

# Gene expression markers for genetic risk groups and survival in chronic lymphocytic leukemia

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**Online Supplementary Table 1.** Candidate gene characteristics, primer sequences, references, and expression pattern in non-B-cells. For: forward primer; Rev: reverse primer. ABI: Applied Biosystems (Weiterstadt, Germany).

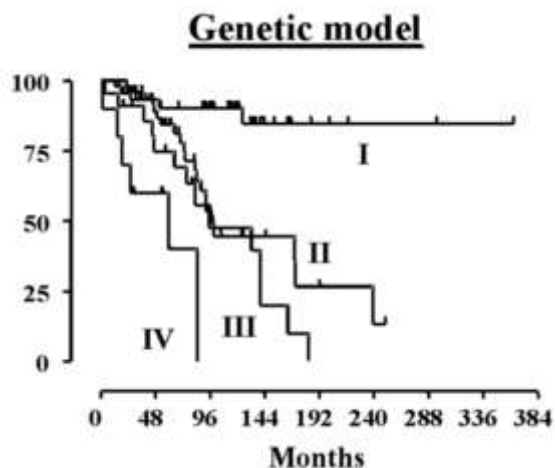
Gene Symbol	Chromosomal localization	Putative function	Assay ID / Primer sequence	Primer reference	Selection criterion	Overexpressed in Non-B-cells *	Investigated in CD19+ purified cohort
ADAM29	4q34	cell-cell / cell-matrix interactions	for:CAATACTCCTGTGATCGTATAA rev:CACTGCTCCTTTCCACTGC	adopted from van't Veer <i>et al.</i> , <sup>30</sup>	overexpression in VH mutated CLL (Oppezso <i>et al.</i> ) <sup>22</sup>	no	yes
ATM	11q22-q23	DNA damage and cell cycle control	Hs00175892_m1	ABI	differential expression in 11q- CLL (Kienle <i>et al.</i> ) <sup>28</sup>	no	yes
CLLU1	12q22	disease-specific expression	for:AGCTTGCAGATGGCAGATCA rev:CATAAAGGGCAGCGAAATGC probe:TATCTCCAGGCCTTTCATTGG	adopted from Buhl <i>et al.</i> ) <sup>20</sup>	disease-specific overexpression (Buhl <i>et al.</i> ) <sup>19,20</sup>	yes	yes
DMD	Xp21.2	cytoskeletal protein	Hs00187905_m1	ABI	overexpression in VH unmutated CLL (Rosenwald <i>et al.</i> ) <sup>16</sup>	no	yes
GLO1	6p21.3-p21.1	enzyme in glutathione metabolism	Hs00198702_m1	ABI	overexpression in VH unmutated <sup>18</sup>	no	no
HCLS1 (HS1)	3q13	transcription factor	Hs00232048_m1	ABI	phosphorylated form overexpressed in VH unmutated CLL (Scielzo <i>et al.</i> ) <sup>25</sup>	yes	yes
KIAA0977	2q24.3	unknown	Hs00383292_m1	ABI	overexpressed in VH mutated CLL ( <i>personal communication</i> )*	no	yes
LPL	8p22	enzyme in triglyceride and lipoprotein metabolism	Hs00173425_m1	ABI	overexpression in VH unmutated CLL (Oppezso <i>et al.</i> ) <sup>22</sup>	yes	yes
MGC9913	19q13.43	unknown	Hs.23133	SuperArray	overexpression in VH mutated CLL (Haslinger <i>et al.</i> ) <sup>18</sup>	no	yes
PCDH9	13q14.3-q21.1	neuronal receptor, signal transduction	Hs.492696	SuperArray	overexpression in VH mutated CLL (Haslinger <i>et al.</i> ) <sup>18</sup>	no	no
PEG10	7q21	negative regulator of TGF-β pathway	Hs01122880	ABI	overexpression in high risk CLL <sup>26</sup>	no	no
SEPT10	2q13	cytoskeletal protein with GTPase activity	Hs00376351_g1	ABI	overexpressed in VH unmutated CLL ( <i>personal communication R. D.-F.</i> )	yes	yes
TCF7	5q31.1	Wnt signaling pathway	Hs00175273_m1	ABI	overexpression in VH mutated CLL <sup>18</sup>	yes	yes
TCL1	14q32.1T-	and B-lymphocyte differentiation	Hs00951350_m1	ABI	potential pathogenic relevance <sup>23,24</sup>	no	yes
TP53	17p13.1	induction of apoptosis, cell cycle arrest and DNA repair	Hs00153349_m1	ABI	differential expression in 17p- CLL <sup>28</sup>	no	
VIM	10p13	intermediate filament (mesenchymal tissue)	Hs00185584_m1	ABI	prognostic factor <sup>27</sup>	yes	yes
ZAP70	2q12	T-cell receptor signaling	Hs00277148_m1	ABI	overexpression in VH unmutated CLL <sup>10-13</sup>	yes	yes
ZNF2	2q11.2	transcription factor	Hs00368338_m1	ABI	overexpression in VH unmutated <sup>18</sup>	yes	yes

\*defined as at least equal median expression level in the CD19 negative fraction of healthy donors compared to the positive fraction, or in the CD19 negative fraction of CLL patients compared to the positive fraction.

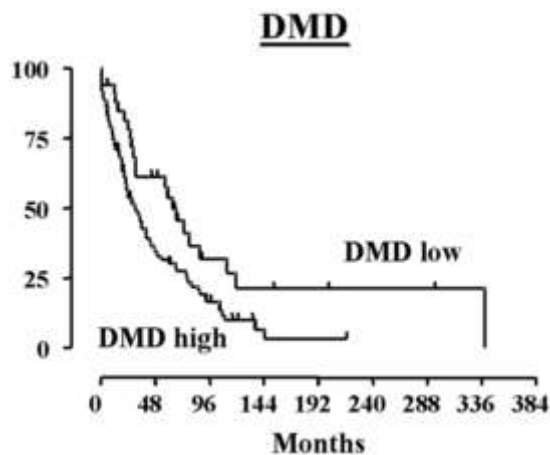
**Online Supplementary Table 2.** Associations between gene expression and genetic subgroups in unpurified patient samples. Only genes with a significant association after adjustment of *p* values are shown (adjusted *p*<0.05), ordered by strength of association.

Marker	AUC	Dadjusted p
<b>VH unmutated</b>		
LPL	0.827	<0.001
TCF7	0.211	<0.001
ADAM29	0.273	0.001
DMD	0.721	0.002
KIAA0977	0.283	0.002
MGC9913	0.692	0.007
SEPT10	0.668	0.030
ATM	0.342	0.049
<b>11q-</b>		
ATM	0.176	0.001
HS1	0.263	0.029
<b>Overall survival</b>		
TCF7	-3.314 *	0.010

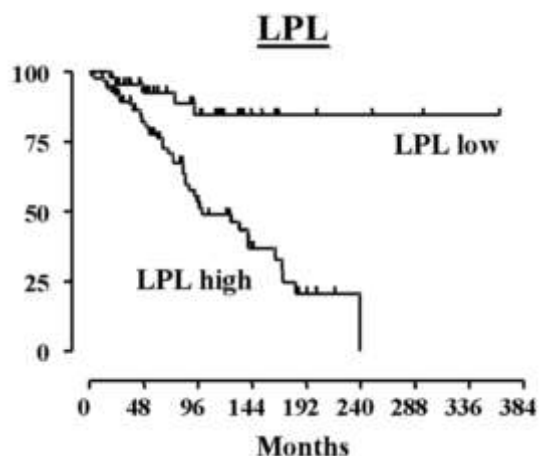
*AUC: estimated area under the ROC curve. The AUC gives the strength and direction of association; values > 0.5: high expression is associated with the respective genetic feature, values < 0.5: low expression is associated with the respective genetic feature. Value of 1 or 0: maximal association. Negative Wald statistics: high expression is associated with prolonged survival times. No significant associations were observed for the 17p- subgroup and V3-21 usage. \*Wald test statistics.*



**Online Supplementary Figure 1.** Overall survival curve (Kaplan-Meier) according to the hierarchical genetic model (Kröber et al. (7)). I. VH mutated without V3-21, 11q-, 17p-; II. VH unmutated / V3-21 usage without 11q-, 17p-; III. 11q- without 17p-; IV. 17p-. Median OS subgroup I: undefined, II: 97 months, III: 95 months, IV: 59 months.



**Online Supplementary Figure 2.** Treatment-free survival curves (Kaplan-Meier) according to DMD expression. Median TFS for low expressers: 63 months, high expressers: 30 months.



**Online Supplementary Figure 3.** Overall survival curves (Kaplan-Meier) according to LPL expression. Median OS for low expressers: undefined, high expressers: 99 months.