Assessment of CD٨٣ Expression as a Prognostic Factor in Chronic Lymphocytic Leukemia

Thesis

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List of Abbreviations

ALC	Absolute lymphocyte count
alloHSCT	Allogeneic hematopoietic stem cell transplantation
APC	Antigen presenting cell
AT	Ataxia telangectasia
ATM	Ataxia telangectasia mutation gene
BM	Bone marrow
CBC	Complete blood count
C.CD٨٣	Cytoplasmic CD٨٣
CLL	Chronic lymphocytic leukemia
CRM١	Chromosome region maintenance ١
CTL	Cytotoxic T-cells
DCs	Dendritic cells
DNA	Deoxyribonucleic acid
EAE	Experimental autoimmune encephalomyelitis
EBV	Ebstein Barr virus
ELISA	Enzyme Linked Immunosorbent Assay
FAB	French American British

FCM	Flow Cytometry
FISH	Fluorescence in situ hybridization
FITC	Fluorescin isothiocyanate
GM-CSF	Granulocyte monocyte-colony stimulating factor
HCL	Hairy cell leukemia
HCMV	Human Cytomegalovirus
HCV	Hepatitis C virus
HLA	Human leukocyte antigen
HPV	Huma n papillomavirus
HSV-١	Herpes simplex virus type ١
IAP	Inhibitors of apoptosis protein
ICC	Invasive cervical cancer
iDCs	Immature dendritic cells
Ig	Immunoglobulin
Ig VH	Immunoglobulin heavy-chain variable region
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgHV	Immunoglobulin variable region
IgM	Immunoglobulin M

IL-١٠	Interleukin-١٠
iwCLL	International workshop on CLL
LDH	Lactate Dehydrogenase
LDT	Lymphocyte doubling time
LPS	Lipopolysaccharide
MBL	Monoclonal B-cell lymphocytosis
mCD٨٣	Membrane-bound CD٨٣ form
MCL	Mantle cell lymphoma
mDCs	Mature dendritic cells
MHC	Major histocompatibility complex
MLR	Mixed leukocyte reaction
MLRs	Mixed leukocyte reactions
MoDCs	Monocyte-derived dendritic cells
MRD	Minimal residual disease
mRNA	Messenger Ribonucleic acid
MZ	Mantle zone
NCIWG	National Cancer Institute Working Group
NHL	Non Hodgkin's lymphomas
PB	Peripheral blood

PCNA	Proliferating cell nuclear antigen
PCR	Polymerase Chain Reaction
PLL	Prolymphocytic leukemia
S.CD٨٣	Surface CD٨٣
sCD٨٣	Soluble CD٨٣ form
SIg	Surface immunoglobulin
SLVL	Splenic lymphoma with circulating villous lymphocytes
s-TK	Serum thymidine kinase
TAP	Transporter associated with antigen processing
TEC	Thymic epithelial cells
TK	Thymidine kinase
VEGF	Vascular endothelial growth factor
WBC	White blood cell
ZAP-٧٠	Zeta chain associated protein ٧٠

Introduction

Chronic lymphocytic leukemia (CLL) is a hematopoietic neoplasm of lymphocytes found in the peripheral blood, bone marrow, and /or lymph nodes. The morphology reveals a monomorphic small round cell population of lymphocytes. It is the most common adult leukemia, with a variable clinical course. Some experience an aggressive disease course that lead to premature death while others live for decades and never require therapy ***(Glassman and Hayes, 2005 and Shanafelt et al., 2008).***

Although the pathogenesis of CLL depends primarily on intrinsic defects within the leukemic cells, interaction with the microenvironment of bone marrow, lymph node and spleen as well as other components of the immune system are likely to affect the clinical course of the disease ***(Ghia et al., 2003).***

The glycoprotein CD٨٣, which is expressed by activated lymphocytes, dendritic cells (DC) and neutrophils, plays a central role in immunoregulation and is the focus of considerable interest as a therapeutic target ***(Prazma and Tedder, 2008)***. It is clear however that CD٨٣ plays a critical role in thymic CD٤+ T cell development and the involvement of CD٨٣ in increasing not only DC function but also lymphocyte survival, differentiation and immunosuppressive activity has been reported ***(Prechtel and Steinkasserer, 2007 and***

Kretschmer et al., 2007).

More than ٩٥٪ of acute myeloid leukemia (AML) and multiple myeloma (MM) patients have normal or only weakly increase in CD٨٣ expression, while ٢٠٪ of chronic lymphocytic leukemia (CLL) patients and ٥/٧ of mantle cell lymphoma (MCL) patients have significantly increased expression of CD٨٣ ***(Hock et al., 2009).***

The report of significantly elevated expression of CD٨٣ in patients with CLL together with the immunosuppressive activity of CD٨٣ raises the possibility that CD٨٣ may play a role in enabling CLL cells to escape Immunosurveillance ***(Hock et al., 2009).***