Chapter

Precision Medicine of Autoimmune Diseases

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Abstract

Genomic-based information is an essential key to precise therapy referred to as personalized medicine. Its application in autoimmune disease treatment will bring the required breakthrough in medicine. Autoimmune diseases are the disease conditions where the body's immune system recognizes and generate an immune response against self-antigens. There exist different approaches of which precision medicine data can be utilized in the clinical management of autoimmune diseases; this includes diagnosis, prognosis, stratification and treatment response prediction. Different markers exist to guide clinical decision while several others are still being identified and proposed. This chapter highlights data and databases in precision medicine of autoimmune diseases and the pathway for data sharing. The precision medicine of selected autoimmune diseases was discussed, and the different biomarkers utilized in the diagnosis, prognosis, stratification and response monitoring of such condition were considered.

Keywords: autoimmune diseases, databases, genomic data, personalized medicine, precision medicine

1. Introduction

The functional responsibility of the immune system (humoral and cell-mediated alike) is to protect against infection by destroying various infectious agents when such agents attack the body or are introduced through vaccination [1]. The functioning of the immune system is coordinated and maintained by a sequence of highly regulated and physiological mechanisms which aids the identification and recognition of both body cells and foreign cells [2].

The body's immune units usually coexist with other cells of the body that carries a self-marker molecule. Immune reactions are only triggered when an antigen which could be a microbe, part of a microbe or a molecule is presented to the surface of the cell and perceived by the body defenses [3].

The immune system of humans is made up of two divisions which are innate and acquired immunity. The innate immunity forms the first line of defense immediately after infectious agents are recognized by the body while acquired immunity functions in the removal of pathogens at the later phase of infection [3].

When the immune system is stimulated, it targets and destroys foreign units. Still, in some abnormal situation, the immune system might be insensitive to antigens, hypersensitive to antigens or recognize the cells with self-marker as foreign cells [2].

There are disease conditions that affect the immune system, which leads to different degree and types of conditions known as the Immune diseases. Diseases of the immune system include inherited and acquired immunodeficiency and immune-proliferative disorders which includes malignancies of the immune system (multiple myeloma, lymphoma, and leukemia), autoimmune diseases (rheumatoid arthritis), and immune hypersensitivities (allergies) [4]. Inherited immunodeficiency, also is known as primary immunodeficiency, refers to a large number of immune disorders which alters either or both development and function of the immune system. Primary immunodeficiency implies conditions resulting from loss of function, a gain of function or loss of expression due to monogenic germline mutations [5]. External and environmental factors can induce an adverse effect on the immune system, and this is regarded as secondary or acquired immunodeficiency, which is encountered commonly in clinical practice and could arise from quite a number of conditions [6].

The evolvement of medical practices especially diagnosis and treatment from the usual "one size fits all" approach to a more genetic and detailed patient stratification in a bit to acquire more information about the disease condition and the patient is known as personalized medicine [7].

The complexity of the body defense system and the ability of the cells associated with it to shift between different activation states under physiological and pathological conditions are some of the reasons for diversity in the treatment approach. The immune diseases at times are diverse, and this result in variations in response to therapy. The difference in the disease course also create reasons why there should be the identification of personalized marker for diagnosis of immune disease. Therefore, the use of genetic assessment to determine the best possible therapeutic approach from the numerous available options with different mechanisms, risks, and efficacy are essential [7, 8].

The Precision medicine data types, genomic data in precision medicine, genomic and personalized medicine databases, data sharing, access and use are discussed in this chapter. Also, the use of genomic methods and data in the understanding, diagnosis of diseases using specific biomarkers, monitoring of prognosis using prognosis biomarkers, personalized treatment of immune disorders, monitoring of response to treatment using response biomarkers are also described in this chapter.

2. Precision medicine of specific autoimmune diseases

2.1 What is immunity?

Immunity is the ability of the body to prevent infection by resisting the invasion of such a body by harmful microorganism knows as infectious agents. Immunity can be categorized broadly into two types which are:

i. Innate or Natural Immunity and

ii. Acquired Immunity

2.1.1 Innate or natural immunity

The initial host protection against diseases- causing agents is the innate immunity which is mediated by phagocytes. Through germline-encoded pattern-recognition receptors (PRRs), the innate immunity of the human body recognizes

microorganisms invading its body. For the immune cells to be activated, different classes of the PRRs, which include Toll-like receptors and cytoplasm receptors recognize distinct and important microbial component of invading microorganisms thereby activating immune cells [3, 9].

2.1.1.1 Mechanism of action of innate or natural immunity

Immediately after the detection of non-self-agents by PRRs which could be exhibited on the outer membrane of the cell, in intracellular parts, or released in the bloodstream and fluids of the body tissues, the PRRs then perform the function of opsonization, stimulation of complement and coagulation outflow, phagocytosis, initiation of pro-inflammatory signaling pathways, and inception of apoptosis. These cascades of intracellular signaling induce the expression of overlapping and unique genes which are involved in the inflammatory immune responses and essential in precision medicine. The reaction by the innate immune system is carried out by phagocytes (neutrophils, monocytes, and macrophages), inflammatory mediators releasing cells (basophils, mast cells, and eosinophils), and natural killer (NK) cells [3, 10].

2.1.2 Acquired immunity

Acquired immunity is the immunity that is developed against an infectious agent by the body after the previous encounter with a pathogen or a type of immunity developed by a child by the exchange of protective materials from mother to child before and after birth or by the injection of such substances. The mediation of adaptive immunity is the function of clonally distributed T and B Lymphocytes whose characteristics are the possession of specificity and memory. Many at times, activation of the innate immune response can trigger acquired immunity. The generation of Helper T cells subsets and the production of cytokines influence adaptive immunity [11, 12].

2.1.2.1 Mechanism of action of acquired immunity

When naïve T-helpers cells are stimulated by Antigen-presenting Cells otherwise known as APCs, they differentiate into two subsets of T helper (T_H) cells such as T_H1 and T_H2. Interferon-γ (IFN-γ) is produced by T_H1 cells that solely promote cellular immunity. T_H2 cells, on the other hand, produce interleukin 4, 5, 10 and 13 (IL-4, IL-5, IL-10, and IL-13). Whereas, IL-12 is the propelling source of T_H1 separation while IL-4 stimulates T_H2 distinction. T_H2 is majorly involved in the promotion of humoral immunity [12].

2.1.3 Pathogenesis of immune diseases

The occurrence of the immunological disease is consequent to the dysregulation of numerous and different part of the human immune system. Fundamentally, the response of the immune system recognizes and eliminates antigens but tolerates its tissues. However, predominant immunopathology lesion is the basis on which the characterization of immune-mediated diseases is based. Immune-mediated disorders can be grouped into immediate hypersensitivity, autoimmunity, immune-complex disease, and delayed-type hypersensitivity. Autoimmunity can be further classified into those mediated by adaptive immunity and those mediated by innate immunity. Most of the disorders lie between the two, which will be best described

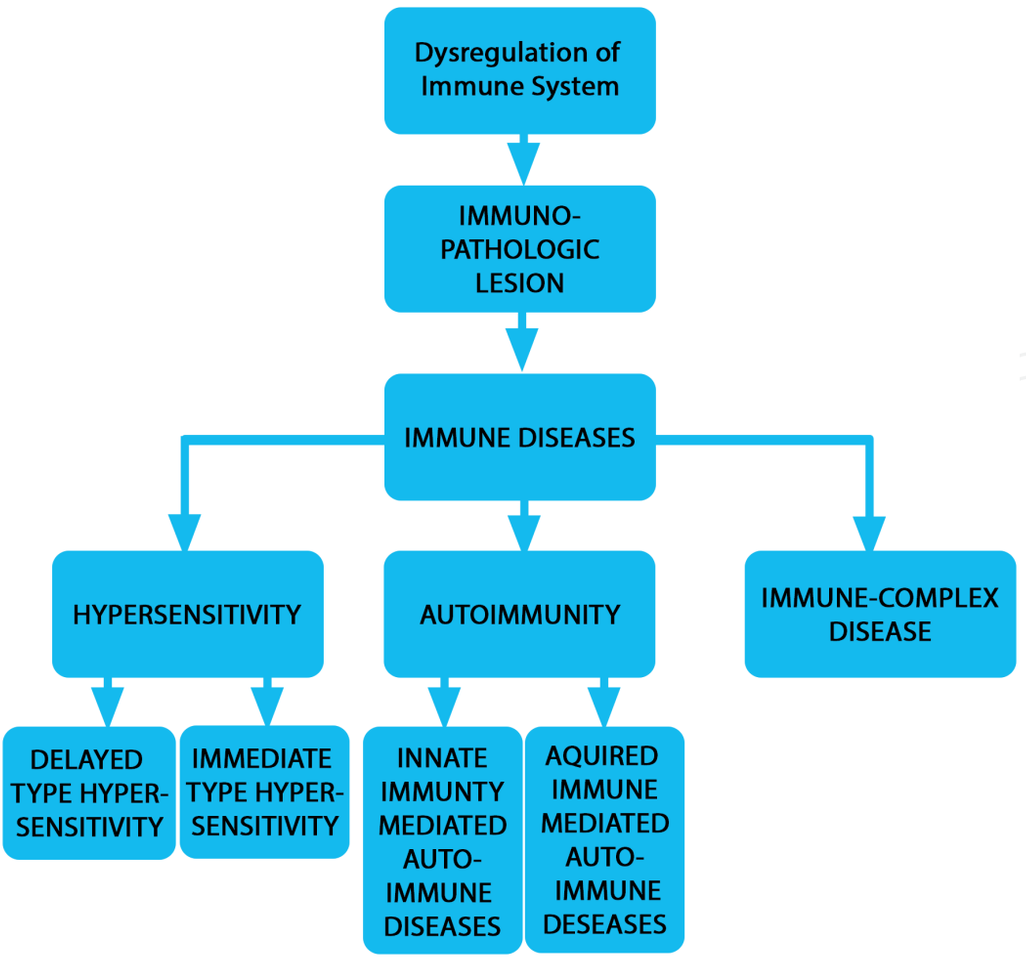

Figure 1.
Schematic representation of the pathogenesis of immune diseases.

as positive pathological feedback between innate and adaptive immune mechanisms [13]. **Figure 1** below represents the pathogenesis of immune diseases.

2.2 Personalized medicine

Personalized medicine is the process of tailoring the diagnostic procedures, treatment, and preventive measures towards the characteristics of individual patients to get an optimal outcome for each patient while emphasizing easy accessibility and cost-effectiveness [14]. In the practice of personalized medicine, the characteristics of an individual, including the uniqueness of its genetic profile guide the clinical decision in the treatment. Prognostic, diagnostic and predictive biomarkers are always being searched to guide these clinical decisions, at the same time, ensure that the best treatment is offered to the right patient at the best time [15]. The division of personalized medicine is illustrated in **Figure 2**.

While the method of application of precision medicine is given in **Figure 3.**

2.2.1 Personalized medicine and genomic data

Generally, personalized medicine compose of a vast collection of genetic data. The development of power systems has helped to increase the effective use of big data in personalized or precisions medicine over time. Also, the evolution of genomics data offers limitless possibilities in the design of clinical procedures, diagnostic, prevention, addressing and prediction of most favorable therapeutics for many diseases that are related to different regions and lineage [16].

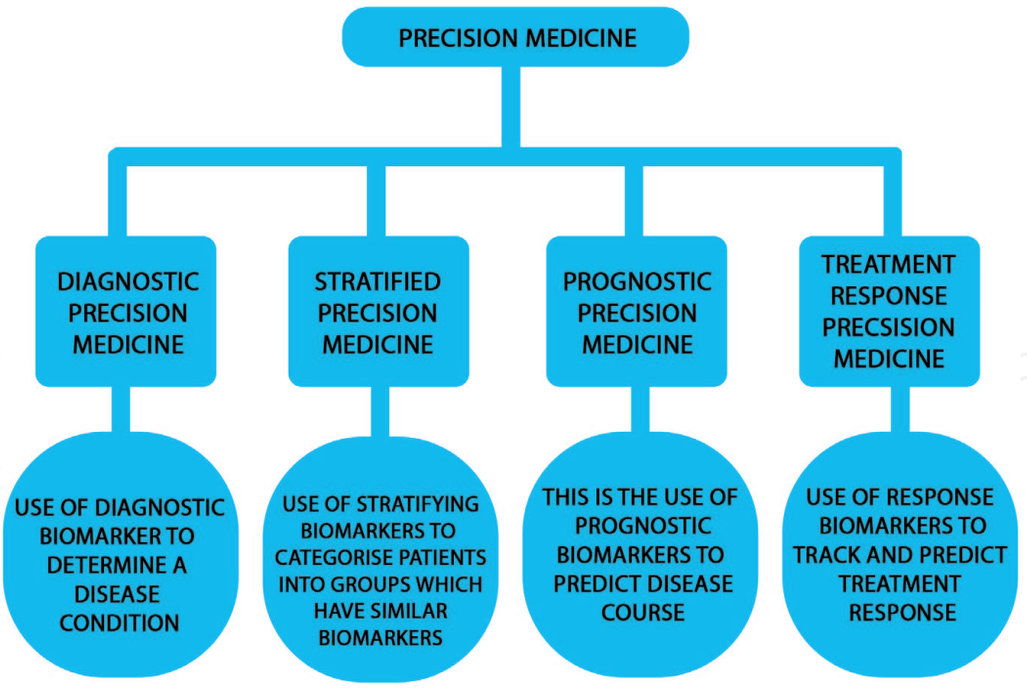

Figure 2.
Diagram showing the different division of precision medicine.

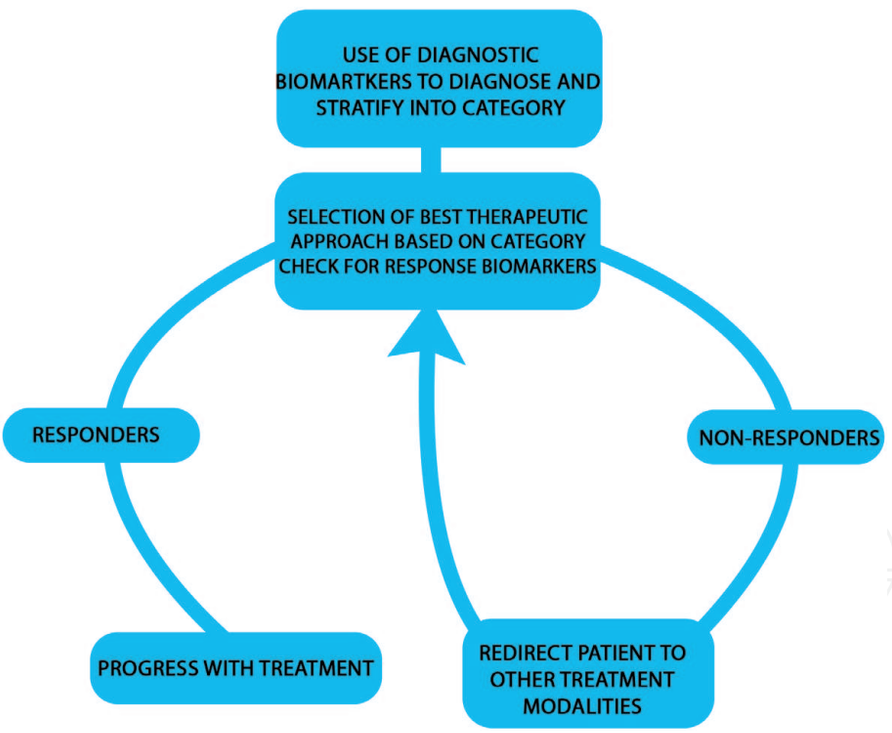

Figure 3.
A flow chart representing application method of precision medicine.

2.2.2 Precision medicine data types

The systematic collection of patient information is now accumulating and gaining complexity, as seen in the case of neuroimaging, which is currently producing above ten petabytes of data every year [17]. Studies in the field of precision medicine research make use of relevant data types such as Imaging data (CT, PET, UltraSound and MRI), bio-sample data (serum, plasma and urine value), molecular data, genomics data (nucleotide sequences), proteomic profiling data (mass

spectrometry), digital pathology data, biomedical instrument data (blood pressure, heart rate and insulin level) and clinical data (death/survival data, demographics and medical-based questionnaire) and others [18].

Some of the achievement in Precision medicine has led to solutions, such as the birth of personalized brain models for a patient with intractable epilepsy [19] and the success in epigenetics mechanism of hematopoiesis [20]. The combination and integration of these data types require a sound understanding of the different fields of informatics (data science, data management and data curation) and bioinformatics [18].

2.3 Genomic and personalized medicine database

A database is an ordered set of structured information or data usually controlled by the database management system (DBMS) in an electronic computer. The data, DBMS and the applications associated with them are called database system or database in short. Each database contains certain types of data; here, we will be introducing some of the database associated with personalized or precision medicine.

2.3.1 Immune epitope database (IEDB)

The IEDB is a free to use database that is very useful in vaccine and drug development, this database catalogs data such as experimental data on antibodies, Major histocompatibility complex (MHC) binding data from different antigenic sources, Helper T lymphocyte (HTL) and Cytotoxic T Lymphocytes (CTL) epitopes for human and other animal species. This database also aids in prediction and analysis of varieties of epitopes [21]. This database can be accessed through https://www.iedb.org/.

2.3.2 Prostate cancer related lifestyle database (PCaLiStDB)

Lifestyle medicine is the study of association between lifestyle, chronic and immune diseases. PCaLiStDB is a lifestyle database that is channeled towards precision in the prevention of prostate cancer and other diseases associated with lifestyle. The data found in this database are lifestyle associated genes, lifestyle type biomarkers and personalized lifestyle-disease associated predictors [22]. The database link is http://www.sysbio.org.cn/pcalistdb/.

2.3.3 Clinical genome resources (ClinGen)

ClinGen database provides data that are of clinical importance, this database is funded by the National Institute of Health (NIH), and it is aimed at collecting necessary data for use in precision medicine and research. Data such as clinically relevant gene and variants are retrieved from this database in making precise diagnosis and treatment [23]. This database is accessed via https://clinicalgenome.org/.

2.3.4 Personal genome project (PGP)

One of the breakthroughs of medical informatics is the personal genome project database. This is an open-access database that is channeled towards the development of a tool for personalized medicine and advancing research. The database provides a wide range of data for different regions (PGP-UK, PGP-AUSTRIA, PGP-CHINA, PGP-CANADA and PGP-UNITED STATE, etc.). Data such as Genome,

Methylome, transcriptome and phenotype data are retrieved from this database for use in the procedure of precise medicine [24]. The database can be linked through https://www.personalgenomes.org/.

2.3.5 Online mendelian inheritance in man (OMIM)

This database was initiated in the early 1960s, and the online version was created in 1985. OMIM is an open-access database that is mainly built for professionals concerned with genetic disorders, a genetics researcher and advance students in medicine. Data such as human gene, genetic disorders, clinical features, phenotype and genes are available [25, 26]. This database address is https://www.omim.org/.

2.3.6 Human gene mutation database (HGMD)

This is a variant-related database that collates already known gene lesion that is responsible for human inherited diseases. The database includes precision medicine data such as gene symbol, genomics coordinates, splicing, different disease, phenotype and mutations in the human genome [27, 28]. This database is accessible via http://www.hgmd.cf.ac.uk/ac/index.php.

2.3.7 Clinical genome database (CGD)

Clinical Genomic Database fills the critical niche in the field of clinical and genomic medicine; it also encompasses medically significant genetic data with available interventions. For each entry in the database, the CGD gives out data such as allelic conditions, gene symbol, clinical categorization (both manifestation and interventions), affected age groups mode of inheritance and pathogenic mutation for all diseases so far captured [27]. This database can be accessed via https://research.nhgri.nih.gov/CGD/.

2.3.8 Other database related to precision/personalized medicine

There are other ongoing database projects to improve the existing ones, an example of this is The Human Variome Project [29]. Also, there are many websites and databases linked to precision medicine that this chapter cannot introduce all. **Table 1** below provides more of the database related to precision medicine in general and their links [30].

2.4 Genomic and personalized medicine data utilization

Data sharing is the potential inherent in the exchange of the same data resource with many applications or users; it encompasses the transferring of copies, accessing and enabling the reuse of data. Data can be open access (publicly available) or controlled (restricted), also, sharing data encompasses both sharing of primary (in case of nucleotide sequences) and secondary data (already used or analyzed data) [31].

Figure 4 above illustrates that precision medicine data encompasses both hospital data (information), GIS and PGHD. Sharing of the Precision medicine information (clinical data) can be accessed openly or otherwise restricted, whereby authorization will be needed by an authorized person to access and use the specified data for therapeutic, diagnostic and research purpose.

Database	Link
Pathway Interaction Database	http://pid.nci.nih.gov/
VirusMINT (interaction between viral protein and human)	http://mint.bio.uniroma2.it/virusmint/Welcome.do
AutDB (animal model resources)	http://autism.mindspec.org/autdb/AMHome.do
Pathogen Interaction Gateway ((host and pathogen interaction)	http://molvis.vbi.vt.edu/ or http://pathogenportal.net/pig/
NetPath (signal transduction)	http://www.netpath.org/
Entrez – (encompasses sub-Databases)	http://www.ncbi.nlm.nih.gov/sites/gquery
GeneCards	http://www.genecards.org/
Human Genome Resources	http://www.ncbi.nlm.nih.gov/projects/genome/guide/human/
Ensembl Human Genome Browser	http://www.ensembl.org/IIomo_sapiens/Info/
Online Mendelian Inheritance in Man (OMIM)	http://www.ncbi.nlm.nih.gov/omim/
GeneCards	http://www.genecards.org/
Entrez Gene	http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene
National Institute of Neurological Disorders and Stroke (NINDS): Clinical and Translational Resources	http://www.ninds.nih.gov/research/scientific_resources/clinical/
Database of Genotypes and Phenotypes (dbGaP)	http://www.ncbi.nlm.nih.gov/sites/entrez?db=gap
NIH Chemical Genomics Center	http://www.ncgc.nih.gov/]
Gene Expression Omnibus	http://www.ncbi.nlm.nih.gov/geo/
ENCODE Project: ENCyclopedia of DNA Elements, NHGRI	http://www.genome.gov/ENCODE/
PubChem	http://pubchem.ncbi.nlm.nih.gov/
PhenX Toolkit	https://www.plienxtoolkit.org/
Human Genome Project, NHGRI	http://www.genome.gov/10001772
NCBI BioSystems	http://www.ncbi.nlm.nih.gov/biosystems/
National Human Genome Research Institute (NHGRI)	http://genome.gov
Kyoto Encyclopedia of Genes and Genomes	http://www.genome.jp/kegg/
HUPO Brain Proteome Project	http://www.hbpp.org/5602.html
ExPASy Proteomics Server	http://expasy.org/
HUPO: Human Proteome Organization	http://www.hupo.org/
European Proteomics Association (EuPA)	http://www.eupa.org/

Table 1.
Database linked to precision medicine in general and their links [30].

2.5 Precision medicine of specific autoimmune diseases

Autoimmune diseases are disease conditions where the immune system respond to self-antigens as a result of damage or dysfunction or disorder in the tissues. It is controlled by a whole lot of factors of which host gene and environment play a vital role. It could affect the entire body, selected systems or selected organs and an

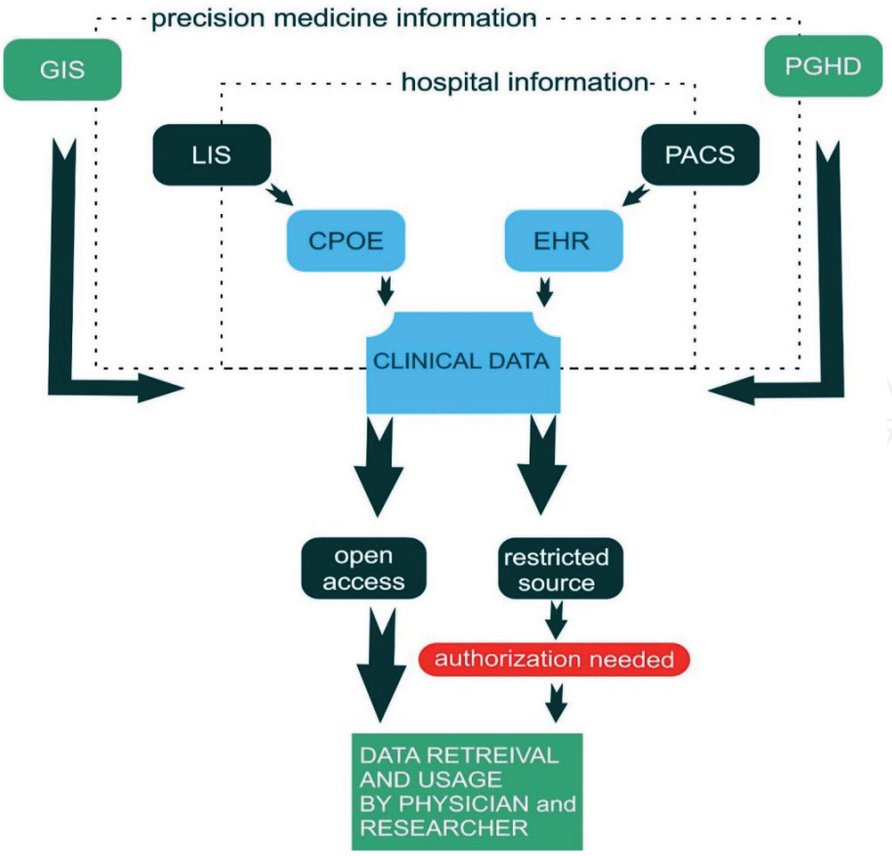

Figure 4.
*Semantic diagram of genomic and personalized medicine data sharing (**LIS**: Laboratory Information System; **GIS**: Genome Information System; **EHR**: Electronic Health Record; **PGHD**: Person Generated Health Data; **PACS**: Picture Archives and Communication System; **CPOE**: Computerized Physician Order Entry).*

interplay between genetic makeup with environmental factors and the self-antigen presented for recognition controls which organ or system of the body that will become the target of the immune system [32, 33].

The precision medicines of the following autoimmune diseases are discussed below:

1. Multiple Sclerosis
2. Myasthenia Gravis
3. Pernicious Anemia
4. Rheumatoid Arthritis
5. Sjogren Syndrome
6. Lupus Erythematosus
7. Type 1 Diabetes

2.5.1 Genomic assessment of multiple sclerosis

Multiple sclerosis is an inflammatory/autoimmune disorder that selects the myelin in the central nervous system which is capable of affecting patients of all age and causing neurologic disability when not adequately managed [34, 35]. More than

200 loci have been identified as an independent contributor to the pathogenesis of multiple sclerosis [36]. Multiple sclerosis is usually diagnosed between age 30 and 50 in most patients and occurs more often in females than male. The best way to understand the pathogenesis of multiple sclerosis is to address it from a multifactorial perspective with a model that proposes the interaction among genetic, epigenetic, infectious, dietary, climatic, or other environmental effects, together with sunlight exposure, and smoking. These interacting factors leads to self-intolerance and depreciation of immune homeostasis in the central Nervous system [34]. The brain and spinal cord tissues get infiltrated by stimulating peripheral mononuclear cells, and this leads to the loss of myelin, gliosis, which often leads to neurological dysfunction. Two primary approach of treatment has been given to the patient with multiple sclerosis due to the autoimmune model of the pathogenesis of such disease [34]. The former treatment is the use of global immunosuppressive agents which are aggressive. At the same time, the latter is the use of more specific agents to target specific elements of the immune system.

The contribution of common variants to multiple sclerosis has been probed, and different HLA alleles variants have been modeled for their contribution to multiple sclerosis and were found to be almost as common in control as it is in the sample as it was observed that OR of the statistical analysis tends towards 1 with an increase in sample size [37]. Biomarkers are important in the genetic assessment of Multiple Sclerosis as they possess the ability to express diverse aspects of multiple sclerosis heterogeneity. They also help in the diagnosis, stratification, and disease course prediction, identification of beneficial therapies and development of a precise treatment based on the predicted treatment response. As of 2016, MRI has turned to the most appropriate tool in the diagnosis of MS. The recommendation for brain MRI is the use of 1.5 T field strength, but 3.0 T is deemed preferable. However, using 7 T field strength has been supported by recent evidence to detect central vein in brain lesion of MS patients, but this can also be depicted using T2-weighted sequences at 3 T which help in the differentiation from microangiopathic lesions. The use of MRI for the diagnosis of MS seems simplified but its complexity sets in the differentiation of MS from other disease conditions like neuromyelitis optical spectrum disorders (NMOSD) which also has short spinal cord lesion at the onset. T2-weighted and contrast-enhanced T1-weighted brain MRI are recommended for the monitoring of disease progression while MRI of the spinal cord is not encouraged. Other than the MRI biomarkers there exist a few body fluid biomarker which could mark different stages of MS disease and differentiate each step from other similar disease conditions [34].

Body fluid biomarkers can be divided into three main groups, including those marking the early phase of MS, those associated with disease course and those associated with treatment response. Low vitamin D level in Cerebrospinal fluid is a marker of the initial stage of MS. Astrocyte-derived chitinase 3-like 1 (CHI3L1) in the CSF is also a prognostic marker of which an increased level of CHI3L1 in the CSF is a significant independent risk factor connected with the progression of disability in multivariate Cox regression models. Utilizing a proteomic approach and verification of result with ELISA confirmed that CHI3L1 would be the best predictors of the conversion to MS in CIS patients. CSF CHI3L1 level with MRI and age were the best predictors of MS risk in a multivariable analysis. Neurofilaments (NF-L) has also been implicated as a biomarker in the early phase of MS [36, 37].

Transcriptional regulator high-mobility group box protein 1 help differentiates patients with relapse-onset MS from patients from primary progressive MS. Proteomic studies show that two isoforms of vitamin D-binding protein and apolipoprotein E permit discrimination between MS patients with aggressive and benign disease courses [36]. During the disease course, calcium-binding protein

secretogranin-1 is decreased in the CSF when compared with the early phase of MS. Stable MS patients, when compared with relapsing patients, possess an increase in B cell activating factors in their plasma samples. Solute carrier family 9, subfamily A (SLC9A9) is a biomarker associated with the non-response to IFN beta. Upregulation of the NLR family, pyrin domain containing 3 (NLRP3) inflammasome is also a biomarker for non-responsive IFN beta treatment. Biomarkers of glatiramer acetate response are feedback gene to complement 32 (RGC-32), FasL, and IL-21. Up-regulated mRNA expression levels of RGC-32 and FasL and reduced expression of IL-21 seen in peripheral blood cells from responders in contrast to non-responders forms the basis for the use of these biomarkers [34, 36, 37].

2.5.2 Genomic assessment of myasthenia gravis

Myasthenia gravis (MG) is an autoimmune disease treated with chronic immunosuppression due to the actions of autoantibodies against the diverse structure of the neuromuscular intersection [38]. The variation of the patient's response to treatment and the variation in side effects to such treatment is the justifying reason for the recognition of the biological markers to predict the effectiveness of each treatment in each patient. Presence of anti-AChR antibodies is a beneficial biomarker in the diagnosis of MG. Still, it cannot judge disease severity as no specific correlation was found between MG severity and anti-AChR antibodies level [39]. MiR-323b-3p, −409-3p, −485-3p, −181d-5p, and − 340-3p has been predicted and suggested as response biomarker to project immunosuppressive drug sensitivity in MG patients.

The miRNAs can be tested in the blood, which would make it a potent response biomarker for treatment response, and any patient detected not to respond as expected will be addressed to other treatments thereby increasing cost-effectiveness. MiR-323b-3p, −409-3p and − 485-3p were downregulated in Non-responding patients while miRNA-181d-5p, and − 340-3p were upregulated in the Non-responding patients [39, 40]. A significant association has been identified between patient's response to azathioprine and two haplotypes, the TPMT3E haplotype in the thiopurine S-methyltransferase and a haplotype in the ATP-binding cassette sub-family C member 6 transporter. The glucocorticoid therapy non-responsive MG patients were found to possess a genetic variant in the secreted phosphoprotein 1 (SPP1) gene encoding osteopontin, which associates it with the non-responsive group [40].

2.5.3 Genomic assessment of pernicious anemia

Pernicious anemia (PA), is an autoimmune disease which results from a long-standing infection by *Helicobacter pylori* and the end-stage of atrophic body gastritis (ABG). The condition which is still active gradually phased out by an autoimmunity reaction that depletes the gastric mucosa irreversibly. The deficiency of vitamin B12 has been implicated in the etiology also. Therefore the goal of a clinician in treating pernicious anemia may be to avert the signs and symptoms of anemia itself, manage its complications such as damage to the nerve and heart tissues, and identifying the specific cause where precision medicine comes in [41]. The National Heart, Lung, and Blood Institute (NHLBI) are currently carrying out basic and clinical researches that could incorporate precision medicine and improve the treatment of the condition.

2.5.4 Genomic assessment of rheumatoid arthritis

Rheumatoid arthritis (RA) is a heterogeneous disease which can range from mild, self-limiting arthritis to fast progressive joint damage. It is triggered by a complex interaction between the human genetic makeup and the environment. Still,

both environmental influence and genetics cannot exhaustively account for the heterogenic clinical features of the disease condition. It is also characterized by synovial hyperplasia and joint destruction, which can lead to joint deformity or [42].

Currently, the treatment of RA is based on the control of inflammation with which an effective therapy that comes early ensures a drastic reduction in the risk of joint damage, mortality and disability. As of 2017, major researches has focused on the identification of biomarkers that can predict patient's response to only Methotrexate (MTX) which is the first non-biologic therapeutic agent administered. Also, TNF inhibitors (TNFi) has been established to be ineffective in about 30% of patients but remains the first choice of available biologic therapeutic agents. Solute carrier family 19 member 1 (SLC19A1) gene possess the most consistent and relevant evidence. It is one of the many transport carriers that allow the transport of MTX into the cell [43].

Anti- CCP antibodies a genomic marker associated with poor prognosis as it relates to the severity of disease and the extent of damage caused on the joint, HLA-DRB1 alleles coding for shared epitope is another marker for severity in RA [44].

2.5.5 Genomic assessment of sjogren syndrome

Sjögren's syndrome (SS) is a form of B cell hypersensitivity which is manifested in the formation of excess autoantibodies and a strong propensity for NHL of B cell emergence [45]. About 5% of patients of primary SS are at risk of lymphoma development. However, it is vital to have a specific biomarker to identify such patient early to be able to monitor and detect early and select appropriate therapy. The diagnostic biomarkers will guide in the diagnosis, and the predictive biomarkers are meant to show another aspect of clinical decision. Cytopenias is an established prognostic biomarker for the development of lymphoma [46]. A lot of proposed biomarkers in the assessment of SS are yet to be confirmed in more extensive studies before adoption into clinical use [47].

2.5.6 Genomic assessment of systemic lupus erythematosus

The systemic lupus erythematosus (SLE) has a broad spectrum of signs and symptoms which varies among patients and involves numerous organs with skin, joints, kidneys, lungs and CNS included. It is a chronic inflammatory autoimmune disease [48]. An association has been established between SLE and human leukocyte antigen (HLA) haplotypes (HLA-DR3; DR9; DR15; DQA1*0101 especially). The extensive association has also been found between vitamin D matching up with serum concentrations and vitamin D-receptor genomic binding domains [49].

2.5.7 Genomic assessment of type 1 diabetes

The type 1 diabetes (T1D) takes place as a result of autoimmune beta-cell destruction, which leads to insufficient production of insulin and results in hyperglycemia [50]. Although the role of precision medicine in type 1 diabetes is not well defined, patient with T1D severity varies with difference in their pancreatic autoantibodies profile and the rate at which their beta cells destroy [51].

In genetic studies (an important feature of precision medicine), identification of over 50 genetic signals in notably HLA region has been found to influence T1D predisposition [52]. The diagnostic biomarkers (serum biomarkers) use in the diagnosis of T1D includes the combination of glucose, C-peptide, glycated molecules and autoantibodies established for T1D. Still, these molecules often mark the late stage of the disease [53].

So far, advance in genomic research introduces the administration of islet autoantigens or peptides into a recipient with the risk of T1D; these studies suggest promising changes in immune regulation of islet autoimmunity. The challenges remain dosing frequency, dosage, route of administration, and adjuvants use.

2.6 Future perspectives

i. A systemic follow up of variant genes like the TNFRSF1A that is connected with multiple sclerosis risk should be closely investigated by researchers. This gene could give an essential perception of the etiology of multiple sclerosis and new treatment strategies.

ii. Myasthenia gravis-related loci may display their involvement in the pathogenesis of immune disease by increasing immune response, repression of the mechanism involved in immune suppression, alteration of procedure that differentiates between autologous and heterologous molecular configuration through immune tolerance, therefore investigations into Single nucleotide polymorphisms (SNPs) in the general population that is associated with Myasthenia gravis will improve diagnosis, therapy and its outcome.

iii. Genome editing technologies have been used with a degree of success in the treatment of sickle cell disease and β-thalassemia, this could be introduced into the precise treatment of pernicious anemia with proper study of the gene encoding for mitochondrial transport of vitamin B12.

iv. Rheumatoid arthritis research should focus on discovering more associated genes and their resultant effects. Transcriptomic and epigenomic strategies should also be used in discovering biomarkers of response to treatments and pathways that are related to therapies. Integration of genetic, clinical and environmental data are also crucial in achieving the aim of precision medicine in the treatment of rheumatoid arthritis.

v. Selection of novel treatments could be achieved for sjogren syndrome by identification of genetic risk factors like that of profound interferon signaling pathway by IRF5 and STAT 4 genes.

vi. Prevention of systemic lupus erythematosus by assaying genetic profile, developing new biomarkers of immune activation and alteration is the precise future treatment of this condition.

vii. Investigations into genes and pathways of type 1 diabetes may reveal on time the pathogenic role of the destruction of β-cell and production of clinical disease by the innate and adaptive immune system. Type 1 Diabetes Genetics Consortium (T1DGC) international have resources that could help in diagnosis, interventions, and monitoring outcomes of treatment of type 1 diabetes.

As the era of 'Big Health Data' continues, it is essential for the diagnosis, prognosis and treatment monitoring efforts on autoimmune diseases to take advantage of the data and different machine learning and deep learning algorithms to establish patterns and clusters within the disease groups. This will help in the identification of more relevant biomarkers and also help in the easy transition of biomarker researches to the bedside.

Indeed, the application of precision medicine in autoimmune diseases depends on the progress of next-generation sequencing program, which at the same time will strive to provide not only a whole-exome, or transcriptome, but at an exact process that is cost-efficient.

3. Conclusions

The information provided by the Genomics data is an indispensable component of precision medicine as it holds the key to the explanation in individual variability and evolution [54]. But, the clinical use of genomic data still needs to be improved on to overcome challenges stated by Kim et al. [55] like:

a. The incongruity between the form of genomic and clinical information: as a result of extensive (several tens of gigabytes of sequence) data in the genomic data, clinical data cannot be processed in the clinical practice without additional processing [55, 56].

b. The difference in the properties of genomic data and observational data used in the clinical settings: given that the genomic workflows hold a large number of data, data obtained from this workflows is undoubtedly different from systems parallel to the clinical plan [57].

c. Difficulty in mapping the genomic and clinical data for medical interpretation: as seen in the case of targeted sequencing, where most data are processed before medical analysis [58].

Also, there is no international validation for biomarkers in use; there is a need for international collaboration to validate biomarkers presently in existence.

Overcoming these challenges will open up more opportunities for the use of genomic data in clinical practices.

Conflict of interest

The authors declare no conflict of interest.

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