Study of Podocalyxin as an Identifying Marker of Leukemic Blast Cells in Acute Myeloid Leukemia

Thesis

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SUMMARY

AML describes a heterogenous group of hematological disorders characterized by block in the terminal differentiation of particular hemopoietic cell lineage. The accurate diagnosis of AML is important for appropriate treatment and management. Flow cytometric immunophenotyping (FCI) has a well-established role as a diagnostic modality in acute leukemias, particularly as a tool for assigning lineage & facilitating further pathologic classifications.

Diagnostically, detection of CD34 has a central role in the immunophenotypic identification of abnormal blast populations in bone marrow, peripheral blood and tissues by flow cytometric and immunohistochemical analysis. However, not all leukemic blasts express CD34.

The aim of this work was to study the expression of podocalyxin in leukemic myeloblasts and whether its detection can increase the ability to immunophenotypically identify leukemic blasts compared with detection of CD34 alone. We also aimed to study the prognostic relevance of Podocalyxin expression in acute myeloid leukemia patients.

This study was carried out on 30 adult patients newly diagnosed with acute myeloid leukemia. They were 18 males

list of Abbreviations

ABL1: Abelson murine leukemia viral oncogene homolog 1

Akt: AKT8 virus oncogene cellular homolog

AKT: Protein kinase B

AML: Acute myeloid leukemia

APC: Adenomatous polyposis coli

APL: Acute promyelocytic leukemia

ARF: Alternate reading frame of the INK4a/ARF locus

BAD: Bcl-2-associated death promoter

Bax: Bcl-2-associated X protein

Bcl2: B cell lymphoma 2

BCR: Breakpoint cluster region

Bim: Pro-apoptotic protein belonging to the BH3-only group of

family members

BM: Bone marrow

CBFA: Core binding factor alpha

CBFβ: Core binding factor beta

Cd34-/-: CD34 negative cells

cdc42: Small GTPase of Rho family

CDK2: Cyclin dependent kinase 2

CDK4: Cyclin dependent kinase 4

cDNA: Complementary DNA

CEBPA: CCAAT/enhancer-binding protein alpha

CEBPa: CCAAT/enhancer-binding protein alpha

C-FMS:	Human cellular homologue of the retroviral oncogene v-

fms- formerly McDonough feline sarcoma viral

oncogene

C-KIT: Proto-oncogene tyrosine-protein kinase

CGH: Comparative genomic hybridization

CR: Complete remission

CREB: CAMP response element-binding protein

CRKL: The adapter protein Crk like

CyclD: Cyclin D protein

CyclE: Cyclin E protein

DW: Distilled water

E2F: Transcription factor family including E2F- and DP-like

subunits

EGFR: Epidermal growth factor receptor

Erk: Extracellular signal-regulated kinase

ER: Status -a score of estrogen receptor

ETO: Eight twenty-one

EVI1: Ectopic viral integration site 1

FADD: Fas-associated protein with death domain

FAK: Focal adhesion kinase

Fas: TNF superfamily receptor 6

FCM: Flowcytometry

FcR: Fc receptor

FISH: Fluorescence in situ hybridization (FISH)

FLT3: Fms-like tyrosine kinase3

Fos: V-fos FBJ murine osteosarcoma viral oncogene

homolog

Fyn: A Src family tyrosine-protein kinase

GCTM2:	Germ cell tumor marker2
Gli:	Gli family transcription factors
gp135:	Glycoprotein 135
GPCR:	G protein coupled receptor
GRB:	Growth factor receptor-bound protein
GSK:	Glycogen synthase kinase
HSCs:	Human stem celles
IGF1:	Insulin-like growth factor 1
Jak:	Janus-family tyrosine kinase
JAK2:	Janus activated kinase
Jun:	Is the name of a gene and protein that in combination with c-Fos forms the AP-1 early response transcription factor
Mad:	Max dimerization protein 1
MAPK:	Mitogen-activated protein kinase
MCF7 breast cancer:	Michigan Cancer Foundation - 7 breast cancer cell line
MDCK cells:	Madin-Darby Canine Kidney Cells
Mdm2:	Murine double minute 2, a p53-associated oncogene
MDS:	Myelodysplastic syndrome
MEK:	MAPK/Erk kinase
MEKK:	MAPK/Erk kinase kinase
MKL1:	Myocardin like protein 1
MLL:	Mixed lineage leukemia
MLLT3:	Mixed lineage leukemia translocated to 3
MMP1:	Matrix metalloprotease1
MMP9:	Matrix metalloprotease 9
MPO:	Myeloperoxidase

Mt:	Mitochondria
MTG8:	Myeloid translocation gene on chromosome 8
Myc:	Myelocytomatosis oncogene cellular homolog
MYH11:	Myosin heavy chain 11
NEC:	Non-erythroid cells
NF1:	Nuclear factor-1
NF-kB:	Nuclear factor κ B
NHERF1:	Na (+)/H (+) exchanger regulating factor 1
NMP1:	Nuclear matrix protein 1
NPM:	Nucleophosmin
NSGCT:	Nonseminomatous germ cell tumors
P15:	Protein of 15 killodalton,
P16:	Protein of 16 killodalton,
P21:	Protein of 21 killodalton,
p27:	Protein of 27 killodalton,
P53:	Protein of 53 killodalton,
PB:	Peripheral blood
PC3:	One of the prostate cancer cell line
PCLP1:	Podocalyxin like protein 1
PCR:	Polymerase chain reaction
PDAC:	Pancreatic ductal adenocarcinomas
PDGFRA:	Platelet derived growth factor alpha receptor
PDGFRB:	Platelet derived growth factor beta receptor
PI3K:	Phosphoinositide 3 kinase
PKA:	Protein kinase A
PKC:	Protein kinase C

PLC:	Phospholipase C
PLZF:	Promyelocytic leukemic zinc finger gene,
PML:	Promyelocytic leukemia
PODXL:	Podocalyxin
Podxl-/-:	Podocalyxin negative cells
PTEN:	Phosphatase and tensin homolog deleted on chromosome 10
Pu.1:	Spleen focus forming virus (SFFV) proviral integration oncogene spi1
Raf:	Proto-oncogene serine/threonine-protein kinase
RARA:	Retinoic acid receptor alpha
RARα:	Retinoic acid receptor alpha
RAS:	Rat sarcoma
Rb:	Retinoblastoma protein
RBM15:	RNA binding motif protein 15
RT -PCR:	Reverse transcriptase polymerase chain reaction
RTK:	Receptor tyrosine kinase
RUNX1:	Runt-related transcriptional factor 1
RUNX1T1:	Runt-related transcription factor 1translocated to 1 (cyclin D-related)
SBB:	Sudan Black B
Shc:	SH2-containing collagen-related proteins
SMO:	Smoothened a G-coupled transmembrane protein
SOS:	Son of sevenless guanine nucleotide exchange factor
Src:	Rous sarcoma oncogene cellular homolog

Side scatter

SSC:

₹ List of Abbreviations

Stat:	Signal transducer and activator of transcription, B-cell lymphoma-extra-large
TCF:	T cell factor
TNF:	Tumor necrosis factor
TNF:	Tumor necrosis factor
Tra-1-60:	Tumor rejection antigen 1-60
Tra-1-81:	Tumor rejection antigen 1-80
Wnt:	Was coined as a catenation of Wg (wingless) and Int and is pronounced 'wint'

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