SUPPLEMENTARY APPENDIX

Distinct gene expression profiles in subsets of chronic lymphocytic leukemia expressing stereotyped *IGHV4-34* B-cell receptors

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Online Supplementary Table S1. ***IGHV-IGHD-IGHJ*** **rearrangements included in the present study.**

Patient	Subset *	*IGHV* usage	*IGHD* usage	*IGHJ* usage	% identity	HCDR3	HCDR3 amino acid sequence
1	16	IGHV4-34	IGHD1-26	IGHJ6	95.0	24	CAGRFYCYGGNCNNANYYYYYGMDVW
2	16	IGHV4-34	IGHD2-21	IGHJ6	92.9	24	CARRFYCAGDGCQSPNYYYYHGLDVW
3	16	IGHV4-34	IGHD2-15/2-2	IGHJ6	95.8	24	CAGSFYCSGATCDSPRYYYHYGVDVW
4	16	IGHV4-34	IGHD2-15	IGHJ6	93.0	24	CAGRFYCSGDTCLSPSFHYYHGLDVW
5	16	IGHV4-34	IGHD2-2	IGHJ6	93.2	24	CAGRFYCSGATCSSPNYFYYYGLDVW
6	4	IGHV4-34	IGHD3-3	IGHJ6	91.2	20	CARGYGFMESTRRYYYYGFDVW
7	4	IGHV4-34	IGHD5-5	IGHJ6	95.2	20	CARGWGDTAVIRRYYYYGMDVW
8	4	IGHV4-34	IGHD5-5	IGHJ6	94.8	20	CARGYGDSSDVRRYYYYGLDVW
9	4	IGHV4-34	IGHD5-5	IGHJ6	94.5	20	CVRGYPDTAVVKRYYYYGMEVW
10	4	IGHV4-34	IGHD5-5	IGHJ6	92.9	20	CARGYPDTDVVRRYYYYGMEVW
11	4	IGHV4-34	IGHD4-17	IGHJ6	94.8	18	CASGSTPTTRRYYYYGMDVW
12	4	IGHV4-34	IGHD3-10	IGHJ6	91.2	20	CARGYADSDVIRRYYYYGMDVW
13	4	IGHV4-34	IGHD5-12	IGHJ6	91.9	20	CARGYADTPTFRRYYYYGMDVW
14	4	IGHV4-34	IGHD5-12	IGHJ6	93.2	20	CARGYGTSATTKRYYYYGMDVW
15	4	IGHV4-34	IGHD4-17	IGHJ6	93.1	20	CARGYGSTATTRRYYYYGMDVW
16	4	IGHV4-34	IGHD3-10	IGHJ6	95.9	20	CARGYPDTPVVRRYYYYGMDVW
17	-	IGHV4-34	IGHD6-13	IGHJ6	94.4	17	CARGVTNIRYDYYYGMDVW
18	-	IGHV4-34	IGHD3-3	IGHJ3	92.8	17	CARRYLEWSVHKNDGFDIW
19	-	IGHV4-34	IGHD3-10	IGHJ3	93.5	15	CARGHSSGSYYAPFDSW
20	-	IGHV4-34	IGHD1-26	IGHJ6	93.2	19	CARGPIQKSGRNFYYYYMDVW
21	-	IGHV4-34	IGHD1-26	IGHJ6	92.0	17	CARLAGSSYNFYQYGVDVW
22	-	IGHV4-34	IGHD2-15	IGHJ4	94.6	15	CAREDCSGGGCYTLDSW
23	-	IGHV4-34	IGHD6-25	IGHJ6	92.1	17	CARGTTPAHYSYYYYMDVW
24	-	IGHV4-34	IGHD3-3	IGHJ6	98.3	28	CARGVTNELSYDFWSGSYHPGHHYFGIDVW
25	-	IGHV4-34	IGHD2-15	IGHJ6	100	30	CARGRRDIVVVVADTIILNPKNYYYYYGMDVW
26*	16	IGHV4-34	IGHD2-15	IGHJ6	96.3	24	CAGRFYCSGAGCDSEGFYYYYGLDVW
27*	16	IGHV4-34	IGHD2-2	IGHJ6	95.1	24	CAGRFYCSGASCDRVDFYYYYGLDAW

**All subset #4 cases carried* IGKV2-30 *rearrangements whereas all subset #16 cases showed* IGKV3-20 *rearrangements. *Additional subset #16 samples for RQ-PCR validation only.*

Online Supplementary Table S2. Identification of 111 significantly differentially expressed genes with at least a 1.5 times difference in average expression between subsets #4 and #16.

Genes	Adjusted *P* value	Probe Set ID	Fold change
IL15: interleukin 15	8.99E-08	217371_s_at	3.31
VDR: vitamin D (1.25- dihydroxyvitamin D3) receptor	4.76E-06	204254_s_at	2.37
RPL37: Ribosomal protein L37	9.24E-04	224766_at	1.75
PSIP1: PC4 and SFRS1 interacting protein 1	1.57E-03	210758_at	1.77
HOXA1: homeobox A1	2.10E-03	214639_s_at	2.20
IGK: immunoglobulin kappa constant	2.27E-03	211644_x_at	10.80
PDIK1L: PDLIM1 interacting kinase 1 like	2.44E-03	227255_at	1.85
PTPMT1: protein tyrosine phosphatase. mitochondrial 1	2.49E-03	223808_s_at	1.80
C1orf69: chromosome 1 open reading frame 69	4.35E-03	1558896_at	1.64
MCCC2: methylcrotonoyl-Coenzyme A carboxylase 2 (beta)	6.87E-03	1560033_at	1.77
METTL2A/2B: methyltransferase like 2A/2B	6.95E-03	221079_s_at	1.53
DDAH1: dimethylarginine dimethylaminohydrolase 1	7.04E-03	209094_at	1.96
TM9SF1: transmembrane 9 superfamily member 1	7.04E-03	238948_at	1.79
TSN: translin	8.22E-03	201513_at	1.68
REPS1: RALBP1 associated Eps domain containing 1	8.22E-03	215201_at	1.55
TLK1: tousled-like kinase 1	8.44E-03	210379_s_at	2.13
CCT8: chaperonin containing TCP1. subunit 8 (theta)	8.44E-03	210436_at	1.72
PIGC: phosphatidylinositol glycan anchor biosynthesis. class C	8.44E-03	215242_at	1.61
SLC35E1: solute carrier family 35. member E1	8.44E-03	222263_at	1.55
PCGF3: polycomb group ring finger 3	8.72E-03	1559528_at	1.89
LRMP: lymphoid-restricted membrane protein	9.00E-03	240718_at	1.76
KIF11: kinesin family member 11	1.18E-02	204444_at	1.91
FBXO38: F-box protein 38	1.25E-02	219608_s_at	2.09
ZNF268: zinc finger protein 268	1.25E-02	209989_at	2.03
KCTD2: potassium channel tetramerisation domain containing 2	1.26E-02	34858_at	1.67
SLC44A5: solute carrier family 44. member 5	1.33E-02	235763_at	3.19
EIF3M: eukaryotic translation initiation factor 3. subunit M	1.47E-02	240513_at	2.35
SFRS3: splicing factor. arginine/serine-rich 3	1.62E-02	235324_at	1.73
HECTD1: HECT domain containing 1	1.62E-02	241683_at	2.51
SNAP29: Synaptosomal-associated protein 29	1.62E-02	239084_at	1.56
TPM4: tropomyosin 4	1.64E-02	209344_at	2.56
CCDC6: coiled-coil domain containing 6	1.72E-02	204716_at	2.70
G3BP1: Ras GTPase-activating protein-binding protein 1	1.72E-02	244396_at	1.89
C7orf46: chromosome 7 open reading frame 46	1.72E-02	228600_x_at	1.88
C14orf169: chromosome 14 open reading frame 169	1.72E-02	219526_at	1.86
WDR57: WD repeat domain 57 (U5 snRNP specific)	1.72E-02	215905_s_at	1.89
THAP1: THAP domain containing. apoptosis associated protein 1	1.72E-02	219292_at	1.75
PNRC2: proline-rich nuclear receptor coactivator 2	1.72E-02	222406_s_at	1.55
SSFA2: sperm specific antigen 2	1.75E-02	236207_at	1.83
GLTP: glycolipid transfer protein	1.88E-02	219267_at	2.52
APPBP2: amyloid beta precursor protein (cytoplasmic tail) binding protein 2	1.88E-02	202631_s_at	1.96
LARP4: La ribonucleoprotein domain family. member 4	1.99E-02	214155_s_at	2.03
HNRPH1: heterogeneous nuclear ribonucleoprotein H1 (H)	2.06E-02	213472_at	3.74
COX7B: cytochrome c oxidase subunit 7B. mitochondrial	2.16E-02	239252_at	2.15
LSM5: LSM5 homolog. U6 small nuclear RNA associated (S. cerevisiae)	2.16E-02	211747_s_at	1.79
NUTF2: nuclear transport factor 2	2.17E-02	202397_at	1.74
DTWD1: DTW domain containing 1	2.28E-02	219291_at	1.56
HNRPUL2: heterogeneous nuclear ribonucleoprotein U-like 2	2.36E-02	66053_at	2.10
TTC30B: tetratricopeptide repeat domain 30B	2.37E-02	1554588_a_at	3.90
PPCS: phosphopantothenoylcysteine synthetase	2.40E-02	218341_at	1.54
TIGD2: tigger transposable element derived 2	2.46E-02	229983_at	2.26
INHBC: inhibin. beta C	2.46E-02	207688_s_at	1.78
C17orf89: chromosome 17 open reading frame 89	2.46E-02	225967_s_at	1.70
TCP1: t-complex 1	2.46E-02	222011_s_at	3.00
SFRS12IP1: SFRS12-interacting protein 1	2.56E-02	235390_at	1.54

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PLEKHA2: pleckstrin homology domain containing. family A (phosphoinositide binding specific) member 2	2.67E-02	238013_at	3.84
TMEM70: transmembrane protein 70	2.72E-02	219448_at	2.12
CSNK2A: casein kinase 2. alpha 1 polypeptide	2.82E-02	212073_at	1.73
ZHX1: zinc fingers and homeoboxes 1	2.83E-02	223214_s_at	2.03
FAM55C: family with sequence similarity 55. member C	2.85E-02	235030_at	2.35
HERPUD2: HERPUD family member 2	2.85E-02	1558699_a_at	1.93
LUC7L3: LUC7-like 3	2.87E-02	229193_at	1.84
C12orf43: chromosome 12 open reading frame 43	2.87E-02	219022_at	1.82
TPR: translocated promoter region (to activated MET oncogene)	2.89E-02	1557227_s_at	2.06
TUFM:Tu translation elongation factor. mitochondrial	2.89E-02	238190_at	2.69
ARGLU1: arginine and glutamate rich 1	3.07E-02	227448_at	2.72
METAP2: methionyl aminopeptidase 2	3.07E-02	227993_at	1.71
COL4A3BP: collagen. type IV. alpha 3 (Goodpasture antigen) binding protein	3.13E-02	223465_at	1.77
ZNF770: zinc finger protein 770	3.22E-02	238687_x_at	1.89
BAG5: BCL2-associated athanogene 5	3.24E-02	230427_s_at	2.31
SIP1: survival of motor neuron protein interacting protein 1	3.24E-02	205063_at	1.88
TLK2: tousled-like kinase 2	3.29E-02	212986_s_at	1.75
TPM4: tropomyosin 4	3.30E-02	212481_s_at	1.79
AIG1: androgen-induced 1	3.31E-02	223136_at	1.82
LYRM2: LYR motif containing 2	3.35E-02	221311_x_at	2.21
CSRP2BP: CSRP2 binding protein	3.35E-02	228543_at	2.08
KDELR2: KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	3.40E-02	200698_at	1.72
TPP2: tripeptidyl peptidase II	3.43E-02	1569857_s_at	2.44
MBD6: methyl-CpG binding domain protein 6	3.43E-02	226076_s_at	1.66
ASNS: asparagine synthetase	3.43E-02	215024_at	1.58
UTX: ubiquitously transcribed tetratricopeptide repeat. X chromosome	3.44E-02	203990_s_at	2.55
CHIC2: cysteine-rich hydrophobic domain 2	3.52E-02	219492_at	1.59
PAPD5: PAP associated domain containing 5	3.66E-02	229043_at	1.83
ZNF555: zinc finger protein 555	3.66E-02	239839_at	1.56
RANBP9: Ran-binding protein 9	3.73E-02	210098_s_at	2.00
COBLL1: COBL-like 1	3.74E-02	215393_s_at	1.99
ZNF678: zinc finger protein 678	3.76E-02	242923_at	1.74
C17orf79: chromosome 17 open reading frame 79	3.76E-02	225096_at	1.68
GNA12: guanine nucleotide binding protein (G protein) alpha 12	3.76E-02	221737_at	1.88
PPP2CA: protein phosphatase 2 (formerly 2A). catalytic subunit. alpha isoform	3.81E-02	235502_at	1.77
ZCCHC10: zinc finger. CCHC domain containing 10	3.84E-02	1559399_s_at	1.88
SEPT7: Septin 7	3.84E-02	1565823_at	1.65
STOML2: stomatin (EPB72)-like 2	3.84E-02	215416_s_at	1.61
ZNF57: zinc finger protein 57	3.84E-02	1554628_at	1.51
IPO9: importin 9	3.84E-02	244703_x_at	1.53
MT1P3: metallothionein 1 pseudogene 3	3.87E-02	221953_s_at	1.52
RPS27L: ribosomal protein S27-like	4.05E-02	238935_at	1.72
WAC: WW domain containing adaptor with coiled-coil	4.05E-02	219679_s_at	2.15
PRKACB: protein kinase. cAMP-dependent. catalytic. beta	4.27E-02	202742_s_at	1.94
UFM1: ubiquitin-fold modifier 1	4.50E-02	222502_s_at	1.87
PLCXD1: phosphatidylinositol-specific phospholipase C. X domain containing 1	4.56E-02	222795_s_at	1.55
YRDC: yrdC domain containing (E. coli)	4.57E-02	218647_s_at	1.76
ARF6: ADP-ribosylation factor 6	4.66E-02	203311_s_at	1.56
ENSA: endosulfine alpha	4.68E-02	221487_s_at	1.61
EIF4E3: eukaryotic translation initiation factor 4E family member 3	4.68E-02	225941_at	1.54
MUT: methylmalonyl Coenzyme A mutase	4.74E-02	202959_at	1.63
ZNF493: zinc finger protein 493	4.75E-02	235604_x_at	1.53
TPM4: tropomyosin 4	4.79E-02	1567107_s_at	1.79
C6orf62: chromosome 6 open reading frame 62	4.85E-02	213875_x_at	2.23
BCAP29: B-cell receptor-associated protein 29	4.85E-02	230150_at	1.53
PHF12: PHD finger protein 12	4.96E-02	231815_at	1.63

Online Supplementary Table S3. Overview of the functional characteristics of the differentially expressed genes in subset #4 *versus* subset #16.

Functionality	Genes	Accession number	Implicated role in cancer	Reference
Enhancing proliferation and tumorigenesis/ prognosis related	*STOML2*	NM_013442.1	Overexpressed in many human cancers and involved in the promotion of cell growth, cell adhesion and tumorigenesis	(1)
	METAP2	NM_006838.3	Important role in tumor transformation and proliferation	(2)
	CCDC6	NM_005436.3	Oncogenic protein, overexpressed in cancer with the ability to increase cell proliferation and transformation	(3)
	HOXA1	NM_005522.3	Overexpression of *HOXA1* gene results in oncogenic transformation and transcriptional up-regulation of Bcl-2	(4)
	PPP2CA	NM_002715.2	Overexpressed in breast tumors and implicated in the negative control of cell growth and division	(5)
	APPBP2	NM_006380.2	Shown to be highly expressed in breast cancer	(6)
	ARF6	NM_001663.3	Overexpressed in breast cancer and shown to be involved in its invasion and metastasis	(7)
	SSFA2	NM_001130445.1	Overexpression promotes multiple myeloma cell adhesion, clonogenic growth and tumorigenicity	(8)
	KIF11	NM_004523.3	Overexpressed in many cancers and is a potential anti-tumor target as its inhibitor has been shown to induce cell-cycle block and subsequent death in AML cells	(9)
	ASNS	NM_001673.3	Shown to be a biomarker for ovarian cancer treatment	(10)
	ZNF268	NM_001165881.1	Potential prognostic factor and implicated in human hematologic malignancies	(11)
PI3K/AKT/ NFκB pathways	*PRKACB*	NM_002731.2	Acts as a potential marker for prostate cancer progression by enhancing PKA and AKT pathways	(12)
	VDR	NM_000376.2	Plays an essential role in the regulation of inflammation by negatively modulating the pro-inflammatory NF-κB pathway	(13)
	PLEKHA2	NM_021623.1	Member of the PI 3-kinase family and involved in the synthesis of PtdIns(3,4,5)P3 from PtdIns(4,5)P2 as a result of stimulation with growth factors	(14)
p53 pathway	*RPS27L*	NM_015920.3	Promotes apoptosis and is directly regulated by the *p53* gene	(15)
	G3BP1	NM_005754.2	Acts as an negative regulator of p53 where its decreased expression results in up-regulation of p53 and degradation of MDM2	(16)
Facilitating viral adhesion and replication in host cells	*SIP1*	NM_003616.2	Catalyzes the integration of viral cDNA and its decreased expression results in reduced HIV-1 infection in human primary monocyte-derived macrophages	(17)
	PSIP1	NM_021144.2	Facilitates viral adhesion and integration by acting as a chromatin docking factor for lentiviruses such as HIV	(18)
	RANBP9	NM_005493.2	Binds and enhances the transactivation activity of the viral protein Rt, which is critical for Epstein-Barr virus lytic activation	(19)
	TSN	NM_004622.2	Interacts with the hepatitis C virus and hence is shown to be involved in the mechanism for hepatocellular carcinoma and lymphoma caused by HCV	(20)
	EIF3M	NM_006360.3	The C terminus of this gene contains a functional region that acts as a receptor for herpes simplex virus entry	(21)
Anti-apoptotic genes	*IL15*	NM_000585.2	It is a pluripotent anti-apoptotic cytokine and is regarded as a highly promising agent in cancer therapy	(22)
	CSNK2A1	NM_177559.2	It acts as a key player in cell growth and proliferation and has been shown to be a potent suppressor of apoptosis in prostate cancer	(23)
	BAG5	NM_001015048.1	Member of the BAG1 related anti-apoptotic protein family which functions through interactions with a variety of apoptosis and growth related proteins	(24)
Pro-apoptotic genes	*THAP1*	NM_018105.2	Functions as a pro-apoptotic factor that links apoptosis response protein to promyelocytic leukemia nuclear bodies	(25)
	COL4A3BP	NM_031361.1	Shown to increase apoptosis in keratinocytes	(26)
Drug resistance/ drug target	*REPS1*	NM_001128617.1	Shown to mediate multidrug resistance and hence acts as a potential target in the treatment of leukemia	(27)
	PTPMT1	NM_175732.2	Potential drug target for the treatment of type II diabetes as its knockdown in the pancreatic insulinoma cell line has been shown to enhance insulin secretion	(28)
	YRDC	NM_024640.3	Overexpression affects cellular sensitivity to anticancer drugs and has been shown to be involved in multidrug resistance mechanisms	(29)

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