ANTI-SSB IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELATION TO DISEASE CHARACTERISTICS, ACTIVITY AND ORGAN DAMAGE

Thesis

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List of Abbreviations

Ab	Antibody
ACEI	Angiotensin Converting Enzyme Inhibitor
aCL	anti Cardiolipin
ACR	American College of Rheumatology
AHA	Anti histone antibodies
AICD	Activation-induced cell death
ANA	Anti-nuclear antibodies
Anti-B2GPI	Anti–β2-glycoprotein I
Anti-dsDNA	Anti-double stranded DNA
Anti-Sm	Anti-smith
Anti-SSA	Anti-Sjögren's Syndrome type A
Anti-SSB	Anti- Sjögren's Syndrome type B
AP1	Activator protein1
APC	Antigen presenting cell
aPL	Antiphospholipid
APRIL	A proliferation-inducing ligand
aPTT	activated partial thromboplastin time
AVN	Avascular necrosis
AZA	Azithromycin
BAFF	B cell activating factor
BILAG	British Isles Lupus Assessment Group
BLys	B lymphocyte stimulator
BUN	Blood urea nitrogen
C_1q	Complement 1q
C_3	Complement 3
C_4	Complement 4
Cardiac-NL	Cardiac neonatal lupus
CD40L	CD40 ligand
CDR1	Complementarily determining region 1
CHB	Complete heart block
CLIFT	Crithidia luciliae immunoflourescence test
CMV	Cytomegalovirus
CNS	Central nervous system

List of Abbreviations (Cont.)

Cox-2	Cyclooxygenase 2
CRP	C-reactive protein
CSA	Cyclosporine A
CTLA-4	Cytotoxic T lymphocyte antigen 4
CYC	Cyclophosphamide
DCs	Dendritic cells
DHEA	Dehydroepiandrosterone
DLE	Discoid lupus erythematosus
DNA	Deoxyribonucleic acid
dRVVT	Dilated Russell Viper Venom test
EBNA 1	Epstein Barr Virus nuclear antigen 1
EBV	Epstein-Barr virus
ELISA	Enzyme-linked immunosorbent assays
EM	Electrone microscope
EPZ	Epratuzumab
ESR	Erythrocyte sedimentation rate
FcR	Fc receptor
FDA	Food and Drug Administration
G6PD	Glucose-6-phosphate dehydrogenase
GFR	Glomerular filteration rate
HCQ	Hydroxychloroquine
HLA	Human leukocyte antigens
HR	Hazard ratio
HRQoL	Health related quality of life
IF	Immunofluorescence
IFN	Interferon
IFN-K	IFNα kinoid
IL	Interleukin
IL-1Ra	IL-1 receptor antagonist
IRES	Internal ribosomal entry elements
ISN	International Society of Nephrology
ISTH	International Society of thrombosis and haemostasis
IVIG	Intravenous immunoglobulin therapy
KCT	Kaolin clotting time

List of Abbreviations (Cont.)

LAC	Lupus anticoagulant
LAI	Lupus activity index
LN	Lupus nephritis
LupusQoL	Lupus quality of life
mAb	Monoclonal antibody
MAC	Membrane attack complex
MHC	Major histocompatibility complex
MMF	Mycophenolate mofetil
MPA	Mycophenolic acid
6-MP	6-Mercaptopurine
MTX	Methotrexate
NAC	N-acetylcysteine
NET	Neutrophils extracellular traps
NLE	Neonatal lupus erythematosus
NLS	Neunatal lupus syndrome
NPSLE	Neuropsychiatric systemic lupus erythematosus
NPV	Negative predictive value
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
PCNA	Proliferating cell nuclear antigen
PDE	Phosphodiesterases
PIP	PCNA interacting peptide
PP2A	Protein phosphatase 2A
PPV	Positive predictive value
PSS	Progressive systemic sclerosis
QoL	Quality of life
RA	Rheumatoid arthritis
RBCC	Ring-B-box coiled-coil
RIA	Radio immuno assay
RISC	RNA-induced silencing complex
RNA	Ribonucleic acid
RNA	Ribonucleic acid
RNP	Ribonucleoprotein
ROC	Receiver operating characteristics
RPS	Renal Pathology Society

List of Abbreviations (Cont.)

RRM	RNA recognition motif
RTX	Rituximab
SBM	Short basic motif
SDI	SLICC/ACR Damage Index
SF-36	36-Item Short-Form Health Survey
SLAM	Systemic Lupus Activity Measure
SLAM-R	Systemic Lupus Activity Measure-Revised
SLAQ	Systemic Lupus Activity Questionnaire
SLE	Systemic lupus erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collaborating Clinics
SNP	Single-nucleotide polymorphism
snRNP	Small nuclear ribonucleoprotein
SPF	High skin protection factor
TCR	T cell receptor
TGF- β	Transforming growth factor- beta
Th	T helper cell
TLRs	Toll-like Receptors
TMP-SMX	Trimethoprim/sulfamethoxazole
TNF	Tumor necrosis factor
TPMT	Thiopurine methyltransferase
TRIM21	Tripartite Motif 21
UPA	Urokinase plasminogen activator
UPAR	Urokinase plasminogen activator receptor
UV	Ultraviolet
ZAP70	Zeta-associated protein 70

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Introduction

Systemic lupus erythematosus (SLE) is a prototype of autoimmune diseases affecting many systems. Both antibodies and autoreactive T cells play significant roles in its pathogenesis. Experimental data and clinical observations indicate that autoimmunity and end organ damage are under separate genetic controls and that there are significant interactions between these two pathways. Experimental evidence has been obtained to support the hypothesis that autoantibodies and autoreactive T effector cells may be initiated by environmental factors through molecular mimicry and the inherent polyreactive nature of antigen receptors. A unified hypothesis has been postulated for the pathogenesis of SLE that has practical implications ***(Lewiset al., 2013).***

Systemic lupus erythematosus most often harms the heart, joints, skin, lungs, blood vessels, liver, kidneys, and nervous system. The course of the disease is unpredictable with period of illness (called flares) alternating with remission ***(Song-Chou and Chia-Li, 2013).***

Autoantibodies play a significant role in the early diagnosis and treatment of autoimmune diseases. Anti-Sjögren's syndrome type B (SSB) antibodies are one of the most common autoantibodies in the serum of SLE patients and also one of the earlier autoantibodies to be produced. The anti-SSB antibodies were produced prior to the SLE symptoms appearing ***(Routsias and Tzioufas 2010 &Eriksson et al., 2011).***

With improvement in mortality in SLE, the functional status of these patients, assessed using health – related quality of life (HRQoL) instruments, is increasingly being recognized as an important out commeasure in clinical research. Domains of HRQoL of particular importance to systemic lupus

erythematosus patients include fatigue, ability to work, good health, independence, social and family life, learned helplessness, (reflecting the unpredictability of lupus), pain and the home environment. The(SL-36) currently appears to be the best available generic instrument ***(Strand et al., 2006).***

A study done by ***Kulczycka et al. (2010)*** found that systemic lupus erythematosus patient's quality of life (QoL) as assessed by short form 36 and satisfaction with life (SL) was rather low. Those with photosensitivity as well as neurological symptoms presented lower QoL in particular domains, while those with renal manifestations of systemic lupus erythematosus assessed their QoL as higher. Similar observations were made for SL only in relation to neurological symptoms. Moreover their findings showed that although hSL is part of HRQoL, both these parameters should be distinguished in order to fully assess the state of the patient. It has been shown that SLE patients have poorer functional status than the general population, and that specific manifestations of systemic lupus erythematosus (disease activity, previous renal involvement and fibromyalgia) may influence HRQoL ***(Grootscholten et al., 2003).***

HRQoL in systemic lupus erythematosus patients has been improved by (1) psycho-educational interventions including telephone counselting, a self-help course, group psychotherapy; (2) therapies ***(Thumboo and Strand,2007).***