Markers For Systemic Lupus

Systemic lupus is one of the most common outoimmuno diseases, charactarized by chronic inflammation of many systems and formation of antibodies to nuclear and cytoplasmic antigens. It is most common between women than men. There are many symptoms to SLE such as malar rash, Ulcers/mucocutaneous involvement and Renal involvement (proteinuria, urinary cellular casts) . Some lab tests used in diagnosis of SLE such as ESR or CRP level, Serum creatinine and CBC with differential, and there are some imaging studies reauired for diagnosis such as Joint radiography, Chest radiography and chest CT scanning, crdiac and brain MRI [2].

Manifestations of SLE are varied, ranging from mild to serious so accurate assessment of disease activity is important for better therapeutic decision-making and data presentation useful for new drug development. In laboratory monitoring of disease activity , there Several immunologic markers, including complement and antidouble stranded DNA (dsDNA) antibody. These are many ways to assess disease activity such as Isles Lupus Assess-ment Group (BILAG) and SLE Disease Activity Index (SLEDAI) [4]. Biomarkers of systemic lupus can be devided into categories of epigenetic, protein (such as cytokines, autoantibodies and complement activation proteins) and metabolomic biomarkers.

Epigenetic biomarkers

Epigenetic modification can influence gene expression by changing chromatin structure that modulates the access to transcription factors and alters cellular function without modifying the genomic sequence[5]. Binding between trancription factors and DNA targets must be tightly for modulation of gene expression so this is an efficient mechanism to avoid the expression of a target gene is to disrupt the binding of transcription factor to DNA through DNA methylation [6]. These epigenetic mechanisms are acting by autoantibody production and regulating immunogenicity [6]. These epigenetic markers containing some types such as DNA methylation, Histone modification and miRNA.

DNA methylation is an efficient biomarker which done by cytosine methylation in the regulatory regions of DNA results in the transcriptional inactivation of genes, as SLE results from hypomethylation which associated with the activation of transcription, and insufficient DNA methylation has been found in T, B or NK cells of SLE patients [5].

Histone modification, modifications of histones such as methylation and acetylation, results in rmodeling of chromatin, which reduce and change the accessibility of DNA to transcription factors[7].

miRNAs, Dysregulated miRNA levels could play an important role in SLE pathogenesis, miRNAs control differentiation OF immune cell and regulate innate and adaptive immune responses. Several studies saied that that miRNAs is an important biomarkers that help monitor disease activity, There are many several types of blood cells that produce miRNA such as platelets and endothelial cells.In SLE, there is increased expression of miR- 142–3p and miR-181a and decreased expression of miR-106a, miR-17, miR-20a, miR-203 and miR-92a [8].

Protein biomarkers

' Cytokines & cytokine receptors ', these markers play a vital role in in lupus pathogenesis, and their balance determines disease activity[9]. The imbalance of these cytokines may result in local inflammatory processes and tissue damage, as they are soluble factors for maturation and activation of the various immune cells [10]. Serum levels of IL-6, IL-10, IL-17, type I interferon (IFN), soluble IL-2 receptor (sIL-2R) and soluble tumor necrosis factor receptor (sTNFR) suggest important functions in maturation and activation of various inflammatory cells, and may be promising biomarkers of disease activity in SLE. IL-6 is one of the first cytokines evaluated in systemic lupus pathogenesis due to its close link with B lymphocytes [10]. Studies showed that patients of SLE had elevated levels of serum IL-6, and there is a relation between these levels and disease activity. IL-10, its levels were higher in patients with SLE than normal controls, it is produced by T cells and monocytes, and it is considered a potent stimulator of B cell proliferation and immunoglobulin production during the disease [9].

Autoantibodies, these antibodies are used in the classification criteria of SLE, and these are many types such as antinuclear antibody (ANA), anti-dsDNA antibody and anti-Sm antibody, these antibodies are different in its sensitivity, that ANA is insensitive but anti-dsDNA antibody is highly specific and sensitive about 57.3% [11]. These autoantibodies include antichromatin/antinucleosome anti-bodies and anti-C1q antibodies which are promising markers for diagnosis or as new measures of renal involvement [12]. The fundamental unit of chromatin is nucleosome, chromatin is a molecule including DNA and histone found in the nucleus of eukaryotic cells and is a normal product of cell apoptosis. In SLE, it is a defective removal of apoptotic materials so immune system recognizes massive amounts of circulating nucleosomes. Antichromatin antibodies is a highly accurate and sensitive (45% to 100%) diagnostic marker for SLE [13].

C1q autoantibodies, its deficiency is one of the strongest risk factor for SLE, The presence of anti-C1q antibody in patients with SLE ranges from 30 to 60%, and its presence is related with disease activity and severity of systemic lupus nephritis [14]. After studies, It is suggestted that anti-C1q antibody may give a useful means to monitor renal involvement or predict renal flares.