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Proteomics and Its Role in Diagnosis of Auto Immune Diseases

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Abstract

The "proteome" is the entire protein composition of a cell that is described at a given moment in terms of localisation, interactions, post-translational changes and turnover. Although it is far more complicated than genomics, proteomics is one of the most important methodologies for understanding gene function. It is critical for early illness diagnosis, prognosis and disease progression monitoring. It also plays an important function in medication development as target compounds. Biological fluids obtained from individuals with Auto Immune Diseases (AIDs) may be used to profile autoantibody reactions and proteomics methods have proven to be quite useful in this process. To identify proteins, proteomics methods such as tissue array and mass spectrometry (MS) in various forms are used. Scientists attempting to identify novel biomarkers in illnesses such as AIDs have recently been more interested in protein microarray technology. The goal of this study was to bring attention to the latest developments in proteomic analysis and to determine its function and clinical value in the diagnosis of autoimmune disorders.

Keywords: Proteomic analysis - Autoimmune diseases- Biomarkers- diagnosis.

1. Introduction

Human proteomics is currently in its early stages, but it will certainly become the most important tool for understanding human biology and disease. Expecting a home plan to properly explain all the complexity of the royal house is as straight forward as expecting a house plan to fully describe all the complexities of the royal house [1]. The proteome is the home, if the genome is a blueprint. Proteome analysis cannot be replaced by deoxyribonucleic acid (DNA) sequencing and messenger ribonucleic acid (mRNA) expression analysis [2]. Post-translational modifications, which occur at many locations in eukaryotic cells in a variety of ways, complicate proteomics [3]. Proteins are biological function effectors, and their quantities are influenced not just by mRNA levels, but also by translation control and host regulation. As a result, proteomics will be regarded as the most important data collection for characterizing biological systems [4]. Around 3% to 5% of human illnesses are categorized as Auto Immune Diseases (AIDs), and the clinical symptoms, disease course and prognosis of these diseases are typically diverse [5].

Post-translational modifications (PTMs) of antigens, which causes host proteins to be

identified as "non-self" or "dangerous," causing an adaptive immune response, is a crucial characteristic that underlies many autoimmune disorders [6]. The alteration of the amino acid side chain of some proteins after biosynthesis is referred to as PTM [7]. Proteins having important structure/function, such as secreted proteins, membrane proteins and histones, are commonly subjected to post-translational changes [8]. There is a significant unmet medical need to (i) improve the diagnosis and prediction of outcomes of complex autoimmune diseases and (ii) develop innovative therapies for complex autoimmune diseases such as systemic lupus erythematosus (SLE), multiple sclerosis (MS), rheumatoid arthritis (RA), Crohn's disease (CD) and systemic sclerosis [9].
The final objective of long-term treatment of individuals with autoimmune disorders is individualized medication therapy that leads to lasting relief rather than merely symptom alleviation. Genomic and proteomic technology has made significant progress in finding novel pharmacological targets and molecular features associated with clinically relevant disease states, disease subgroups and treatment responses [10]. The goal is to discuss how to employ proteomic methods to find accurate biomarkers for illness diagnosis from a variety of materials, including blood, tissue, tissue interstitial fluid (TIF), saliva and urine [11].

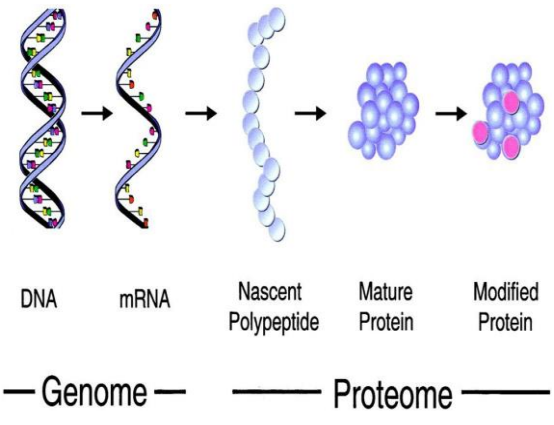

Figure 1: Depicts the connection between genetic elements and the proteome [3].

2. Current Proteomic Technology

Proteomic analysis consists of three major stages for identifying biomarkers in specific illnesses. They include (1) protein extraction and separation, (2) protein identification and (3) protein verification [12].
The following are the last steps: (1) a database search, (2) a study of protein-protein interactions (PPIs) and (3) a statistical analysis [13].

2.1. Sample Collection, Pretreatment and Preparation

To begin, gather several sorts of samples from a number of patients, including pleural effusion, saliva, blood, urine, tissue and TIF from each patient. Second, for proteomics investigations, a suitable sample-pretreatment process is necessary to overcome the sample-analytical method mismatch. Sample pretreatment is critical in the analytical workflow for proteomics investigations in order to get the useful, high-quality quantitative data required to reduce discrepancies between laboratories. Dissolution, extraction, interaction with certain chemical species, crushing, treatment with a chelating agent (e.g., EDTA), masking, filtration, dilution, sub-sampling and many more procedures may be used in sample preparation. The sample is treated in order to make it ready for examination by specific analytical equipment. Pretreatment and sample preparation varies depending on the kind of sample; for example, tissue samples require different pretreatment and preparation processes than blood samples. As a result, various samples require different lysis buffers, saline and digesting methods. Furthermore, the environment and conditions in which valid test samples must be stored vary [14].

2.2. Protein extraction, separation and purification Technology

Proteomics techniques for extracting and separating proteins are being used in a number of new research to identify viable biomarkers for a variety of illnesses. They include one-dimensional electrophoresis (1-DE), two-dimensional differential gel electrophoresis (2-DDIGE) and two-dimensional gel electrophoresis/mass spectrometry (2-DE / MS) [15].

2.2.1. Laser capture microdissection

In proteomics research, LCM may be used to harvest the precise cells required from a sample. A tiny infrared laser was used to target thin, quickly postfixed tissue slices. The heat melted tiny polymer film connected to a cap over the sample and the film stuck to the cells of interest. As a result, researchers use LCM to ensure that these cells are fully isolated from other cells in the sample as well as preserving the cells' molecular features. The difficulty of anatomical resolution in tissues has been solved by LCM. The spectrum of proteins discovered in previous investigations has widened thanks to new extraction methods. By diluting the signals of certain proteins, this technique can identify protein signals with low presence. Proteomics researchers employ a powerful method that combines LCM and 2-DE to identify novel targets and biomarkers [16].

Chromatography is used in traditional protein purification procedures such as size exclusion chromatography (SEC), ion exchange chromatography (IEC) and affinity chromatography [17]. The SEC is used to separate low-molecular-weight proteins and might be a useful technique for purifying non-covalent multi-meric protein complexes in biological settings [18]. Many different types of ligands have been isolated and utilized in antibody purification. Lectins are used to purify immunoglobulin (Ig) M and IgA molecules, whereas proteins A and G are used to purify IgG molecules [19].

2.2.2. Gel-based approaches: Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis (SDS-PAGE)

The SDS-PAGE is a high-resolution method for separating proteins depending on their size, which aids in estimating molecular weight [20].

2.2.3. Two-dimensional gel electrophoresis

Two-dimensional polyacrylamide gel electrophoresis (2-DPAGE) is a fast and accurate technique for sorting proteins based on their mass and charge. Based on the size of the gel, 2-DPAGE may resolve roughly 5,000 distinct proteins in a single run [21].

2.3. Protein identification

Genes code for proteins, which are complex molecules that catalyze processes, convey signals and create three-dimensional cellular support structures that are structured spatially and temporally. The goal of many early proteomic studies was to figure out how individual proteins related to biological processes. Despite the success of this endeavor, it's crucial to remember that proteins don't always have the same function or part in physiology (for example, pleiotropy), therefore revealing the varied biological activities and work of proteins in cells is a big problem in proteomics. Other advancements in proteomics have focused on determining protein post-translational changes, protein-protein interactions and protein locations in cells [22]. Protein activities and functions are divided by organelle spatial structure. The identification of proteins found in organelles (such as mitochondria) aids in the definition of protein roles and possible functions that may occur inside the compartment and this knowledge can assist to better characterize the organelles' functions. Proteomic research aims to

understand the structure and folding of proteins on a large scale and in vivo [19].
To move forward with protein understanding, new equipment and techniques are required [23].
There are several proteomics methods for identifying proteins, including tissue array and mass spectrometry (MS) in various forms [24].

2.3.1. Protein Microarray

Protein microarrays, also known as protein chips, are a novel type of proteomics technology that allows for high-throughput detection with a small sample size. Functional protein microarrays, analytical protein microarrays and reverse-phase protein microarrays are the three types of protein microarrays [25].

2.3.1.1. Analytical protein microarray

Antibody arrays that specialize in protein detection are the most common type of analytical protein microarray. The target protein is identified in these microarrays via direct labeling or using a reporter antibody in a sandwich assay technique [26].

2.3.1.2. Functional protein microarray

Protein interactions, such as protein binding and enzyme-substrate reactions, may be studied using functional protein microarrays [26]. Purified recombinant proteins or peptide fragments are assembled into functional arrays that may be utilized for discovery-based research, such as the investigation of protein-protein, protein-DNA, protein-lipid, protein-drug and protein-peptide interactions [27].

2.3.1.3. Reverse phase protein microarray

Cell lysates from various cell states are arrayed on nitrocellulose slides that have been probed with antibodies against target proteins. Antibodies are detected via fluorescence, chemiluminescence and colorimetry. Reference peptides are written on slides to measure proteins. These microarrays are used to detect proteins that have been changed or are dysfunctional in specific illnesses [28] as shown in Figure. 2. can be probed with cell lysate to determine protein expression levels and the specificity of the interaction that results. (Middle) Functional: Can be used to investigate target proteins' biochemical characteristics and activities. (Right) Reverse phase: Can be used to look into post-translational changes and identify biomarkers [26]. Protein microarray has lately gotten a lot of attention from scientists looking for novel biomarkers in various illnesses. Protein microarray technology is a strong platform when compared to mass spectrometry. Its benefit is that it just takes a little number of proteins to simultaneously investigate numerous analytes inside the original sample. As a result, protein microarrays are extremely effective in the identification of biomarkers [27].

2.3.2. Mass spectrometry

Mass spectrometry has been used to identify native proteins and native protein complexes with great success. MS is currently being used to investigate entire cells in the hopes of calculating the status of protein folding in whole proteomes [29]. Although mass spectrometry has achieved several advances in the previous decade, there are certain clear patterns. The need for high-quality, high-resolution precision instruments, particularly Orbitrap and time-of-flight (TOF) mass analyzers, has driven the development of high-quality, high-resolution precision equipment [30]. In addition, the development of novel biological therapies has increased the need to describe intact proteins in order to

confirm their structure, sequence and changes. To elicit sequence information, fragmentation of amide bonds in intact proteins necessitates more powerful techniques than fragmentation of peptides. Electron transfer dissociation (ETD) and ultraviolet light dissociation (UVPD) are two techniques that have been used to achieve more effective fragmentation of intact proteins, particularly when used simultaneously. The possibilities for top-down MS have considerably increased as a result of these significant advancements in MS capabilities [31].

There has been a rising interest in utilizing ion mobility spectrometer (IMS) technology to provide ion separation capabilities to mass spectrometers during the last 20 years. The trapped IMS (TIMS) device traps ions in a flowing gas using electric and radiofrequency fields. Parallel Accumulation-Serial Fragmentation (PASEF), a method for the large-scale selective release of peptide ions from TIMS devices, was born out of the success of TIMS [32].

The combination of two approaches (TIMS / PASEF) yields a new way for separating complicated ion mixtures in order to increase the number of tandem mass spectra of collected peptides, resulting in more protein identifications [32].

The enzyme-linked immunosorbent assay (ELISA) and Western blotting are used to analyze specific proteins. These methods are limited to analyzing a small number of specific proteins and cannot identify the amount of protein expression [17].

2.3.3. Enzyme immunosorbent assay

This test attaches enzyme-conjugated antibodies to an antigen or antibodies on a solid surface. Then it evaluates changes in enzyme activity that is proportional to antibody and antigen concentrations in the biological sample [33].

Because ELISA is a useful technique for measuring serum antibody concentrations it may be used as a serological blood test to identify a variety of illnesses, including coeliac and autoimmune disorders [34]. The ELISA can be used to test for food allergies, blood types, the presence of the pregnancy hormone human chorionic gonadotropin (hCG), clinical and laboratory research, forensic toxicology and a number of other diagnostic scenarios [35].

Antinuclear antibodies (ANA) are a key indication of autoimmune disorders. Laboratory tests are useful in the diagnosis, treatment, prognosis and prediction of pathological changes produced by disease activities because clinicopathological categorization of autoimmune disorders is difficult without laboratory assistance. ELISA is the most used approach for most regular laboratories, despite the fact that there are other detection methods that can detect ANA. Despite being the "gold standard," the Indirect Immunofluorescent Antibody (IFA) test is not frequently utilized. The IFA-ANA test is a useful screening tool because it can identify anti-mitochondrial and other cytoplasmic antibodies, which ELISA cannot do [36].

The diagnostic usefulness of the recently developed solid-phase screening test Connective Tissue Disease-Screen (CTD-Screen) in identifying ANA in a "real world situation" was assessed. They discovered that the novel ANA-ELISA had diagnostic accuracy comparable to that of the IFA-ANA, which is frequently used in CTD. The benefit of ANA-ELISA over indirect immunofluorescence is that it is less manual, does not rely on performance and is more sensitive and specific [37].

2.3.4. Western blot

The Western blot approach, which involves electrophoresis of proteins, transfer to nitrocellulose membranes and accurate detection of target proteins using enzyme-linked antibodies, is a very significant and powerful technique for identifying low-abundance proteins [38].

Edman degradation may also be used to

determine the amino-acid sequence of particular proteins. Quantitative proteomics has recently produced isotope-coded affinity tags (ICAT), stable isotope labeling with amino acids in cell culture (SILAC) and isobaric tags for relative and absolute quantification (iTRAQ). X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy are two high-throughput methods for determining the three-dimensional (3D) structure of proteins, which can help researchers, better understand their biological activities [39]. To increase the resolution and sensitivity for high-performance protein analysis, NMR can be coupled with other techniques such as liquid chromatography (LC) or ultra-high performance liquid chromatography (UHPLC) [40].

3. Bioinformatics analysis

Proteomics necessitates the use of bioinformatics. As a result, with the introduction of high-throughput technologies based on strong data analysis, its relevance is progressively rising. This new field introduces a unique technique for managing data from massive and heterogeneous proteomics for discovery operations [18]. Descriptions of protein function, domain structure, subcellular distribution, post-translational modifications, variations, similarities to other proteins, structural categorization and so on are all accessible in bioinformatics. Proteomics relies on computational approaches to describe changes in the 3-D structure and stability of proteome proteins as a function of sequence variations and to make predictions about the proteome's functional state [41].

4. Proteomics and biomarkers in autoimmune diseases

Autoimmune disorders are a group of illnesses in which the patient's own organs or tissues are attacked by autoantibodies. Autoantibodies are clinically validated as biomarkers for diagnosis, prognosis and patient stratification [1]. They play an essential part in the pathophysiology of AIDs. Changes in cytokines, chemokines, protein glycosylation and other molecules also give useful information for assessing AIDs progress [27]. Blood, various bodily fluids and tissues all contain these biomolecules [42].

Biomarkers are categorized as follows, Consistent with the Food and Drug Administration:

• Diagnostic biomarkers: these are substances that are used to detect or confirm the presence of a disease or a condition, or to identify people who have a certain disease subtype. Hemoglobin A1c (HbA1c), for example, is the most often utilized biomarker for diagnosing prediabetes and diabetes [43].

• Prognostic biomarkers: used to predict the likelihood of a clinical occurrence, recurrence, or development of a disease. For instance, elevated prostate-specific antigen (PSA) is a predictor of prostate cancer clinical progression [44].

• A safety biomarker is a type of biomarker that may be used to detect the presence or severity of toxicity as an adverse impact that can be evaluated before or after exposure to medicinal goods or from environmental sources. Transaminases, for example, have been used as indicators for potentially hepatotoxic medications [45].

• Monitoring Biomarker: a continuous measurement used to determine the severity of disease or medical problems, as well as proof of medicinal product or environmental exposure. For example, in children with pulmonary hypertension, B-type natriuretic peptide is used to assess vascular and ventricular function [46].

• Pharmacodynamics reaction: When exposed to medicinal goods or certain environmental factors, a biomarker is utilized to indicate that a biological reaction occurs. For example, while modifying anticoagulant treatment, the international normalized ratio (INR) is

critical [47]. A good biomarker should be able to offer information on diagnosis, prognosis and therapy. Additionally, they must be derived from the patient's clinical data and possess the following chemical-analytical properties:

• High specificity: A biomarker's measurement must be disease specific.
• Specimen: sample collection must be as painless as possible. Saliva, for example, is superior to pee, while urine is superior to blood.
• Representativeness: the number of biomarkers in the sample must correspond to the number of biomarkers in the organism.
• Stability: It's important to understand how things work [48].

4.1. Biomarkers in systemic lupus erythematosus

From a serological and clinical standpoint, it might be argued that systemic lupus erythematosus is the most varied autoimmune disease. Immunopathological abnormalities are continuously being identified and individual patient clinical presentations vary greatly. In SLE patients, immunological dysregulation leads to an over production of autoantibodies and immune complexes, over activation of complement and potential tissue inflammation, all of which lead to multi-organ involvement and unexpected clinical symptoms [49]. With the growing number of cytokines and chemokines, as well as advances in cytokine biology, these molecules have emerged as key players in the pathogenesis of SLE or as indirect indicators that indicate the disordered response in SLE [50] as shown in Table. 1. BAFF, B-cell activating factor; CNS, central nervous system; CSF, cerebrospinal fluid; IFN, interferon; IL, interleukin; NPSLE, neuropsychiatric systemic lupus erythematosus; TNF, tumor necrosis factor; RANTES, Regulated on activation normal Tcell produced and released; MCP-1, Monocyte chemoattractant protein-1; IP-10, interferon-induced protein 10; MIP-3B, Macrophage Inflammatory Protein-3 beta; SIGLEC-1, Sialic Acid Binding Ig Like Lectin 1; anti-dsDNA, anti-double-stranded DNA; anti-U1-RNP, anti-uridin1ribonucleoprotein complex; BLys, B lymphocyte stimulator [51].

Recent studies comparing the levels of IL-1 cytokines in patients with Immune thrombocytopenic purpura (ITP) to those with SLE-associated thrombocytopenia (SLE-TP) and SLE without thrombocytopenia (SLE-NTP) found that ITP patients had significantly lower levels of IL-1β, IL-18, IL-36α, IL-36β, IL-36γ and IL-33 which may help in their discrimination [52].

4.1.1. Biomarkers of lupus nephritis

Renal involvement is one of the most prevalent symptoms of SLE and it continues to cause considerable morbidity and death. In 25-50 percent of people with SLE and 80 percent of children with SLE, lupus nephritis develops [53].

4.2. Autoantibody biomarker in rheumatoid arthritis

The most common systemic illness is rheumatoid arthritis. It's characterized by synovial inflammation, which can lead to joint injury and impairment, and it has been linked to an increase in the incidence of systemic manifestations, cardiovascular comorbidities, for example [54].

Circulating autoantibodies in biological fluids, inflammatory cytokines, chemokines and alterations in metabolism are all common features of the pre-RA stage, which can persist from months to years before the emergence of the disease

Table (1): Cytokine and chemokine abnormalities associated with SLE.

Cytokine/Chemokine	Abnormality	Disease Association
IFN-α/β	Serum and CSF levels are elevated.	Fever; CNS and hematological symptoms
IFN signature	IFN-regulated genes have their expression levels increased.	Hematologic, renal and CNS (cerebritis) manifestations
IFN-inducible chemokines		
MCP-1 (CCL2)	Enhanced serum and/or urine concentrations; increased gene expression	Disease activity/flares
RANTES (CCL5)		Lupus nephritis
MIP-3B (CCL19)		NPSLE
IP-10 (CXCL10)		Hypocomplementemia
SIGLEC-1		Autoantibodies (anti-dsDNA, anti-U1-RNP; Ro, Sm)
CXCL1		
CXCL16		
IFN-γ	Elevated serum levels	Disease activity
IL-17	Elevated serum levels	Disease activity
IL-6	Elevated levels in serum and urine	Disease activity; anti-dsDNA elevated levels. low serum C3/C4; lupus nephritis
IL-10	Elevated serum levels	Disease activity; anti-dsDNA elevated levels; low serum C3/C4
IL-12	Elevated or decreased levels reported in different studies	Lupus nephritis (elevated levels of IL-12 in serum and urine)
IL-15	Elevated serum levels	Disease pathogenesis
IL-21	Elevated serum levels	Disease activity; disease pathogenesis
IL-2	Decreased serum levels	Disease pathogenesis
IL-1	Elevated serum levels	Disease activity
IL-1 receptor antagonist (IL-1ra)	Decreased serum levels	Lupus nephritis
BAFF (BLys)	Elevated serum levels	Disease activity
TNF-α	Elevated levels in serum and kidneys	Disease activity; correlated with serum IFN-α levels

phenotype [55]. Anti-citrullinated protein antibodies (ACPA), which are assessed in vitro as anti-citrullinated cyclic peptide (anti-CCP) antibodies are utilized as a major clinical diagnostic biomarker for RA, develop in around two-thirds of RA patients [56]. Synovial fluid antigens were discovered. There were 24 proteins found in synovial fluid that had previously been identified as shown in Table. 3 [57]. Post-translationally changed vimentin, such as phosphorylation, ubiquitination, carbamylation and citrullination, has been investigated extensively [59]. According to current research, mutant citrullinated vimentin (MCV) is a potential RA diagnostic and prognostic marker with sensitivity and specificity equivalent to anti-CCP [60]. Native vimentin's involvement in RA is less well understood, although it might be a helpful biomarker [57].

Table (2): Summary of biomarkers for lupus nephritis.

Traditional Biomarkers
Serum Creatinine levels
Serum C3/C4 levels
Anti-dsDNA levels
Urine protein levels
Urine sediments
Kidney biopsy
Candidate Biomarkers (Serum, peripheral blood and kidney)
Anti-nucleosome antibodies (serum)
Anti-C1q antibodies (serum)
Complement C4d (kidney biopsy)
Complement C4d (erythrocyte-bound; peripheral blood)
Candidate Biomarkers (Urinary proteins)
Monocyte chemo attractant protein-1 (MCP-1)
Neutrophil gelatinase-associated lipocalin (NGAL)
Tumor necrosis factor-like weak inducer of apoptosis (uTWEAK)
Transferrin (TF)
α1-acid glycoprotein (AGP; AAG)
Ceruloplasmin (CP)
Lipocalin-type prostaglandin D-synthetase (L-PGDS)
Hepcidin
Tumor growth factor- β (TGF-β)

4.3. Autoantibody biomarker in rheumatic diseases

Myositis is a systemic illness that predominantly affects muscles, with extra-muscular organ involvement occurring occasionally. There are many clinical subgroups of myositis, each with its own clinical presentations and autoantibody profiles, suggesting that disease pathogenesis is heterogeneous. Various autoantibodies have been identified in myositis, some specific to myositis, Anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies and anti-Jo-1 or anti-histidyl-tRNA-synthetase antibodies are the most frequent myositis-specific autoantibodies (MSAs), whereas anti-U1-ribonucleoprotein (anti-U1-RNP), anti–Sjögren's-syndrome-related antigen A/Ro (anti-SS-A/Ro), anti-polymyositis/scleroderma (anti-PM/Scl) and anti Ku70/80 heterodimer (anti-Ku) autoantibodies, Ku (Ku70/80) is a DNA-binding protein have a role in repairing DNA, are the most common myositis-associated autoantibodies (MAAs) [61].
The MSAs are a good tool for subdividing patients and predicting disease courses and outcomes because of their high specificity for myositis and the strong connection between different MSAs and unique clinical characteristics. Despite its use, the European League Against Rheumatism/American College of Rheumatology Classification (EULAR/ACR) criteria for adult and juvenile myositis in 2017 included just anti-Jo-1 to identify individuals with myositis [61].

4.4. Autoantibodies in Systemic Sclerosis (SSc)

The pathogenic triad of SSc includes abnormal immune activation as evidenced by disease-specific autoantibodies, obliterative vasculopathy and ischemia caused by endothelial cell damage/apoptosis, intimal proliferation, luminal obstruction, vasoconstriction and tissue fibrosis caused by excess extracellular matrix (ECM) accumulation [62]. Autoantibodies are seen in nearly all SSc patients. Antinuclear antibodies (ANAs) such as anti-centromere antibody (ACA), anti-topoisomerase I antibody (ATA), anti-RNA polymerase (RNAP) III antibody and others were found in SSc. Individual SSc-specific ANAs, like MSAs, are directed against ubiquitous nuclear proteins and are linked to particular clinical manifestations of SSc [63].

5. Conclusion

For large-scale protein studies, mass spectrometry-based techniques and micro arrays have recently become the most popular technology. Over the last decade, mass spectrometry-based proteomics has

Table (3): Synovial fluid proteins identified as auto antigens in RA.

Gene Name	Protein Name	Localization
TKT	Transketolase	Intracellular and extracellular
TPM3	Tropomyosin alpha-3 chain	Intracellular and extracellular
VIM	Vimentin	Intracellular and extracellular
CEACAM1	Carcinoma embryonic antigen-related cell adhesion molecule1	Intracellular and extracellular
EEF1G	Elongation factor 1-gamma	Intracellular and extracellular
IMPDH1	Inosine-5'-monophosphate dehydrogenase 1	Intracellular and extracellular
KRT19	Keratin 19	Intracellular and extracellular
LDHB	L-lactate dehydrogenase B chain	Intracellular and extracellular
MIF	Macrophage migration inhibitory factor	Intracellular and extracellular
TKT	Transketolase	Intracellular and extracellular
TPM3	Tropomyosin alpha-3 chain	Intracellular and extracellular
VIM	Vimentin	Intracellular and extracellular
CAMK2G	Calcium/calmodulin-dependent protein kinase type II subunit gamma	Intracellular
CARHSP1	Calcium-regulated heat-stable protein 1	Intracellular
EEF1D	Elongation factor 1-delta	Intracellular
IFI35	Interferon-induced 35 kDa protein	Intracellular
ILF2	Interleukin enhancer-binding factor 2	Intracellular
PRKAR1A	cAMP-dependent protein kinase type I-alpha regulatory subunit	Intracellular
PSME3	Proteasome activator complex subunit 3	Intracellular
RPLP1	60S acidic ribosomal protein P1	Intracellular
RUFY1	RUN and FYVE domain-containing protein 1	Intracellular
SSB	Lupus La protein / SSB	Intracellular
STAT1	Signal transducer and activator of transcription 1-alpha/beta	Intracellular
TPM1	Tropomyosin alpha-1 chain	Intracellular

emerged as a promising technique that is experiencing rapid advancement in a variety of domains, including mass spectrometric instruments, peptide identification algorithms and bioinformatics computational data analysis. Protein microarrays are effective instruments for determining relative protein quantity and tracing posttranslational changes. Reverse-phased protein microarrays might be a potential and novel microarray application for predicting disease progression, guiding treatment selection and monitoring therapy response. Biomarkers are valuable instruments that are utilized in many aspects of biology, from study to diagnosis. Proteomics has the potential to aid in the development of advanced biomarkers in a variety of illnesses, including autoimmune disorders. For diagnostic and prognostic purposes in autoimmune disorders, a variety of proteomics systems are now accessible.

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