

Significance Of CD27 Expression In B Cell Precursor ALL Patients

Thesis

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List of Abbreviations

ABL	Ableson proto-oncogene; gene on chromosome 9
AIDS	Acquired immunodeficiency syndrome
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
AUL	Acute undifferentiated leukemia
BCP-ALL	B cell precursor-Acute lymphoblastic leukemia
BCR	Breakpoint cluster region; gene on chromosome 22
BM	Bone marrow
Bso	Basophilic
C CD3	Cytoplasmic CD3
C Ig	Cytoplasmic immunoglobulin
CALLA	common acute lymphoblastic leukemia antigen
CBC	Complete blood count
CBF	Core binding factor
CD	Cluster of Differentiation
CD27 L	CD27 ligand
CNS	Central nervous system
CR	Complete remission
CSF	Cerebrospinal fluid
DCs	Dendritic cells

DLDichroic lenses
DS.....Down syndrome
EBVEpstein-Barr virus
EDTAEthylene diamine tetra-acetic acid
EM.....Electron Microscope
EMO.....Extramedullary involvement
EOEosinophilic
FABFrench–American–British
FABFrench-American-British.
FCM.....Flowcytometry
FITC.....Flourescein isothiocyanate
FSForward scatter
GPA.....Glycophorin A
Hb.....Hemoglobin
HIVHuman immunodeficiency virus
HLAHuman leukocyte antigen
HOX genes....HOX: Homeobox genes, master transcriptional
regulators of early development
HSCS.....Histiocytes
IAPInhibitor of apoptosis proteins
IgImmunoglobulins
IL.....Interleukin
IPTImmunophenotyping

JAKJanus Kinase
kDakilodalton
LDHLactate dehydrogenase
LNsLymph nodes
MIC-MMorphologic Immunophenotyping Cytogenetic
and Molecular genetic
MLLMixed-lineage leukemia
MLL-AF4Mixed-lineage leukemia- ALL1 fused gene from
chromosome 4
MoAbMonoclonal antibody
MPALMixed phenotype acute leukemia
MPOMyeloperoxidase
MRDMinimal residual disease
MSMultiple Sclerosis
NGFNerve growth factor
NKNatural Killer
NOSNon other specific
PASPeriodic-acid-schiff
PBPeripheral blood
PBSPhosphate buffered saline
PBX1Pre-B-cell transforming gene on chromosome 1
PCRPolymerase chain reaction
PEPhycoerythrin

PLTPlatelets
PMTs.....Photomultiplier tubes
RBRetinoblastoma protein/gene
RBCSRed blood cells
S IgSurface immunoglobulin
SBBSudan black
SCCSide light scatter
SDStandard deviation
SS.....Side scatter
T effsEffector T cells
TCR.....T-cell receptor
TdTTerminal deoxynucleotidyl transferase
TELTranslocation ETS leukemia (ETS is a family of transcriptional factors)
TEL-AML1...Translocation ETS leukemia-acute myeloid leukemia-1
ThT helper cells
TLCTotal leukocytic count
TNFTumor necrosis factor
TregsRegulator T cells
WBC.....White blood cell count
WHOWorld Health Organization

INTRODUCTION

Acute Lymphoblastic Leukemia (ALL) is characterized by the malignant proliferation and accumulation of early lymphoid precursor cells in the bone marrow, blood and lymphoid organs. This disease is the most frequent form of leukemia in children & comprising almost one-third of all pediatric cancers (*Trehan et al., 2009*).

Combination chemotherapy together with central nervous system prophylaxis has improved the treatment of ALL, and overall cure rates now approach 80%. Despite this improvement, about 20-25% of the patients still relapse (*Lee-Sherick et al., 2010*).

A number of clinical and biological factors at the time of presentation are relevant to the prognosis and affect the response to treatment (*Amirghofran et al., 2011*). These prognostic factors include age, gender, number of blasts, white blood cells (WBC) and platelet number, cytogenetic abnormalities, extramedullary involvement (EMI) and immune phenotype (*Fathi et al., 2012*).

CD27 is a member of the tumor necrosis factor family. It is expressed on T cells, Nk cells and memory B cells. The interaction between CD27 and its ligand CD70 plays an

Introduction

important role in the maturation and activation of these cells (*Croft et al., 2009*).

It plays an important role in lymphoid differentiation and apoptosis. Induced on normal B lymphocytes after antigenic challenge it is a marker of memory B cells. Increased expression of the membrane form of CD27 on ALL blasts has been reported and ligation of CD27 has been shown to induce apoptosis (*Nilsson et al., 2005*).

Interestingly, the CD27 antigen can be detected both as transmembrane protein and as soluble protein in serum, as a shorter metalloprotease cleavage product (sCD27). Increased levels of sCD27 have been associated with immune activation in diseases such as AIDS, multiple sclerosis and systemic lupus erythromatosus. However, its role in B cell ALL is still not clear (*De Miltio et al., 2002*).