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# Systematic Reveiw of Potential Uses of Biomarkers in Human Disease Identification

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***Abstract:*** **Biomarkers of all types have actually been utilized by generations of researchers, physicians, and epidemiologists to study human disease. The application of biomarkers in the diagnosis and management of heart disease, infections, hereditary and immunological conditions. This systematic review aimed to discuss and evaluate the potential uses of biomarkers in detection of human despises through based evidence previous trails. Electronics search was performed through different databases such Midline, and Embase and the date last searched was November 2016. Results were screened manually to identify relevant publications based on title and/or abstract. Publications that did not focus on the identification or evaluation of biomarkers were excluded. Several evidance have found that a majority of diseases might not be connected to a disease-specific protein biomarker in either the blood plasma or urine proteomes. Amongst the unique disease conditions represented in the microarray information.**

***Keywords:*** **Biomarkers, Potential uses, diagnosis and management of heart disease.**

## 1. INTRODUCTION

Biological markers (biomarkers) have been defined earlier as cellular, molecular or biochemical changes that are quantifiable in biological media such as human tissues, cells, or fluids [(1)]. More just recently, the meaning has actually been expanded to consist of biological qualities that can be objectively determined and examined as a sign of typical biological procedures, pathogenic procedures, or medicinal actions to a restorative intervention [(2)]. In practice, biomarkers consist of tools and innovations that can help in comprehending the forecast, cause, diagnosis, development, regression, or result of treatment of disease [(2)].

Biomarkers of all types have actually been utilized by generations of researchers, physicians, and epidemiologists to study human disease. The application of biomarkers in the diagnosis and management of heart disease, infections, hereditary and immunological conditions, and cancer are popular [(1,3)]. Their usage in research study has actually outgrown the have to have a more direct measurement of direct exposures in the causal path of disease that is devoid of recall predisposition, which can likewise have the capacity of offering info on the absorption and metabolic process of the direct exposures [(4)].

Surrogate result biomarkers are objectively determined attributes of a disease, which serve as indications of the underlying pathogenic procedure accountable for disease development, consisting of the modification because procedure following a healing intervention [(5,6)].

Biomarkers portraying prodromal indications make it possible for earlier diagnosis or permit the result of interest to be figured out at a more primitive phase of disease. Blood, urine, and cerebrospinal fluid offer the essential biological info for the diagnosis. In these conditions, biomarkers are utilized as a sign of a biological aspect that represents either a subclinical symptom, phase of the condition, or a surrogate symptom of the disease. Biomarkers utilized for screening or diagnosis likewise typically represent surrogate symptoms of the disease. The possible usages of this class of biomarkers consist of [(7)]: A) recognition of people predestined to end up being afflicted or who remain in the "preclinical" phases of the health problem, B) decrease in disease heterogeneity in epidemiologic research studies or medical trials, C) reflection of the nature of disease including the stages of latency, induction and detection, and D) target for a medical trials [(7)].

This systematic review aimed to discuss and evaluate the potential uses of biomarkers in detection of human despises through based evidence previous trails

## 2. METHODOLOGY

Systematic review study of Potential biomarkers for human diseases identification were demonstrated by a primary-literature search performed using PRISR (Preferred Reporting Items for Systematic Reviews) guidelines,

This electronic search was performed through different databases such Midline, and Embase and the date last searched was November 2016. Results were screened manually to identify relevant publications based on title and/or abstract. Publications that did not focus on the identification or evaluation of biomarkers were excluded. The searches were limited to human studies. Only English language articles were included, due to lack of resources for translation. Reference lists of included articles and relevant review articles were checked to identify any studies which the electronic search strategy may have missed.

## 3. RESULTS AND DISCUSSION

We identified several studies that were focusing in biomarkers as identification of different human diseases. The desire for minimally intrusive biomarker techniques has actually put a concentrate on recognized scientific biofluids, such as blood and urine, as sources of putative molecular biomarkers. Both blood and urine are quickly and cheaply gotten from patients as a traditional aspect of scientific care, for that reason biomarker methods leveraging these fluids are especially open to present scientific procedure [8,9]. The development of numerous blood plasma and urine proteome tasks, with objectives to recognize the huge body of gene items consisting of these biofluids, has actually produced brand-new chances for genomics-based methods to the elucidation of scientific molecular biomarkers [10,11]. Microarray analyses of blood and urine have actually determined expression signatures symptomatic of illness such as rheumatoid arthritis [12], Alzheimer disease [13], Chronic Fatigue Syndrome [14], Huntington's disease [15], and glial brain growths [16].

We have actually consisted of in our evaluation an extremely important research study [17] utilized microarray experiments where disease and regular tissues were determined in the exact same experiment. The disease and tissue annotations were by hand evaluated in a post-processing action to guarantee precision. In connecting proteome biomarkers with disease, they have actually discovered that 1,028 (38.5%) plasma and 577 (39.9%) urine proteins were discovered to be considerably differentially revealed in several of the 238 unique disease states represented in the microarray information. Of those, 846 (82.2%) plasma and 490 (84.9%) urine proteins are considerably differentially revealed in more than one disease state. Therefore, less than 20% of putative proteome disease markers show uniqueness for a single disease [17].

Amongst the putative biomarker proteins connected with disease we recognized a variety of enriched gene annotation terms (**Table 1**) [17]. Disease-associated plasma biomarker proteins were improved for plasma membrane proteins, and proteins associated with sugar and carb metabolic process. Disease-associated urine biomarker proteins were improved for extracellular proteins, and proteins associated with amine metabolic process and biotic stimulus reaction.

**Table 1: Annotation enrichment for disease-associated biomarkers**[17]

| GO Term | P-value |
|---|---|
| **Plasma** | |
| (GO:0005975) carbohydrate metabolic process | 3.1E-5 |
| (GO:0019318) hexose metabolic process | 1.1E-4 |
| (GO:0006066) alcohol metabolic process | 4.6E-4 |
| (GO:0044459) plasma membrane part | 5.3E-4 |
| **Urine** | |
| (GO:0009308) amine metabolic process | 7.7E-3 |
| (GO:0044421) extracellular region part | 1.4E-2 |
| (GO:0050896) response to stimulus | 1.8E-2 |

They have found that a majority of diseases might not be connected to a disease-specific protein biomarker in either the blood plasma or urine proteomes. Amongst the unique disease conditions represented in the microarray information [17], 136 (57.1%) were connected to plasma proteins, while 127 (53.4%) were mapped to urine proteins. Of these, 65.4% and 72.4% link specifically to biomarkers shared by other illness in plasma and urine respectively. A choice of disease conditions connected with several disease-specific biomarker proteins are noted in (**Table 2**) [17]

**Table2: A subset of diseases associated with multiple disease-specific protein biomarkers**[17]

| Disease | Disease-specific protein biomarkers |
|---|---|
| Plasma | |
| Idiopathic cardiomyopathy | *MACF1, SF3B2, RFX5, TLN1, FSHR, PCCA, PGK2, NEK1, RGS3, RGN, CYP3A43* |
| Thrombocytopenia | *CYLC2, PIGK, AASS, PANX2, DSPP, XPC, TBL1X, TCERG1* |
| Malignant melanoma | *PDE3A, CALR, PDCD6IP, CHAC, KIAA0586* |
| AIDS | *PAPPA, TRADD, KIAA0649, APRIN, MAP3K5* |
| Huntington's disease | *MAML1, PLGL, RNF10, KIAA0913, OAS1* |
| Urine | |
| Idiopathic cardiomyopathy | *DEFA3, ALDH1L1, CD177, TLN1, SLURP1, BPI, APOH, C8B* |
| Glioblastoma | *WISP2, PRDX3, TIMP2, ACO1* |
| Breast cancer | *ENPP4, PFKP, THBD, IGFALS* |
| Acute promyelocytic leukemia | *CSPG3, LGALS7, HSPA5* |
| Adenovirus infection | *VGF, AGA, UMOD* |

Other included study [18] which compares serum concentrations of 1100 proteins in between 30 primary Sjögren's syndrome (pSS) patients and 30 healthy controls (HCs), with 82 differentially revealed proteins determined as pSS-associated proteins biomarkers. and they evaluated the connection in between differentially revealed proteins and European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI), they have actually discovered Nine proteins were statistically drawn out by Spearman's rho test (Table 3) as follows: ephrin type-B receptor 2 (EPHB-2), C-X-C motif chemokine 13 (CXCL13), signaling lymphocytic activation molecule 2 (SLAMF-2, CD48), β2MG, BAFF, TNF receptor 2 (TNF-R2), lymphocyte activation gene-3 (LAG-3), cluster of differentiation 163 (CD163), and programmed cell death protein 1 ligand 2 (PD-L2) [18].

**Table3: Serum proteins positively correlated with ESSDAI score in patients with pSS in first cohort ($n = 30$)** [18]

| **Protein** | **Spearman's $\rho$** | ***P* value** |
|---|---|---|
| EPHB-2 | 0.65 | <0.0001 |
| CXCL13 | 0.60 | 0.0005 |
| CD48 | 0.56 | 0.0014 |
| β2MG | 0.55 | 0.0018 |
| BAFF | 0.52 | 0.0029 |
| TNF-R2 | 0.51 | 0.0039 |
| LAG-3 | 0.49 | 0.0058 |
| CD163 | 0.49 | 0.0062 |
| PD-L2 | 0.47 | 0.0081 |

And also they stated that There was significant correlation between ESSDAI scores and CXCL13, TNF-R2, CD48, BAFF, and PD-L2 in both the initial and the validation cohorts of patients with pSS[18].

We identified systematic review study [19] that included over 59 trails that focus in biomarkers for disease progression in Alzheimer's disease, and they have actually concluded that they discovered inadequate proof to advise using any biomarker for determining disease development in Alzheimer's disease scientific trials. More assessment of the effectiveness of MRI measurements of ventricular volume and entire brain volume as biomarkers of disease development in Alzheimer's disease does appear to be warranted [19].

However a significant progress in early detection of Alzheimer's disease with high level of sensitivity and uniqueness by imaging methods and analysis of protein biomarkers in cerebrospinal fluid has actually been accomplished [20]. The high expense and invasiveness of these approaches make their application for primary screening of big populations not practical [21]. Numerous techniques to the advancement of minimally intrusive or non-invasive assays for early detection of Alzheimer's disease have actually been evaluated [22,23]. Presently there is no reputable molecular test for identifying AD at the pre-symptomatic or MCI phase. Just recently we proposed a method for early detection of MCI based upon analysis of cell-free flowing miRNAs in plasma by RT-qPCR [22]. Numerous developments were shown to be reliable for choice of possible miRNA biomarkers. We assumed that modifications in concentrations of flowing miRNAs enhanced in the brain, and more particularly in hippocampus and frontal cortex, were more most likely to show Alzheimer's disease - associated pathologic procedures in the brain than other or common organ-enriched miRNAs. Second, we examined miRNAs present in synapses and neurites, dysfunction and damage which is particular of early phases of neurodegeneration, and for that reason, might impact expression and secretion of these miRNAs. Third, to make up for procedures unassociated straight to MCI, e.g. modifications in blood-brain barrier permeability, we used the "biomarker pair" approach [24,25,26].

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