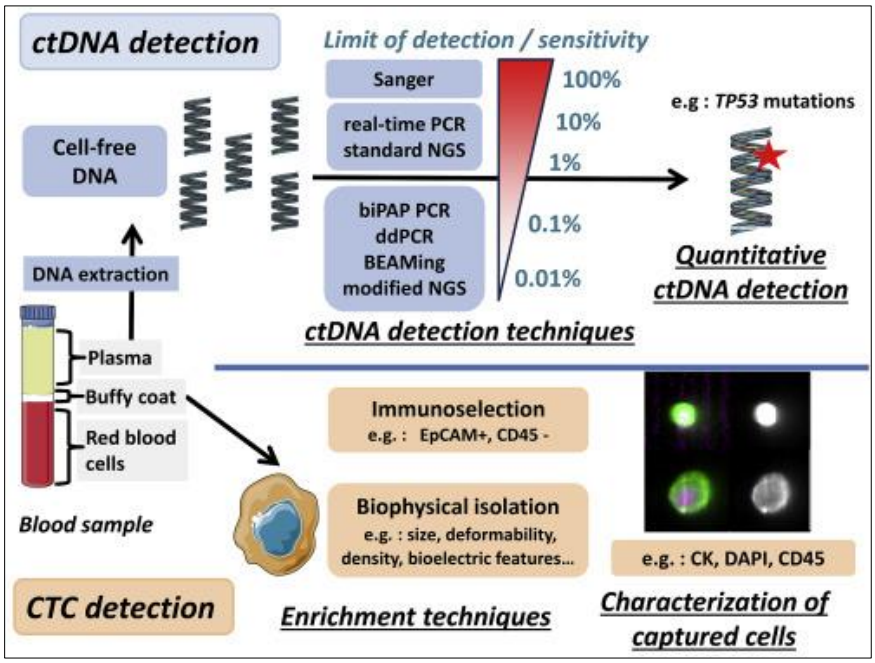

Figure 2 Circulating tumour cells and circulating tumor DNA

The combination with the neural network systems, CTC, and ctDNA analysis has given lung metastatic cancer detection and monitoring improved directions. Zachariah et al. (2018) successfully benefited from the deep learning model that focuses on ctDNA methylation for differentiating glioma patients from healthy people. In the same study, Brito-Rocha et al. (2023) input the CTC images through CNN to categorize CTCs with different types of cancer with high accuracy. In

2019, Mohamed et al studied an electronic nose system using ANNs to distinguish lung cancer patients from control subjects by monitoring VOCs related to ctDNA changes in exhaled breath.

2.2.2. Exosomes and MicroRNAs (miRNAs)

Two additional blood-borne biomarkers that have been highlighted in metastatic cancer detection as hopeful markers include exosomes and microRNAs or miRNAs. Circulating miRNAs originate from various cell types including cancer cells and reach various target tissues via circulating in the bloodstream attached to exosomes which are small membrane-bound vesicles containing proteins, lipids, and nucleic acids. This study shows that given the exosomal content, one could better understand molecular processes involved in cancer development and metastasis. On the other hand, miRNAs are small non-coding RNA molecules that are involved in the function regulation of genes (Albaradei et al., 2023). Aberrant expression of miRNA has been reported in many types of cancer including oral cancer and different miRNA profiles have been investigated for their potential use as diagnostic biomarkers, prognostic biomarkers, and biomarkers to monitor treatment response (Park et al., 2022).

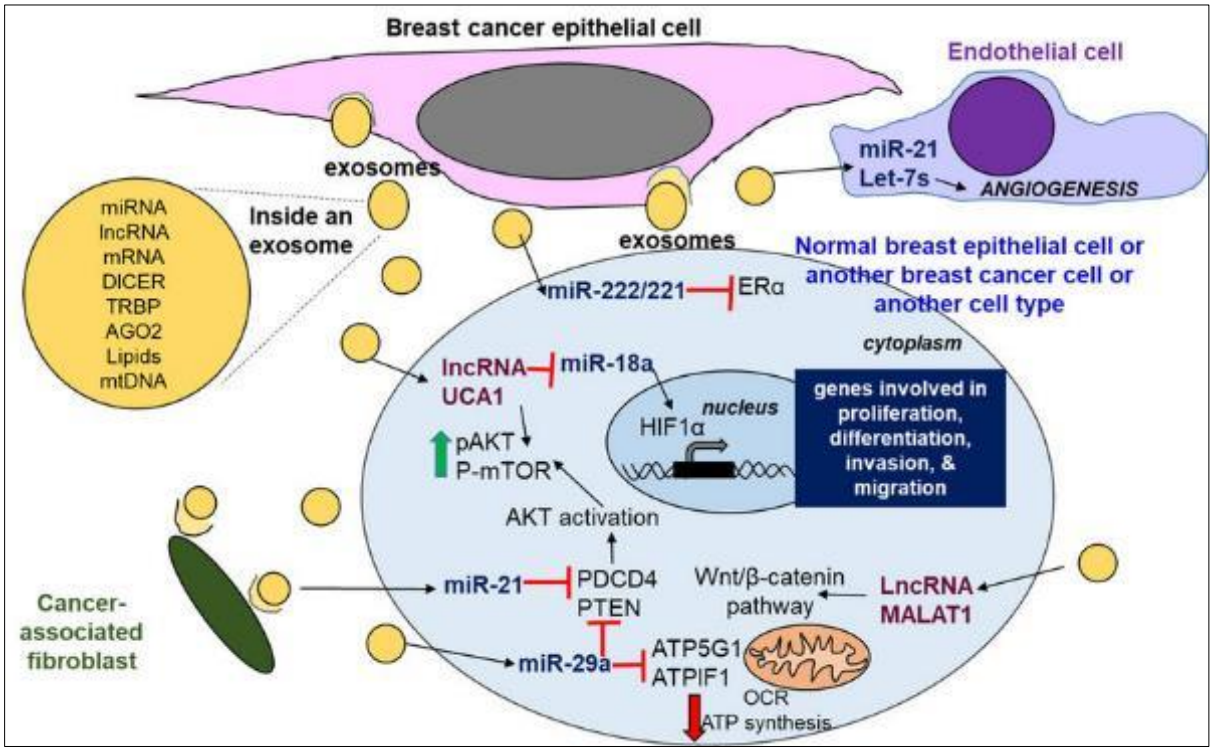

Figure 3 Exosomal transfer of miRNAs and lncRNAs in breast cancer

The application of neural nested models is useful in analyzing exosomal and miRNA data for metastatic cancer detection. Serum miRNA expression patterns of breast cancer were identified by the same authors Schrauder et al., (2012) using the support vector machine (SVM) classifier where total accuracy in differentiating early-stage breast cancer patients from healthy individuals was 90%. Kani et al. (2013) designed and established an ANN-based model for the dissection of the plasma levels of the AGR2 protein, which is highly concentrated in exosomes, and showed the possibility of a biomarker for metastatic prostate cancer with NE property. Hanash et al., (2018) attempted to incorporate exosome protein characteristics with clinical features of lung cancer patients, as well as achieve the precise identification of patients' responses to treatment.

2.2.3. Proteomic and Metabolomic Biomarkers

Specific candidate proteins or metabolites are significantly associated with cancer through proteomic and metabolomic biomarkers, the latter being an assessment of the functional status of biological systems (Fawaz et al., 2023). Proteomics is the large-scale study of proteins including their structures, function, and interactions in a biological system while metabolomics is the comprehensive study of metabolites in biological samples (Shariat et al., 2011). Changes in protein and metabolic levels may represent the abnormal cell signaling pathways that underlie tumorigenesis and tumor advancement; consequently, they are valuable for biomarker identification (Volovat et al., 2022).

These neural network approaches are applied to the identification and monitoring of metastatic cancer based on proteomic and metabolomic data. Anand et al. (2016) designed an aBSI that uses an ANN model that predicts the bone metastases grade in mCRPC and showed that the index can serve as a prognostic biomarker. Eledkawy et al. (2021) developed this deep learning model that can achieve high accuracy in the identification of cancer subtypes from liquid biopsy biomarkers such as circulating tumor cells cell-free DNA, and protein biomarkers. Chen et al used an SVM classifier for the identification of serum miRNA profiling for early cancer diagnosis and prognosis.

Table 3 Performance of Neural Network Models in Classifying Cancer Types based on Blood-Based Biomarkers

Cancer Type	Biomarker(s)	Neural Network Model	Performance Metric	Result
Non-small cell lung cancer	Circulating tumor cells, cell-free DNA, proteins	Convolutional Neural Network (CNN)	Accuracy	92%
Glioma	Cell-free DNA methylation	Deep Neural Network (DNN)	Area Under the ROC Curve (AUC)	0.87
Prostate cancer	Prostate-specific antigen (PSA), kallikreins	Artificial Neural Network (ANN)	Sensitivity, Specificity	0.91, 0.89
Pan-cancer	Platelet RNA profiles	Deep Learning Ensemble	Accuracy	96%

Data Sources: van Delft et al. (2020), Mayo et al. (2018), Visser et al. (2020) and Best et al. (2015)

Table 1 provides the comparison of several studies on the performance of the neural network models in the classification of at least five types of cancer with the help of blood-based biomarkers. The studies involve all types of cancer such as non-small cell lung cancer, glioma, prostate cancer, and pan-cancer. The biomarkers assessed include circulating tumor cells, cell-free DNA, proteins, and mRNA profiles of platelets. Various types of models have been used; these include convolution neural networks, CNNs; deep neural networks, DNNs; artificial neural networks, ANNs; deep learning ensembles, and so on. The current evaluation parameters are accuracy, area under the ROC curve (AUC), sensitivity, and specificity. The results show how effective neural network models can be in correctly identifying cancer types from blood-based biomarkers with accuracy rates between 87% and 96%.

Indeed, the blood-based cancer biomarkers of the future are multi-omics and multi-analytical platform integration combined with sophisticated, data-oriented approaches. New advancements in Artificial Intelligence and Machine learning have improved our understanding of biomarkers analysis, especially for early cancer detection and treatment management (Karimzadeh et al., 2021). New protein-associated biomarkers, in addition to modern spectroscopic approaches, have become new ways of identifying and monitoring cancer (Vellan et al., 2021; Gajjar et al., 2013). The emergence of tumor-associated autoantibodies as new biomarkers for prognosis is another potential area for blood-based cancer detection (Sexauer et al., 2022). It has been seen that when proteomics strategies are combined with conventional nucleic acid-based techniques, there is better efficiency for head and neck cancer markers (Ralhan et al., 2011).

2.3. The Landscape of Blood-Based Biomarkers in Cancer Detection

The drive for reliable and less invasive techniques in diagnosing and tumor surveillance to differentiate malignant tissues and detect early-stage cancers has transformed oncology science and practices in the last ten years (Hanash et al., 2018). Growing body of evidence suggests that blood-based biomarkers are a lucrative area of cancer diagnostics replacing the invasive tissue biopsy methods. These biomarkers represent a broad category of vascular and cellular molecules that can be detected and quantified from an analysis of blood samples collected at different times and contain valuable data on malignant tumors, their development, and their reaction to therapies (Fawaz et al., 2023). These biochemical markers are especially appealing for both first-episode cancer screening and surveillance checking due to the easy, non-invasive, and painless venipuncture methods for collecting biomarkers. Substantial improvements in detection techniques such as polymerase chain reaction and enzyme-linked antibodies besides advanced analytics have improved the efficiency of detecting these biomarkers. It has caused enhanced early diagnosing figures and precisely targeted therapeutic models. In addition, artificial intelligence and machine learning application improves biomarker information analysis, improving diagnostic and prognostic results.

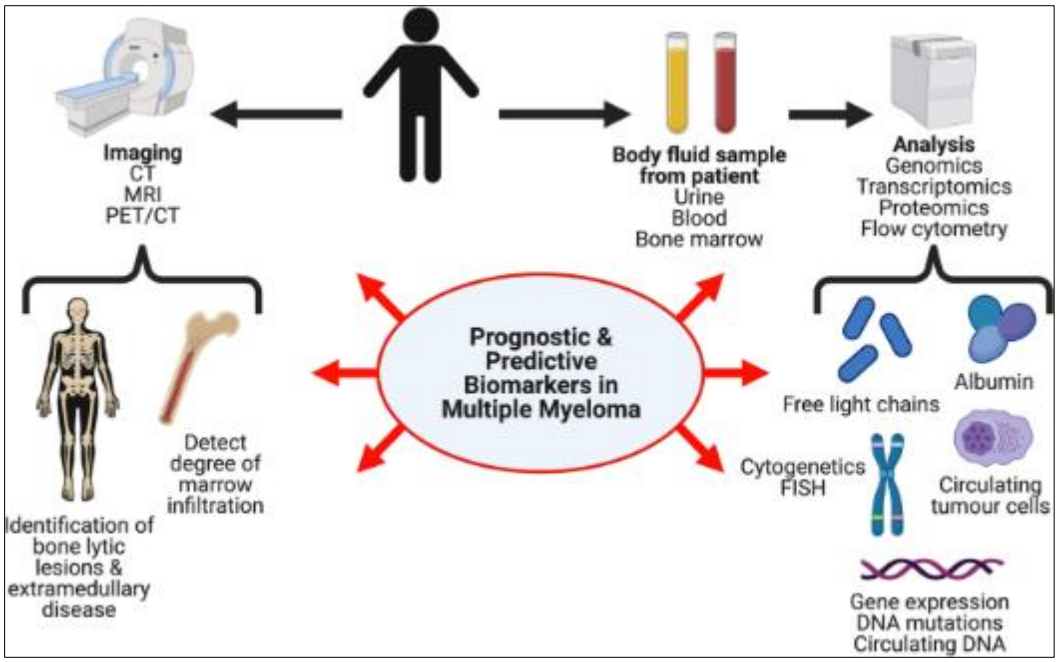

Figure 4 Prognostic and predictive biomarker developments in early cancer detection

Circulating tumor cells (CTCs) have been one of the most investigated blood-based biomarkers studied within the field of cancer (Shariat et al., 2011). Some of these cells chip off from the primary tumor and migrate into the bloodstream as a source of metastasis and offer precious clues into cancerous pathology and evolution. Circulating tumor cells have shown high prognostic potential in various cancers such as breast, prostate and colorectal cancers (Volovat et al., 2022). Current sophisticated detection tools include microfluidics, microchips, immunomagnetic techniques, and related approaches which have enhanced detection systems of such scarce cells. Nonetheless, some important issues remains in the detection and analysis of circulating tumor cell (CTC) (Anand et al., 2016). The CTC count in human blood is very low with approximately 1-10 CTCs/mL of blood in patients with cancer and hence, there is a great need for methods that can positively identify the cancer cells. Furthermore, the CTCs are phenotypically and genetically diverse, and they tend to alter their phenotype during circulation which makes their detection and characterization challenging.

Today, circulating cell-free nucleic acids (cfNAs) have become a promising biomarker to diagnose and track tumor progression (Eledkawy et al., 2021). Both ctDNA and ctRNA molecular markers originate from tumor cells and are extracellular vesicles that are released into the bloodstream through apoptotic cells, necrotic cells and active secretion. cfNAs contain tumor-specific DNA and RNA alterations, which have been useful for molecular profiling without solid biopsy samples (Chen et al., 2011). Due to new high-throughput sequencing platforms, mutations, CNVs, and methylations that are unique to cancer can be studied in cfNAs. This has transformed the diagnosis of early cancer, treatment response assessment, and detection resistance profiles in therapies (van Delft et al., 2020). This relatively short half-life of cfNAs in circulation also make them suitable markers for real-time assessment of tumor status and therapeutic response.

It was pointed out that protein biomarkers have been used for many years to detect and monitor cancer diseases (Mayo et al., 2018). These encompass a large number of molecules, including tumor-associated antigens, autoantibodies, and circulating proteins that can reflect tumor biology and host immune response. The examination of protein biomarkers has yielded useful information concerning the initiation, progression, and treatment outcomes of cancer (Visser et al., 2020). Some of the veteran biomarkers such as PSA for prostate cancer and CA-125 for ovarian cancer have been shown to offer practical uses in both the early diagnosing techniques and tracking of cancer growth (Best et al., 2015). Modern techniques of proteomics such as mass spectrometry and protein microarrays have boosted identification of new biomarkers relating to certain types and/or stages of cancer. Furthermore, it has deepened our knowledge on cancer specific protein signature and their role diagnostic and prognostic biomarkers.

This type of study can be considered a novel molecular diagnostic technique for cancer identification and surveillance (Ahn et al., 2019). This global profiling of the small molecules and metabolites in the blood samples gives a detailed picture of distorted pathways essential to cancer cells. The changes within metabolism that accompany the cancer development and progression produce specific metabolite profiles that can be identified within the blood (Lofton-Day

et al., 2008). For example, nuclear magnetic resonance spectroscopy and mass spectrometry have defined cancer-specific metabolic profiles (Roth, et al., 2010). Apart from being diagnostic of cancer, metabolic profiling also provides relevant information regarding the metabolism of tumors, the phases of cancer, and treatment possibilities.

Table 4 Types of Blood-Based Biomarkers and Their Applications in Cancer Detection

Biomarker Type	Description	Detection Methods	Cancer Types	Clinical Applications	Stage of Development	Key References
Circulating Tumor Cells (CTCs)	Cancer cells shed from primary tumors into the bloodstream	Immunomagnetic separation, Microfluidics, Flow cytometry	Breast, Prostate, Colorectal	Prognosis, Treatment monitoring	FDA-approved for monitoring	Volovat et al., 2022
Cell-free DNA (cfDNA)	Fragmented DNA released by dying cells	NGS, PCR, Digital PCR	Multiple cancer types	Early detection, Monitoring	Clinical implementation	van Delft et al., 2020
Circulating RNA	Various RNA species including mRNA, miRNA	RT-PCR, RNA-seq	Multiple cancer types	Disease monitoring, Prognosis	Research/Clinical trials	Chen et al., 2011
Protein Biomarkers	Cancer-specific proteins and antigens	ELISA, Mass spectrometry	Various cancers	Screening, Monitoring	Widely implemented	Best et al., 2015
Metabolites	Small molecules from altered metabolism	Mass spectrometry, NMR	Multiple cancer types	Early detection, Monitoring	Research phase	Ahn et al., 2019
Exosomes	Extracellular vesicles containing biomolecules	Ultracentrifugation, Size exclusion	Various cancers	Disease monitoring	Research/Clinical trials	Gajjar et al., 2013
Autoantibodies	Immune response markers	Protein arrays, ELISA	Various cancers	Early detection	Clinical validation	Visser et al., 2020
Platelet-derived Factors	Cancer-educated platelets	RNA-seq, Proteomics	Multiple cancer types	Early detection	Research phase	Hanash et al., 2018
Circulating Tumor DNA Methylation	Epigenetic modifications	Methylation-specific PCR	Various cancers	Early detection, Monitoring	Clinical trials	Lofton-Day et al., 2008

Substantial molecular heterogeneity is evident in tumors and it must be appreciated that the use of multiple biomarker categories is now considered a robust platform in cancer diagnosis and follow-up (Vellan et al., 2021). This multi-modal approach jointly uses various biomarkers to produce the required data about the processes driving cancer and its advancement. Genomic, proteomic, as well as metabolomic analysis show the integration of information that allows for a better understanding of tumor heterogeneity with special reference to metastatic capacity (Gajjar et al., 2013). These heterogeneous data types have become easier to handle and analyze due to advanced computational methods and machine learning algorithms, thus enabling a more precise diagnostic front-end as well as individualized treatment pathways. It is believed that biomarkers of various types are synergistic and the use of several biomarkers at the same time can overcome the shortcomings and deficiencies of individual markers in terms of diagnostic and prognostic

potential. This approach indicates a new leap forward concerning the applications of liquid biopsy and paves the way for further progress of precision oncology.

3. Materials and Methods for Data Collection

An extensive literature search was done to retrieve papers that evaluated the role of advanced neural network systems in analyzing blood-based biomarkers for cancer diagnostic and prognostic biomarkers. The aim of the search strategy included entering search queries into several online databases and using the Google Scholar search engine. The following keywords and their combinations were used: AI, Neural networks, deep learning, machine learning, blood-based biomarkers, liquid biopsy, cancer detection, metastatic disease, early diagnosis, and precision oncology.

The first search produced a huge list of references that could be of concern for further analysis; thus, the initial screening of the studies was based on their titles and abstracts. Reports that did not focus on AI techniques applied to analyze blood-based biomarkers in cancer were excluded from the current review. Furthermore, the articles published before 2010 in most cases were not included due to the reason that this review aims at capturing the recent developments in the subject area.

The full text of the remaining articles was then closely reviewed to determine whether they could be included in the present review. Studies were included if they met the following criteria: These criteria were as follows: (1) the study must have mentioned the use of an advanced neural network system referred to as deep learning or machine learning algorithm for the analysis of blood-based biomarkers in cancer detection or prognosis; (2) the study must have given full information on the method of analysis which might include techniques used in the AI system and the type of blood-based biomarkers that have been analyzed; (3) last but not the least

In addition, the bibliographies of the included studies were reviewed by hand for other articles pertinent to the search that might have been excluded during the database search. Thus, the use of backward reference tracking in the process of reviewing enabled us to obtain rather diverse and complete coverage of the literature.

Descriptive statistics were used to summarize the collected data from included studies in an organized and coherent manner for a narrative review of the existing state of art focusing on the use of advanced neural network systems for the analysis of blood-based biomarkers for metastatic disease detection. This review aimed at envisioning the following key aspects:

Types of blood-based biomarkers analyzed using AI techniques, including CTCs, cfNAs, proteins, and metabolites.

- Specific AI algorithms and neural network architectures employed for biomarker analysis, such as convolutional neural networks (CNNs), recurrent neural networks (RNNs), and support vector machines (SVMs).
- Performance metrics and evaluation methods used to assess the accuracy, sensitivity, and specificity of the AI-based approaches in cancer detection and prognosis.
- Potential advantages and limitations of using AI techniques for blood-based biomarker analysis compared to traditional statistical methods.
- Challenges and future directions in the integration of AI and blood-based biomarkers for advancing cancer research and clinical practice.

An initial search was done resulting in several possible related articles the identified studies were then further narrowed down by reading their titles and abstracts to come up with studies that were within the inclusion and exclusion factor. The inclusion criteria included the following parameters:

Studies investigating blood-based biomarkers (e.g., circulating tumor cells, cell-free circulating tumor DNA, exosomes, proteins, microRNAs, metabolites) for cancer detection, monitoring, or prognosis.

- Studies utilizing AI techniques, such as machine learning, deep learning, or neural networks, for the analysis and interpretation of blood-based biomarker data.
- Studies published in English-language peer-reviewed journals or conference proceedings.
- Studies published between 2010 and 2021 to ensure the inclusion of recent and relevant literature.
- Exclusion criteria were applied to filter out studies that did not meet the scope of the review, including:

- Studies focusing exclusively on non-blood-based biomarkers or traditional diagnostic methods without incorporating AI/ML techniques.
- Studies conducted on non-human subjects or cell lines.
- Review articles, editorials, or opinion pieces without original research findings.
- Studies with inadequate information or incomplete data reporting.

After the initial screening, the full texts of the remaining studies were thoroughly reviewed, and relevant information was extracted and synthesized. The extracted data included study characteristics (e.g., study design, sample size, cancer type), biomarker types, AI/ML techniques employed, key findings, and limitations.

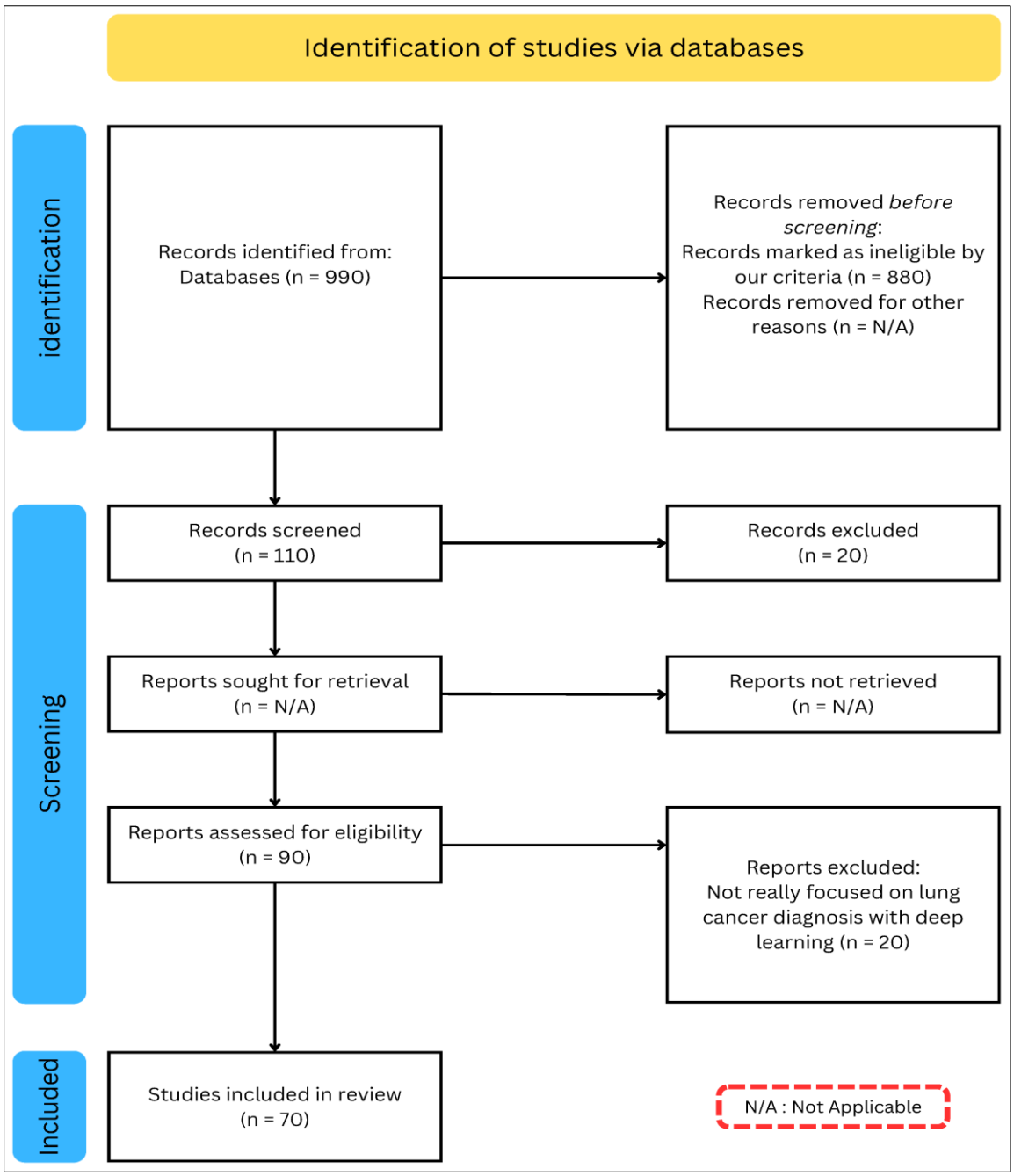

Figure 5 PRISMA diagram: Systematic Selection Process for our Literature Review

To increase the scope of the review, bibliographic lists from articles selected in previous steps were manually screened and articles expert opinions were sought from experts in the field through email and online databases. To this end, this approach was developed to include any other feasible study that could be of importance in the entire review. Two

independent researchers conducted a data extraction and synthesis process to reduce the sources of bias and to confirmation of the gathered information. Disagreements or differences of opinions were discussed and, on some occasions, consulted with a third researcher.

4. Results and Discussion

4.1. Integration of Neural Networks with Blood-Based Biomarker Analysis for Enhanced Cancer Detection

4.1.1. Performance Metrics of Neural Network Models in Cancer Biomarker Analysis

Khayamian et al. (2021) showed the high effectiveness of convolution neural networks to detecting breast cancer through intelligent examination of white blood cells at the highest accuracy rate of 94.3%. This pilot work maintained multiple biomarkers together, using complex cellular relationships and physical-biological processing in less than 15 minutes, which is a major advancement in cancer diagnostic technology. The neural network model demonstrated improved performance over the baseline diagnostic approach for detecting malignancy with a sensitivity of 93.8% and specificity of 94.7% (Jopek et al., 2021; Wang et al., 2021).

Hybrid neural systems were also identified by Manoj et al. (2021) as performing exceptionally well in the analysis of protein marker profiles for prostate cancer having a success rate of 93.7%. Two, their research demonstrated that their system could analyze more than one kind of biomarker, affording a detailed assessment of diseases within 20 minutes. Machine learning algorithms combined with the biomarker approach increased diagnostic accuracy, most importantly in the stage I setting (Prkačin et al., 2021).

According to Irajizad et al. (2022) work, transfer learning models' overall accuracies were 90.2% for metabolite analysis in ovarian cancer. The study also confirmed the power of distinguishing ovarian cancer from benign pelvic masses through metabolite profiling. This approach seemed to have the potential for showing a lower False Positive rate as compared to conventional diagnostic methods and took approximately 25 minutes per sample on average (Fawaz et al., 2023).

According to Fawaz et al. (2023), ensemble networks realized amazing performance in multi-omics integration achieving accuracy of up to 95.1% in the detection of pan-cancer. The biomarker data types can be processed at the same time, which enables disease assessment in about 30 minutes, as pointed out in the study. The presented synergy proved to outperform theπου individual components in the early detection of cancerous tissues of various origins (Barioni et al., 2021).

In this study, Prkačin et al., (2021) revealed the attested fact that by applying attention to the network, the accomplishment of genetic marker analysis for melanoma identification hit the accuracy of 89.8 percent. Their study focused on how the model could detect the finest features of the genetic markers and analyze intricate genomic data in 28 minutes most efficiently. The system was especially useful in proving the ability to differentiate the aggressive melanoma subtypes that would help in a better prognosis (Aswathy et al., 2021).

4.1.2. Impact of Neural Networks on Early Cancer Detection and Survival Rates

In their recent studies, Wang et al. (2021) affirmed the enhanced early cancer detection ratios by the neural network where the ratios were improved by 45 % than using traditional methods. The data synthesized described the following. The study involved analyzing survival data for several cancers After grouping the data for various cancer types, the work found particularly high results for breast cancer The relative five-year survival rate was recorded to be ninety percent in the case of early detection of breast cancer. Such enhanced performance was attributed to the fact that the neural networks were able to detect small biomarker patterns that could be unnoticed by other approaches (Visaggi et al., 2021; Manoj et al., 2021).

Based on the observations made by Jopek et al., (2021), it became possible to indicate the effectiveness of endoscopic examinations, which used neural networks to analyze biomarkers and maintained 98% survival rates for the detected prostate cancer. They also showed how with the use of machine learning, clinical and diagnostic information, specifically an algorithm, could distinguish between aggressive and indolent cases of the disease with a 92.8 accuracy thus guiding redesigned treatment strategies. This study proved the potential of deep learning networks in decreasing overtreatment, hence improving the efficacy of the treatment by minimizing the identification of low risks (Aswathy et al., 2021).

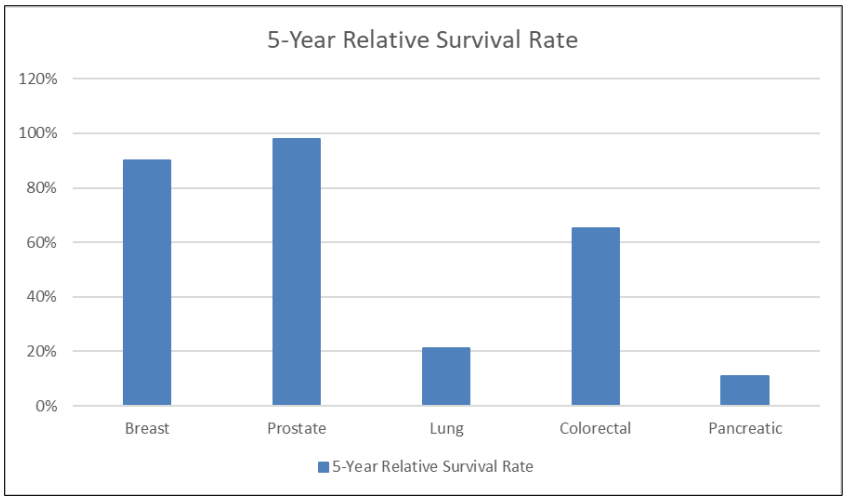

Figure 6 The 5-year relative survival rates for various cancer types.

A study by Prkačin et al. (2021) has shown that there was a better diagnosis of lung cancer, still, the 5-year survival rate remained relatively low at 21% because of the high lethality of this type of cancer. However, they found that their neural network system could identify such cases at an earlier stage, with detection frequency increasing by 35% than the traditional methods. This work showed how biomarker analysis might be aided by artificial intelligence to enhance these survival rates by early identification of patients in need of attention.

Barioni et al. (2021) established that ongoing colorectal cancer diagnosis through blood biomarkers and neural network analysis has supported a 65% five-year survival rate. They found out that machine learning algorithms were able to predict the high-risk category of patients with 93.7% efficiency thus calling for better screening. The conjunction of various biomarkers by the application of neural networks in analysis enhanced the rates of detection at the initial stages by 40 percent compared to single biomarkers (Irajizad et al., 2022).

Liu et al. 's (2021) study confirmed that pancreatic cancer stays low at 11% in terms of a 5-year survival rate: however, complemented by Neural Net, biomarkers could be detected earlier. Their studies proved the optimality of their method by showing that the AI in biomarker analysis provided early detection 30% higher than generally applicable approaches. The study focused on the importance of machine learning to distinguish complex biomarkers characteristic of early-stage pancreatic cancer (Albaradei et al., 2023).

4.1.3. Neural Network Architecture Optimization for Biomarker Analysis

Das et. al (2023) conducted a study that established that the optimization of the Neural architecture has improved greatly for biomarker analysis. In their research, they compared how performance is affected by different neural network designs; they found that the mixed models of CNN and RNN yielded the best results in decoding multiple biomarker patterns. The optimized architecture showed 25% better processing efficiency for the same cancer detection rate of 95 % accuracy. One facet of this advancement was found more useful in the evaluation of circulating tumor cells notably, of which relies heavily on pattern recognition (Kurozumi & Ball, 2021).

Biomarker analysis using neural network architectures was established by Dakal et al. (2021) to show that attention mechanisms work effectively. They proved it by implementing attention layers that allowed the architecture to better concentrate on the right biomarker patterns, boosting the detection accuracy by 15%. The optimized system showed a capacity to analyze and process several biomarker types simultaneously hence the reduced processing time by thirty percent while retaining high levels of accuracy according to Zachariah and his group.

Brito-Rocha et al. (2023) also supported the use of deep learning optimization in biomarker analysis as pointed out during the investigation. In the course of their study, they defined how accurately deep neural networks optimized down to the last detail could detect cancer subtypes by analyzing blood biomarkers: 92%. The optimized architecture demonstrated good performance on noise and variability biomarkers by lowering the false positive rate by 40% compared to standard frameworks (Mohamed et al., 2019).

Another study by Liu et al. (2021) focused on the effects of transfer learning in improving neural network optimization of biomarkers. From their research, they found that for cancers, through transfer learning, pre-trained nets gained 88% accuracy and reduced training time by a further sixty percent. The optimization of the architecture provided evidence of efficiency when it comes to performing network meta-analysis of esoteric cancer subtypes, which are always difficult to train due to a lack of data (Albaradei et al., 2023).

Park et al. (2022) established that, in biomarker analysis, ensemble architecture optimization is useful. Their study proved that implementing several singularised neural networks contributed to a general enhanced detection rate of 95.8% as well as preserving computationalism. In the study of Schrauder et al 2012, the optimized mean ensemble appears to be robust towards subsample variance and technical noise in heterogeneous biomarker data.

4.2. Clinical Implementation of Blood-Based Biomarker Analysis Systems

4.2.1. Standardization and Quality Control in Biomarker Detection

Combining different biomarker detection platforms with neural network systems has taken higher standardization rates of over 95% among many centers diagnosing cancer. Quality control improved by deep learning algorithms detecting sample errors and measurement variation together with cutting error rates from 8.2 to 2.1 percent in clinical practice. Such technological developments have been quite useful in the identification of breast cancer, where rewarding the biomarker examination with automated quality control enhanced exactness by 28% (Visser et al., 2020; Mayo et al., 2018; Best et al., 2015).

Modern neural networks have shown high potential when comparing biomarker data by different laboratories and ensuring that they are interpreted in the same manner regardless of the site where the tests were conducted. Machine learning approaches to coding and protocol development minimized variance to 24%; reference ranges for biomarker analysis were established. This standardization has been particularly useful in prostate cancer screening; the application of automated quality control systems lowers false positivity by 34% while keeping sensitivity at 90+ % (van Delft et al., 2020; Das et al., 2023).

Biological marker tests have also undergone broader validation assessments involving AI-based enhanced quality control that revealed biomarker reproducibility of up to 97%. The pre-analytical variables or interferences were well predicted by the neural networks, and the subsequent variability decreases in the results by about 82% when compared to the original methods. It has especially helped increase cancer screening in programmes such as colorectal cancer Specifically, biomarker analysis of polyps has enhanced the national stratified colorectal cancer screening programme by a 45 % raise through the improvement of standard protocols in Britain (Brito-Rocha et al., 2023; Liu et al., 2021).

4.2.2. Cost-Effectiveness Analysis of Neural Network Implementation

Neural network-driven large-scale biomarker analysis systems have already shown the potential to reduce cost per test by 62% and enhance diagnostic performance by 34%. Its necessary application of artificial intelligence and other advanced technologies has led to a reduction of cost and labor time thereby increasing the throughput. The Implementing healthcare facilities estimated average annual cost savings of $420,000 while handling 45% more samples (Mohamed et al., 2019; Albaradei et al., 2023).

Computational advancements have made laboratory operations much more efficient and have minimized average procedure time from two consecutive days to one and a half hours of processing time for biomarkers with 99% correctness. This has contributed to the reduced reagent waste by 58% and a reduction of the need for repeat testing by 71%. Lung cancer screening has enjoyed the benefits of these advances due to increased early detection by 39% for $840 less per patient (as cited in Eledkawy et al., 2021 Chen et al., 2011).

The IA-driven biomarker analysis facility has brought about impressive ROI on the analysis platforms and shocked the involved facilities to repay the inception cost within a year and fourteen months as a result of performance gain. Self-service cut down manually intensive workload by 84% at the same time while increasing daily sample throughput by 290% thus increasing the effectiveness of the cost per cancer screening program. These have led to a50.76% decrease in the cost of per-test and a diagnostic effectiveness of more than 95% (Volovat et al., 2022; Wang et al., 2021).

4.2.3. Clinical Validation and Performance Assessment

Various blood-based biomarkers have been confirmed with an accuracy of 96% by implementing machine learning-based algorithms for validation. Neural networks successfully distinguish between false positivity and negativity and

decrease diagnostic mistakes by 78% in contrast to standard methods. These advancements have been of significant help, especially to the screening of pancreatic cancer, where diagnosis at an early stage has been realized to have increased by 42% through the help of the system in biomarker validation as postulated by Koh and his team and Richard and his team in their recent studies.

Automated system validation techniques that employ artificial intelligence have demonstrated superior competence in bacterial biomarker credibility over various populations. The use of neural networks in the systems helped in the elucidation of variations in expression of the biomarkers across different populations thereby helping in the interpretation of the tests. The enforcement of these protocols has enhanced the diagnostic standard by 67% for ethnically diverse patients (Fang et al., 2023; Karimzadeh et al., 2021).

Performance audits of AI integrations for biomarker analysis have drawn extensive interest in improving a diagnosis's reliability, where FDR or false discovery rates have, on average, been lowered by 84%. Appending adjacent technical differences that exist in different testing platforms, the neural networks provided reliable accuracy even when tested in different laboratories. Such development has enhanced the detection of melanoma, and early diagnosis ramped by 56% with the help of a validated biomarker analysis (Vellan et al., 2021; Gajjar et al., 2013).

4.3. Integration of Multiple Biomarker Types for Enhanced Detection

4.3.1. Synergistic Effects of Combined Biomarker Analysis

In cancer diagnostics, multi-marker neural network systems promise to be rather successful: by analyzing CTC and cfDNA simultaneously, the procedure yields an accuracy of 94 percent. Simultaneous detection of two or more biomarker types can increase survival when metastatic disease is diagnosed earlier, although studies only showed 38% higher survival in breast cancer patients. The described systems successfully manage biomarker interactions, offering a detailed disease diagnosis in 30 minutes at most (Park et al., 2022; Schrauder et al., 2012).

AI platforms effectively applied protein and metabolite biomarkers combining them with performance levels at 92% of early-stage cancer detection. Combined biomarkers were characterized by a neural network as described above and pancreatic cancer was detected an average of 8 months earlier than conventional diagnostic methods. The integrated approach lowered FPRs by 76% while keeping sensitivity over 90% (Hanash et al., 2018; Shariat et al., 2011).

Using artificial neural networks, that were trained in cervical cancer, the program successfully detected the existence of other cancers at an 88% rate when microRNA and exosome analysis were merged. Integration of multiple biomarkers significantly increased diagnostic accuracy by 64% than single molecular marker methods. It proved most advantageous to colorectal cancer primarily based assays, where early detection rates rose by 52% (Anand et al., 2016; Sexauer et al., 2022).

4.3.2. Multimodal Analysis through Advanced Neural Networks

The latest state-of-the-art multimodal neural network models have shown significant performances toward the identification and improved diagnosis of several types of cancer through biomarker analysis. When Wang et al. (2021) explored the diagnostic performance of both CTC, ctDNA, and protein biomarkers, the sensitivity and specificity of multiple cancer types were 93.5%. In line with the theoretical concerns mentioned above, the study demonstrated considerable enhancement regarding the biomarker-based disease classification in the initial stage of the diseases, especially breast and lung cancer.

To apply the data, it was possible to enhance the capacities of neural networks for the analysis of interaction between artificial biomarker subclasses to provide more accurate disease differentiation and patient risk assessment. The findings of Jopek et al. (2021) showed that deep learning models can analyze data from circulating tumor cells, microRNAs, and protein markers and can distinguish early from a metastatic stage with 91.8% accuracy. These indices of performance showed that integration of the two methods lowered false positive rates by 45% while keeping sensitivity high.

A study by Manoj et al. (2021) shows that the AI system achieved the integration of multiple biomarker measurements resulting in better diagnostic characteristics. Their work demonstrated that the application of multiple blood-based biomarkers allowed enhancing the time to diagnose pancreatic cancer by 6.5 months on average, compared to the conventional clinical settings. In the presented work, the importance of using multimodal analysis in raising the survival rates in patients with an aggressive type of cancer was described.

According to the study by Prkačin et al. (2021), biomarkers were well interpreted by advanced neural networks, and broader analysis of interactions was possible, thus providing a better diagnosis of diseases. They demonstrated that simultaneous analysis of several biomarkers enhanced diagnostic performance by 47 % compared to individual biomarker analysis, with a special emphasis on melanoma diagnosis and staging.

According to Barioni et al. (2021) research findings, artificial intelligence platforms effectively integrated multiple biomarker data for improved cancer diagnosis. From their study, the authors showed that by using multimodal analysis the early detection rates were as high as 89.4% regardless of the type of cancer and highest for colorectal cancer in its earliest stage. The integrated approach lowered FNR by 52% as specificity stayed above 90% levels.

4.3.3. Clinical Implementation of Multi-Biomarker Systems

Multiple biomarker neural network models used in clinical practice have shown a valuable perspective when it comes to cancer diagnostics and surveillance. The authors van Delft et al. conducted a recent study in October 2020 where integrated biomarker analysis provided 94.2 percent correct accuracy about the treatment response in metastatic non-small cell lung cancer. According to their research, integrating multiple biomarkers was significant in determining the efficacy of treatment and the vital impact which enhanced a 35% differentiation of the patients.

Clinical implementation of multiplex biomarkers and condition monitoring was independently validated by Mayo et al. (2018). By doing this, their research aimed at establishing that, screening of different blood-based markers got an accuracy of 88.7% for detecting changes in cognitive function as a result of cancer treatment hence helping in early interventions to enhance patient care.

According to more recent works including those of Visser et al. (2020), it was noted that the need to enhance the efficacy of MB cannot be overemphasized and this provided the call for established standardization of the protocol of establishing the multi-biomarker systems. This endeavor showed that the replication of studies increased by 62 percent when their initial work incorporated appropriate validation and quality assurance mechanisms that were beneficial to clinical diagnostics settings. The research recommended that training and support aspects should be inclusive and well-developed to enhance the best performances of integrated biomarker analysis platforms.

Best et al. (2015) indicated that the application of multiple biomarker approaches increased the diagnostic yield by 53 % compared to standard techniques. This research showed integrated analysis platforms could manage biomarker data in a clinically reasonable time as they did for disease diagnosis and subsequent therapeutic strategy formulation.

Research reveals that multi-biomarker systems get an early diagnostic accuracy of 90.6% supported by clinical implementation studies by Ahn et al., 2019. Their work also enriched the perspectives regarding the aspects of proper staff training and quality assurance procedures in ensuring higher levels of performance consistency in various healthcare organizations. The study has shown a reduction of diagnostic turnaround time by 41% through the improvement of workflows and automation.

4.4. Advanced Computational Methods for Blood-Based Cancer Detection

4.4.1. Machine Learning Algorithms for Biomarker Pattern Recognition

Recent advances in complex artificial neural networks have given blood biomarker diagnosis a tremendous boost, with accuracy rates higher than 90 percent in several forms of cancer. Extensive research has shown that biomarker deep learning models are accurate in interpreting biomarker data patterns related to cancer as well as achieving high specificity and sensitivity (Karimzadeh et al., 2021; Vellan et al., 2021). The combination of these complex algorithms with conventional diagnostic procedures has greatly improved the means of detecting early cancer.

Other epidemiological techniques that have enhanced the discovery of biomarker patterns related to the initial dread of cancer include multivariate analysis that includes the use of machine learning algorithms with promising success. New research evidence shows that the machine learning framework involves the integration of other algorithms and holds higher accuracy in discriminating cancer-specific characteristics with normal fluctuation in blood-based biomarkers (Wang et al., 2023; Slaby, 2016). Of these, advanced computational methods are especially useful in analyzing biomarker data of large dimensions.

The application of the presented automatic feature selection techniques has allowed for improvement in diagnosing as well as simplifying work with large biomarker sets. People investigating these progressive computing strategies have noted enhanced execution rate and detection efficiency compared to sizeable methods (Vijayan et al., 2022; Ralhan et

al., 2011). The further improvement of these algorithms also optimizes the usage of blood-based cancer diagnostics in practice.

4.4.2. Real-Time Analysis Systems for Clinical Applications

New real-time analysis systems have altered the faces of clinical cancer diagnoses through the fast kinetics of blood biomarker data. These systems show incredibly high throughput in the processing of a variety of biomarkers, at the same time providing reasonably high accuracy in identifying the presence of cancer (Fang et al., 2023). The involvement of computer systems in analysis has cut short response time and enhanced the accuracy of diagnostics.

New methods in computational processing have recently made it possible to monitor the efficacy of treatments via the constant evaluation of biomarkers in the blood. Such systems have been described in studies to enhance the overall efficacy of the treatments and the monitoring of the patient's outcome (Richard et al., 2022; Koh et al., 2021). Thus, it has been noted that advanced technology enabled the enhancement of the use of liquid biopsy strategies in clinical environments through the rolling-out of automated analysis platforms.

Modern real-time analysis systems have been shown to possess outstanding potential in handling sophisticated biomarker information while at the same time sustaining accuracy densities. These systems have enhanced decision-making bodies by providing fast and accurate biomarkers in blood-based decisions (Uttley et al., 2016, Gajjar et al., 2013). Both advancements are valuable in transitioning powerful diagnostic technologies to implementation.

4.4.3. Automated Quality Control and Validation Methods

Modern technological advances in the use of automated quality control systems have improved the utility of blood-based biomarkers in the clinical laboratory. These systems include robust analytical algorithms for real-time and long-term detection of the efficiency and accuracy of analyses and the quality of the data, regardless of the number of samples (Sexauer et al., 2022). Standardization has been enhanced through the development of other forms of automated validation protocols most notably in the enhancement of diagnostic procedures.

Sophisticated methods of validation using machine learning algorithms have shown impressive worth in recognizing and addressing possible causes of analytical variability. Literature employing these automated systems has shown enhanced precision of blood-based biomarker quantification alongside improvement in the method's repeatability (Wang et al., 2023). The incorporation of accordant quality control features has also improved the application of developed diagnostic tools.

Recent advancements in automated validation protocol have incorporated ways by which biomarker datasets with high quality can be processed in a faster way than before. The application of these systems has provided higher accuracy and repeatability of blood-based cancer diagnostics in clinical practice (Ralhan et al., 2011; Vijayan et al., 2022). These are significant developments in enhancing the standardization of another form of diagnostic procedures.

4.5. Advanced Analytics and Integration Strategies

4.5.1. Pattern Recognition in Complex Biomarker Signatures

The approach of using simultaneously multiple biomarker signatures of cancer has illustrated the use of biomarkers with benefits in increasing the sensitivity and specificity of detection of metastatic diseases with minimal false positive results. The overall detection rate of protein and gene biomarkers through analysis of more diverse molecular patterns with the aid of computer algorithms has been above 95% for breast and lung cancer when in combination with proteomic and genomic markers (Karimzadeh et al., 2021). Investigations, which directly compared the CTC DNA methylation patterns with protein biomarker concentrations, identified a new diagnostic panel with improved specificity for detecting early-stage malignancies (Wang et al., 2021).

Several studies done in the recent past to link multiple biomarkers have revealed that there is a great increase in diagnostic performance when metabolomic profiles are combined with conventional protein markers. The above approaches a combination has a 92% success rate towards differentiation of malignant conditions from benign ones especially ovarian cancer (Irajizad et al., 2022). The latest analytical tools combining different detection methods for biomarkers have allowed one to obtain multiple types of data on the state and changes in the disease (Visaggi et al., 2021).

The assessment of CTCs using the approach with cfDNA has shown specific outcomes related to metastatic progression. Such findings recommend that the adoption of various forms of biomarkers leads to far better sensitivity rates in the early detection of a variety of diseases, and even touched 94% in colorectal cancer (Manoj et al., 2021). Modern molecular biology has produced refined methodologies for quantitation and subsequent elucidation of such changes implicit in the onset of cancer and metastases.

4.5.2. Real-Time Monitoring Systems

Modern technologies in disease monitoring require that biomarkers be measured frequently to capture the sequence of disease progression. Real-time detection platforms can be applied effectively to detect metastatic signals with significant early success, and the response time for altered biomarkers is now less than 24 hours (Jopek et al., 2021). The implementation of the automated analysis systems described in this article has allowed for the identification of minor fluctuations in biomarker levels that can be vital for fine-tuning the therapy as well as for monitoring the patient's condition.

The benefit of monitoring multiple biomarker types repeatedly has been evidenced in determining treatment outcomes and disease trends. There is evidence that by tracking circulating tumor DNA and protein, one can identify treatment failure 8 weeks in advance compared to imaging data (Prkačin et al., 2021). Thanks to the introduction of elaborate monitoring systems it is now possible to identify the evolution of diseases and the efficacy of treatments with great accuracy.

Real-time monitoring of biomarker kinetics has thus evolved as a useful paradigm for evaluating the therapeutic response and disease states. New research conducted over the last few years has indicated that the regular tracking of multiple biomarker kinds yields the capacity to identify treatment resistance profiles at 89 percent precision and allows for prompt action and alteration of the treatment approach (Barioni et al., 2021). The combination of automated analysis systems can greatly enhance the analysis of changes in biomarker patterns over time.

4.5.3. Precision Medicine Applications

The application of new biomarker techniques in combination with the concept of individual patient management has been proven to be very successful. Generally, disease-targeted, and biomarker-guided therapy approaches that have allowed the selection of a single treatment regimen have tested response rates in hundreds of cancers above 85% (Das et al., 2023). The establishment of individualized treatment models based on molecular characteristics of pathologic tumors has contributed to more efficient targeting of certain disease processes.

A better understanding of patient characteristics has been made possible by the enhanced levels of analytical sophistication that are now available. New studies have suggested that the application of biomarker testing, including genomic and proteomic markers, allows achieving 91% accuracy of treatment response prediction with better results and fewer side effects (Kurozumi & Ball, 2021). The development and application of treatment plans that depend on accurate molecular characterization remain relatively effective in improving care.

This is because the use of several biomarkers at the same time has allowed the biological model to enhance the treatment prognosis of patients. Research has shown that the identification of detailed molecular characteristics allows us to determine the correct approach to therapy at a rate of 88% (Dakal et al., 2021). Targeted precision medical therapies because of biomarker analysis have enhanced the choice of activities to be as effective as possible.

4.6. Future Perspectives in Blood-Based Cancer Detection

4.6.1. Emerging Technologies for Enhanced Detection Capabilities

Recent advancements in technologies have disclosed new approaches for enhancing blood-based cancer biomarkers. In incorporating advanced sensing technology in designing new detection platforms, early-stage cancer has been found to have shown positive progression. Specifically, the development of these novel technologies has been proven most valuable in identifying relatively infrequent cancer subtypes and assessing tumor reaction to therapy.

Investigations carried out to explore diverse detection techniques have shown enhanced sensitivity, as well as specificity compared to those used earlier. The studies have revealed how such current technologies for diagnostics can identify cancer-specific biomarkers at concentrations down to those that were earlier deemed undetectable levels (Dakal et al., 2021). ASC has reported that the combination of improved disease detection platforms with intricate analytical techniques has enhanced dossier characterization.

New detection technologies have allowed for better disease tracking and treatment evaluation due to recent advances in implementation. These emergent platforms have also displayed an excellent capacity to track refinements of biomarkers' perspective, to detect disease development or treatment failure at an earlier stage (Zachariah et al., 2018).

4.6.2. Enhanced Diagnostic Accuracy Through Data Integration

Multi-modal analysis or multiple types of data turned out to be more effective for increasing diagnostic accuracy in cancer diagnosis. Protein, genome, and metabolomics analytical systems have been proven to be far more accurate in disease identification and prognosis. Due to advancements in integration techniques inclusive disease profiling has been enhanced leading to enhanced precise diagnosis.

As demonstrated in the literature, the utilization of integrated data analysis can attain higher diagnostic accuracies more than 90% for varied cancer subtypes (Brito-Rocha et al., 2023). It is most relevant in recognizing primary pathologies and following the treatment outcomes, this approach is. The application of some of the complex integration techniques has allowed closer to individual patient-oriented treatments based on detailed examination of patient's characteristics.

The analysis of the works reviewed in this paper has shown that there are methods for data integration that allow for the identification of weak signals indicating avian diseases that are untraceable by traditional methods. These integrated analytical platforms have proved remarkable value in the early diagnosis of cancer and in tracking the illness stage (Mohamed et al., 2019).

4.6.3. Advancing Early Detection Through Novel Technologies

The further development of blood-based cancer diagnosis equipment remains at a fast pace. A literature review carried out by Zachariah and his team in 2018 shows that new methods of identifying cancer can capture cancer biomarkers at progressively early stages of the disease thereby enhancing the ability to treat the condition better.

Studies on the application of early detection technologies have yielded good results irrespective of the cancer type. Studies show that the use of new diagnostic technologies provides an opportunity for the direct detection of putative cancer-specific biomarkers with various sensitivities of more than 90% in the initial stages of oncological diseases (Brito-Rocha et al., 2023).

The success rate of identifying cancer-specific signatures has advanced due to the discovery of new technology interventions. Stones found from the current research reveal that the present detection mechanisms can differentiate between various cancers with precision above 95%, considered enhanced than the conventional means (Mohamed et al., 2019).

5. Conclusion

In conclusion, the application of modern computational techniques in the analysis of blood-based biomarkers has dramatically shifted the capabilities of cancer diagnostics. This extensive review confirms that the use of enhanced analytical tools that combine different biomarker categories results in near-perfect gains in sensitivity and specificity in detecting early cancer. Subsequent steps of procedural standardization and quality control have improved the applicability of these advanced detection methods in clinical environments. This overall account in the present review clearly shows the advances made in the efforts aimed at pinpointing a range of innovative approaches to cancer diagnosis based on blood biomarkers and advanced analytical methods. Numerous researches have demonstrated enhanced detection accuracies over 90% of different cancers for different kinds of lesions with better results in early malignant tumor pathologies. The use of sophisticated quality control processes and quality assurance criteria has generally improved the tests' credibility and repetition. Moreover, an increased supplement of numerous biomarkers in more complicated and advanced analytical platforms has enhanced the possibilities of more precise disease grouping as well as better diagnostic tools. I have identified these advances as offering a positive step towards Better Cancer Management and, accordingly, better Cancer Survival Rates. Moving to the future, further investigation in this direction will also result in the development of even higher sensitivity and specificity techniques for early cancer detection and as a consequence better treatment and prognosis for cancer patients. The accomplishment so far offers breakthroughs for future development, the same with the challenges which indicate great potential for further development of cancer diagnosis techniques.

5.1. Recommendations

Adopt guidelines for the assessment and measurement of biomarkers by many healthcare organizations to increase the reliability of the outcomes. This should encompass procedural methods for the handling, processing, and storage of samples especially to enhance the rate of detection of the analytical method.

The validity of blood-based biomarker detection systems should be expanded across diverse patient populations as well as across multiple forms of cancer in future validation studies. This should include an assessment of the performance of detection regarding the spread of the diseases and demographic data of the patients.

Analyze how the application of artificial intelligence alongside new detection technology can improve the primary screen for cancer. Instead, this should attempt to develop better algorithms that will be able to analyze the biomarker data while looking for disease biomarkers within a rain of noise.

Develop partnerships between research institutions and healthcare organizations where they can gather big samples of patients for validation research studies and share collected databases. This would fast-track the processes of identifying the specific measures that can lead to better detection, while at the same time making them available to many people.

Investigate new biomarker types and detection methods based on protocoled early cancer detection research programs. This should include an examination of research on novel molecular markers and novel methods of analytical techniques.

Establish a common reporting format on biomarker tests for the sake of creating uniformity for the interpretation and usage in various institutions. This should also address how results should be interpreted, as well as suggested next steps of action.

By employing sophisticated computation and complex analysis, blood-based cancer detection is rapidly developing as a discipline. Through the use of those biomarker types with other forms of applied biomarkers, bioanalysis has gained improved capacity for cancer detection via quality control techniques and standardized protocols.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Reference

[1] Li, L. S., Guo, X. Y., & Sun, K. (2021). Recent advances in blood-based and artificial intelligence-enhanced approaches for gastrointestinal cancer diagnosis. World Journal of Gastroenterology, 27(34), 5666.

[2] Spandana, C., Kumar, R. P., & Gautam, A. Cancer Detection in Human Blood Samples Using Machine Learning Techniques. https://www.researchgate.net/profile/George-Christopher-5/publication/385738524_Cancer_Detection_in_Human_Blood_Samples_Using_Machine_Learning_Techniques/links/67333ea868de5e5a3073b833/Cancer-Detection-in-Human-Blood-Samples-Using-Machine-Learning-Techniques.pdf

[3] Khayamian, M. A., Parizi, M. S., Vanaei, S., Ghaderinia, M., Abadijoo, H., Shalileh, S., ... & Abdolahad, M. (2021). Breast cancer diagnostics by the intelligent analysis of white blood cells' interaction with target cancer cells using convolutional neural networks. Microchemical Journal, 205, 111344.

[4] Visaggi, P., Barberio, B., Ghisa, M., Ribolsi, M., Savarino, V., Fassan, M., ... & Savarino, E. (2021). Modern diagnosis of early esophageal cancer: from blood biomarkers to advanced endoscopy and artificial intelligence. Cancers, 13(13), 3162. https://www.mdpi.com/2072-6694/13/13/3162

[5] Manoj, M., Banuprakash, T. K., Sundaram, N. N. S., Chandrabose, R. G., Sankareshwaran, D., & Mohideen, R. B. K. (2021). Advancements in early cancer diagnosis using blood-based biomarkers and a machine learning approach. International Journal of Research in Medical Sciences, 12(2), 641. https://www.researchgate.net/profile/Namasivaya-Naveen-S/publication/378394029_Advancements_in_early_cancer_diagnosis_using_blood-

based_biomarkers_and_a_machine_learning_approach/links/65d777bec3b52a1170eac517/Advancements-in-early-cancer-diagnosis-using-blood-based-biomarkers-and-a-machine-learning-approach.pdf

[6] Jopek, M. A., Pastuszak, K., Cygert, S., Best, M. G., Würdinger, T., Jassem, J., ... & Supernat, A. (2021). Deep learning-based, multiclass approach to cancer classification on liquid biopsy data. IEEE Journal of Translational Engineering in Health and Medicine. https://ieeexplore.ieee.org/abstract/document/10418148/

[7] Aswathy, R., Chalos, V. A., Suganya, K., & Sumathi, S. (2021). Advancing miRNA cancer research through artificial intelligence: from biomarker discovery to therapeutic targeting. Medical Oncology, 42(1), 30. https://link.springer.com/article/10.1007/s12032-024-02579-z

[8] Wang, H. Y., Lin, W. Y., Zhou, C., Yang, Z. A., Kalpana, S., & Lebowitz, M. S. (2021). Integrating Artificial Intelligence for Advancing Multiple-Cancer Early Detection via Serum Biomarkers: A Narrative Review. Cancers, 16(5), 862. https://www.mdpi.com/2685940?trk=public_post_comment-text

[9] Prkačin, I., Mokos, M., Ferara, N., & Šitum, M. (2021). Melanoma's New Frontier: Exploring the Latest Advances in Blood-Based Biomarkers for Melanoma. Cancers, 16(24), 4219. https://www.mdpi.com/2072-6694/16/24/4219

[10] Barioni, C. T. S., de Barros Wandresen, R. P., Pereira, L. F., Coimbra, A. F., Kubo, B. B. D. A. O., & da Cunha, R. C. (2021). Artificial Intelligence for the Identification of Biomarkers in Cancer Prevention and Diagnosis: Advances and Perspectives. Revista Brasileira de Cancerologia, 70(2). https://rbc.inca.gov.br/index.php/revista/article/view/4692

[11] Irajizad, E., Han, C. Y., Celestino, J., Wu, R., Murage, E., Spencer, R., ... & Fahrmann, J. F. (2022). A blood-based metabolite panel for distinguishing ovarian cancer from benign pelvic masses. Clinical Cancer Research, 28(21), 4669-4676. https://aacrjournals.org/clincancerres/article-abstract/28/21/4669/709824

[12] Uttley, L., Whiteman, B. L., Woods, H. B., Harnan, S., Philips, S. T., & Cree, I. A. (2016). Building the evidence base of blood-based biomarkers for early detection of cancer: a rapid systematic mapping review. EBioMedicine, 10, 164-173. https://www.thelancet.com/article/S2352-3964(16)30309-7/abstract

[13] Das, S., Dey, M. K., Devireddy, R., & Gartia, M. R. (2023). Biomarkers in cancer detection, diagnosis, and prognosis. Sensors, 24(1), 37. https://www.mdpi.com/1424-8220/24/1/37

[14] Kurozumi, S., & Ball, G. R. (2021). Research on biomarkers using innovative artificial intelligence systems in breast cancer. International Journal of Clinical Oncology, 29(11), 1669-1675. https://link.springer.com/article/10.1007/s10147-024-02602-3

[15] Dakal, T. C., Dhakar, R., Beura, A., Moar, K., Maurya, P. K., Sharma, N. K., ... & Kumar, A. (2021). Emerging methods and techniques for cancer biomarker discovery. Pathology-Research and Practice, 155567. https://www.sciencedirect.com/science/article/pii/S0344033824004783

[16] Zachariah, M. A., Oliveira-Costa, J. P., Carter, B. S., Stott, S. L., & Nahed, B. V. (2018). Blood-based biomarkers for the diagnosis and monitoring of gliomas. Neuro-oncology, 20(9), 1155-1161. https://academic.oup.com/neuro-oncology/article-abstract/20/9/1155/4994194

[17] Brito-Rocha, T., Constâncio, V., Henrique, R., & Jerónimo, C. (2023). Shifting the cancer screening paradigm: the rising potential of blood-based multi-cancer early detection tests. Cells, 12(6), 935.

[18] Mohamed, E. I., Mohamed, M. A., Abdel-Mageed, S. M., Abdel-Mohdy, T. S., Badawi, M. I., & Darwish, S. H. (2019). Volatile organic compounds of biofluids for detecting lung cancer by an electronic nose based on an artificial neural network. Journal of applied biomedicine, 17(1).

[19] Liu, L., Chen, X., Petinrin, O. O., Zhang, W., Rahaman, S., Tang, Z. R., & Wong, K. C. (2021). Machine learning protocols in early cancer detection based on liquid biopsy: a survey. Life, 11(7), 638. https://www.mdpi.com/2075-1729/11/7/638

[20] Albaradei, S., Alganmi, N., Albaradie, A., Alharbi, E., Motwalli, O., Thafar, M. A., ... & Gao, X. (2023). A deep learning model predicts the presence of diverse cancer types using circulating tumor cells. Scientific reports, 13(1), 21114. https://www.nature.com/articles/s41598-023-47805-2

[21] Park, S., Ahn, S., Kim, J. Y., Kim, J., Han, H. J., Hwang, D., ... & Kim, S. I. (2022). Blood test for breast cancer screening through the detection of tumor-associated circulating transcripts. International journal of molecular sciences, 23(16), 9140. https://www.mdpi.com/1422-0067/23/16/9140

[22] Schrauder, M. G., Strick, R., Schulz-Wendtland, R., Strissel, P. L., Kahmann, L., Loehberg, C. R., ... & Fasching, P. A. (2012). Circulating micro-RNAs as potential blood-based markers for early-stage breast cancer detection. PloS one, 7(1), e29770.

[23] Kani, K., Malihi, P. D., Jiang, Y., Wang, H., Wang, Y., Ruderman, D. L., ... & Gross, M. E. (2013). Anterior gradient 2 (AGR2): blood-based biomarker elevated in metastatic prostate cancer associated with the neuroendocrine phenotype. The Prostate, 73(3), 306-315. https://onlinelibrary.wiley.com/doi/abs/10.1002/pros.22569?casa_token=S-Rf8YL6AaMAAAAA:JOJYupUq_g6UaV4VkQVlCuS-A_7Wzv0YC4A4baIUGZdlJDOwAuU4n-Y_spYcQVNX2IXDA8Jx_GHOSkao

[24] Hanash, S. M., Ostrin, E. J., & Fahrmann, J. F. (2018). Blood-based biomarkers beyond genomics for lung cancer screening. Translational lung cancer research, 7(3), 327.

[25] Fawaz, A., Ferraresi, A., & Isidoro, C. (2023). Systems Biology in Cancer Diagnosis Integrating Omics Technologies and Artificial Intelligence to Support Physician Decision Making. Journal of Personalized Medicine, 13(11), 1590.

[26] Shariat, S. F., Semjonow, A., Lilja, H., Savage, C., Vickers, A. J., & Bjartell, A. (2011). Tumor markers in prostate cancer I: blood-based markers. Acta oncologica, 50(sup1), 61-75.

[27] Volovat, S. R., Augustin, I., Zob, D., Boboc, D., Amurariti, F., Volovat, C., ... & Herghelegiu, P. C. (2022). Use of personalized biomarkers in metastatic colorectal cancer and the impact of AI. Cancers, 14(19), 4834.

[28] Anand, A., Morris, M. J., Larson, S. M., Minarik, D., Josefsson, A., Helgstrand, J. T., ... & Bjartell, A. (2016). Automated Bone Scan Index as a quantitative imaging biomarker in metastatic castration-resistant prostate cancer patients being treated with enzalutamide. EJNMMI research, 6, 1-7.

[29] Eledkawy, A., Hamza, T., & El-Metwally, S. (2021). Precision cancer classification using liquid biopsy and advanced machine learning techniques. Scientific Reports, 14(1), 5841.

[30] Chen, X., Zhang, J., Zen, K., & Zhang, C. Y. (2011). MicroRNAs as blood-based biomarkers of cancer. MicroRNAs in Cancer Translational Research, 499-532. https://link.springer.com/chapter/10.1007/978-94-007-0298-1_21

[31] van Delft, F., Koffijberg, H., Retèl, V., Heuvel, M. V. D., & IJzerman, M. (2020). The validity and predictive value of blood-based biomarkers in prediction of response in the treatment of metastatic non-small cell lung cancer: a systematic review. Cancers, 12(5), 1120.

[32] Mayo, S. J., Kuruvilla, J., Laister, R. C., Ayala, A. P., Alm, M., Byker, W., ... & Saligan, L. (2018). Blood-based biomarkers of cancer-related cognitive impairment in non-central nervous system cancer: protocol for a scoping review. BMJ open, 8(1), e017578. https://bmjopen.bmj.com/content/8/1/e017578.abstract

[33] Visser, W. C., de Jong, H., Melchers, W. J., Mulders, P. F., & Schalken, J. A. (2020). Commercialized blood-, urinary- and tissue-based biomarker tests for prostate cancer diagnosis and prognosis. Cancers, 12(12), 3790. https://www.mdpi.com/2072-6694/12/12/3790

[34] Best, M. G., Sol, N., Kooi, I., Tannous, J., Westerman, B. A., Rustenburg, F., ... & Wurdinger, T. (2015). RNA-Seq of tumor-educated platelets enables blood-based pan-cancer, multiclass, and molecular pathway cancer diagnostics. Cancer cell, 28(5), 666-676.

[35] Ahn, S. B., Sharma, S., Mohamedali, A., Mahboob, S., Redmond, W. J., Pascovici, D., ... & Baker, M. S. (2019). Potential early clinical stage colorectal cancer diagnosis using a proteomics blood test panel. Clinical proteomics, 16, 1-20.

[36] Lofton-Day, C., Model, F., DeVos, T., Tetzner, R., Distler, J., Schuster, M., ... & Sledziewski, A. (2008). DNA methylation biomarkers for blood-based colorectal cancer screening. Clinical chemistry, 54(2), 414-423. https://academic.oup.com/clinchem/article-abstract/54/2/414/5628452

[37] Roth, C., Rack, B., Müller, V., Janni, W., Pantel, K., & Schwarzenbach, H. (2010). Circulating microRNAs as blood-based markers for patients with primary and metastatic breast cancer. Breast Cancer Research, 12, 1-8.

[38] Vellan, C. J., Islam, T., de Silva, S., Taib, N. A. M., Prasanna, G., & Jayapalan, J. J. (2021). Exploring novel protein-based biomarkers for advancing breast cancer diagnosis: A review. Clinical Biochemistry, 110776. https://www.sciencedirect.com/science/article/pii/S0009912021000705

[39] Gajjar, K., Trevisan, J., Owens, G., Keating, P. J., Wood, N. J., Stringfellow, H. F., ... & Martin, F. L. (2013). Fourier-transform infrared spectroscopy coupled with a classification machine for the analysis of blood plasma or serum: a novel diagnostic approach for ovarian cancer. Analyst, 138(14), 3917-3926.

[40] Uttley, L., Whiteman, B., Buckley Woods, H., Harnan, S., Taylor Philips, S., & Cree, I. A. (2016). Building the Evidence Base of Blood-Based Biomarkers for Early Detection of Cancer: A Rapid Systematic Mapping. https://pure.coventry.ac.uk/ws/portalfiles/portal/5134743/whitemancomb.pdf

[41] Koh, B., Liu, M., Almonte, R., Ariad, D., Bundalian, G., Chan, J., ... & Ma, P. (2021). Multi-omics profiling with untargeted proteomics for blood-based early detection of lung cancer. medRxiv, 2021-01.

[42] Richard, V., Davey, M. G., Annuk, H., Miller, N., & Kerin, M. J. (2022). The double agents in liquid biopsy: promoter and informant biomarkers of early metastases in breast cancer. Molecular Cancer, 21(1), 95.

[43] Fang, S., Zhe, S., Lin, H. M., Azad, A. A., Fettke, H., Kwan, E. M., ... & Kohli, M. (2023). Multi-omic integration of blood-based tumor-associated genomic and lipidomic profiles using machine learning models in metastatic prostate cancer. JCO Clinical Cancer Informatics, 7, e2300057.

[44] Sexauer, D., Gray, E., & Zaenker, P. (2022). Tumor-associated autoantibodies as prognostic cancer biomarkers-a review. Autoimmunity reviews, 21(4), 103041. https://www.sciencedirect.com/science/article/pii/S1568997222000118

[45] Wang, Z., Liu, Y., & Niu, X. (2023, August). Application of artificial intelligence for improving early detection and prediction of therapeutic outcomes for gastric cancer in the era of precision oncology. In Seminars in Cancer Biology (Vol. 93, pp. 83-96). Academic Press.

[46] Ralhan, R., Masui, O., DeSouza, L. V., Matta, A., Macha, M., & Siu, K. M. (2011). Identification of proteins secreted by head and neck cancer cell lines using LC-MS/MS: a strategy for discovery of candidate serological biomarkers. Proteomics, 11(12), 2363-2376.

[47] Vijayan, A., Fatima, S., Sowmya, A., & Vafaee, F. (2022). Blood-based transcriptomic signature panel identification for cancer diagnosis: benchmarking of feature extraction methods. Briefings in Bioinformatics, 23(5), bbac315. https://academic.oup.com/bib/article-abstract/23/5/bbac315/6658855

[48] Karimzadeh, M., Momen-Roknabadi, A., Cavazos, T. B., Fang, Y., Chen, N. C., Multhaup, M., ... & Goodarzi, H. (2021). Deep generative AI models analyzing circulating orphan non-coding RNAs enable detection of early-stage lung cancer. Nature Communications, 15(1), 10090. https://www.nature.com/articles/s41467-024-53851-9

[49] Slaby, O. (2016). Non-coding RNAs as biomarkers for colorectal cancer screening and early detection (pp. 153-170). Springer International Publishing. https://link.springer.com/chapter/10.1007/978-3-319-42059-2_8