

## SUPPLEMENTARY FIGURES AND TABLES

**Table S1.** Baseline characteristics of multiple myeloma (MM) and plasma cell leukemia (PCL) patients used in next-generation sequencing (NGS) and RT-qPCR analysis.

Baseline characteristics <sup>1</sup> :	MM	PCL
No. of patients	34	23
Gender: males - females	29.4 - 70.6	44.2 - 55.8
Age median (min-max) (years)	72 (45- 86)	69 (42 - 83)
ISS stage: I-II-III	17.6 - 41.2 - 41.2	NA - 34.1 - 65.9
ECOG PS: 0-1-2-3-4	14.7 - 35.3 - 32.4 - 11.8 - 5.9	43.8 - 39.6 - NA - NA
Ig isotype: G-A-LC only-M-D-Bicl-NS	64.7 - 17.6 - 14.7 - NA - NA - NA - 2.9	40.0 - 17.5 - 19.2 - 9.1 - NA - NA - NA
Light chains: kappa-lambda	72.7 - 27.3	56.8 - 43.2
Previous treatment lines: 0-1-2-4	NA	50 - 30 - 10 - 10
cPCs (%)	0.2 (0.00 - 4.6)	19.4 (7.0 - 67.5)
<b>Biochemistry at diagnosis<sup>2</sup>:</b>		
Hemoglobin level (g/l)	95.7 (63.2 - 141.0)	93.2 (66.9 - 139.0)
Thrombocyte count (x10 <sup>9</sup> /l)	182.0 (69.4 - 357.0)	83.6 (37.6 - 201.0)
Calcium total level (mmol/l)	2.4 (2.0 - 3.5)	2.5 (1.9 - 4.7)
Albumin level (g/l)	32.5 (19.2 - 46.5)	34.4 (22.5 - 50.0)
Creatinine level (μmol/l)	92.0 (50.0 - 913.0)	164.5 (49.0 - 781.0)
β2-microglobulin (mg/l)	4.4 (2.1 - 50.0)	8.7 (2.4 - 44.9)
Lactate dehydrogenase (μkat/l)	3.6 (1.4 - 7.3)	6.0 (1.2 - 22.9)
C-reactive protein (mg/l)	4.2 (0.0 - 69.2)	10.7 (1.0 - 42.3)
<b>Cytogenetics at MM / PCL diagnosis<sup>3</sup>:</b>		
No. of patients	34 (100%)	12 (52%)
IgH disruption: positive	30.80%	100.00%
Translocation t(11;14): positive	0.00%	100.00%
Translocation t(4;14): positive	31.30%	60.00%
Translocation t(6;14): positive	0.00%	100.00%
Translocation t(14;16): positive	6.70%	33.30%
del(13)(q14)/monosomy 13: positive	76.90%	63.60%
gain 1q21: positive	65.40%	90.90%
del(17)(p13): positive	20.00%	27.30%
Hyperdiploidy: positive	33.30%	37.50%

<sup>1</sup>: Described using N (%) and/ or median (minimum - maximum). <sup>2</sup>: Described using median (minimum - maximum). <sup>3</sup>: Described using N(%). Only 12 samples from PCL patients out of 23 have been analyzed for cytogenetic changes. NA = not available, Bicl – bclonal, NS – non-secretory

**Table S2:** Previous therapy in any treatment line before sPCL diagnosis.

Previous therapy of patients diagnosed with sPCL (N = 11 patients with sPCL) <sup>1</sup>	Statistics <sup>2</sup>
<b>Proteasome inhibitors (PI)</b>	<b>8 (72.7%)</b>
bortezomib	8 (72.7%)
<b>Immunomodulatory drugs (IMiD)</b>	<b>6 (54.5%)</b>
thalidomide	4 (36.4%)
lenalidomide	3 (27.3%)
<b>PI + IMiD</b>	<b>5 (45.5%)</b>
<b>Corticosteroids</b>	<b>9 (81.8%)</b>
<b>Conventional chemotherapy</b>	<b>8 (72.7%)</b>
<b>Transplantation</b>	<b>3 (27.3%)</b>
<b>Number of previous treatment lines</b>	
1	6 (54.5%)
2	3 (27.3%)
4	2 (18.2%)
median (min–max)	1 (1–4)
<b>Time from MM to PCL diagnosis (months), median (min–max)</b>	<b>14.0 (3.8–60.1)</b>

<sup>1</sup>Respective treatment modalities could be combined.

<sup>2</sup>Described using N (%) in categorical variables and median (minimum–maximum) in continuous variables.

**Table S3:** TaqMan Assays of validated long non-coding RNAs (lncRNAs).

LncRNAs	Life Technologies Assay ID	Catalog Number
LY86-AS1	Hs00543584_m1	4331182
VIM-AS1	Hs04402632_m1	4426961
MIR9-3HG	Hs00288663_m1	4331182
PCAT7	Hs04406635_m1	4426961

**Table S4:** LncRNAs with significantly deregulated expression level between multiple myeloma patients and patients with plasma cell leukemia (adjusted  $P < 0.001$ ) as detected by next-generation sequencing analysis during the exploration phase of the study.

LncRNA	ENSG <sup>1</sup>	logFC <sup>2</sup>	AveExpr <sup>3</sup>	P-value	adj P-value
VIM-AS1	ENSG00000229124	1.597	11.059	2.669x10 <sup>-9</sup>	2.034x10 <sup>-5</sup>
AL358053.1	ENSG00000287465	-2.309	3.481	9.307x10 <sup>-8</sup>	1.489x10 <sup>-4</sup>
ZBTB20-AS5	ENSG00000242290	-1.417	6.183	1.038x10 <sup>-7</sup>	1.489x10 <sup>-4</sup>
AL133415.1	ENSG00000234961	1.303	11.585	1.021x10 <sup>-7</sup>	1.489x10 <sup>-4</sup>
AC006296.2	ENSG00000251412	-2.804	1.693	1.087x10 <sup>-7</sup>	1.489x10 <sup>-4</sup>
AC006296.1	ENSG00000248425	-2.708	1.173	1.173x10 <sup>-7</sup>	1.489x10 <sup>-4</sup>
PCAT7	ENSG00000231806	-3.876	3.370	2.308x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
LINC02231	ENSG00000248995	-2.439	0.964	2.124x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
AC012321.1	ENSG00000260772	-1.060	5.570	2.727x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
AC006296.3	ENSG00000287360	-2.470	1.931	2.709x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
Z92544.1	ENSG00000261659	1.089	5.126	2.996x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
AC021979.1	ENSG00000258594	-2.874	1.777	3.126x10 <sup>-7</sup>	1.984x10 <sup>-4</sup>
ZBTB20-AS2	ENSG00000241295	-1.553	4.700	3.682x10 <sup>-7</sup>	2.158x10 <sup>-4</sup>
AC079416.4	ENSG00000280227	-1.000	5.015	5.556x10 <sup>-7</sup>	2.919x10 <sup>-4</sup>
LINC02576	ENSG00000232613	-2.142	5.227	5.748x10 <sup>-7</sup>	2.919x10 <sup>-4</sup>
AL391834.2	ENSG00000273226	-1.267	3.945	6.165x10 <sup>-7</sup>	2.936x10 <sup>-4</sup>
AC087752.3	ENSG00000253878	-1.557	5.359	7.384x10 <sup>-7</sup>	3.309x10 <sup>-4</sup>
AL162719.1	ENSG00000285717	-2.995	2.160	8.139x10 <sup>-7</sup>	3.445x10 <sup>-4</sup>
AC012313.1	ENSG00000232098	1.230	4.096	9.237x10 <sup>-7</sup>	3.520x10 <sup>-4</sup>
AC092155.1	ENSG00000226622	-2.470	2.229	9.642x10 <sup>-7</sup>	3.520x10 <sup>-4</sup>
AC119673.2	ENSG00000286619	-3.273	4.409	1.013x10 <sup>-6</sup>	3.520x10 <sup>-4</sup>
ZBTB20-AS1	ENSG00000241560	-1.199	7.417	1.016x10 <sup>-6</sup>	3.520x10 <sup>-4</sup>
AL450992.1	ENSG00000229021	2.448	2.044	1.218x10 <sup>-6</sup>	4.035x10 <sup>-4</sup>
AC009948.3	ENSG00000279598	-1.988	5.019	1.716x10 <sup>-6</sup>	5.231x10 <sup>-4</sup>
AC093010.2	ENSG00000259976	-1.312	10.739	1.646x10 <sup>-6</sup>	5.226x10 <sup>-4</sup>
LINC01712	ENSG00000231364	-2.378	1.993	1.909x10 <sup>-6</sup>	5.595x10 <sup>-4</sup>
AC068051.1	ENSG00000197585	-1.969	3.451	2.330x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AL161640.1	ENSG00000230404	-3.135	1.409	2.439x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AC008569.1	ENSG00000267379	1.212	6.403	2.425x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
SEMA6A-AS1	ENSG00000248445	-1.068	4.589	2.520x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AL024508.1	ENSG00000272189	-1.610	2.343	2.614x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AC016745.2	ENSG00000272563	-2.614	3.020	2.744x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AL360181.2	ENSG00000235245	1.543	2.792	2.664x10 <sup>-6</sup>	6.335x10 <sup>-4</sup>
AC026333.4	ENSG00000274191	-2.021	2.220	3.656x10 <sup>-6</sup>	8.193x10 <sup>-4</sup>
AP003721.1	ENSG00000256196	1.575	2.802	4.681x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
PLCB1-IT1	ENSG00000225479	2.520	3.080	4.739x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
LY86-AS1	ENSG00000216863	-2.644	4.628	4.698x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
AC068491.2	ENSG00000270190	2.642	1.366	4.567x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
AC079906.1	ENSG00000274723	-2.188	1.122	5.136x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
AC108463.3	ENSG00000271590	2.628	2.792	5.261x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
AL022098.1	ENSG00000287920	-1.251	7.062	5.066x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
MIR9-3HG	ENSG00000255571	-4.075	5.022	5.463x10 <sup>-6</sup>	9.459x10 <sup>-4</sup>
LINC02090	ENSG00000230969	-2.330	3.018	5.747x10 <sup>-6</sup>	9.596x10 <sup>-4</sup>
AP000560.1	ENSG00000278879	-1.135	7.303	5.245x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>

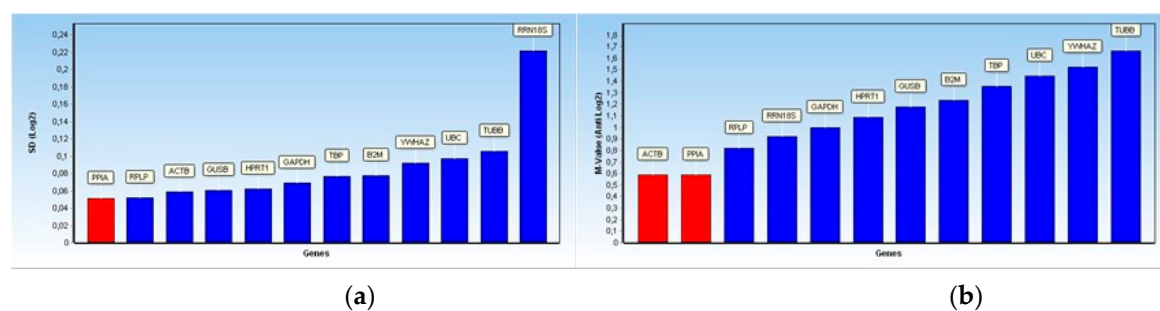
SEMA6A-AS2	ENSG00000249167	-2.223	1.862	5.822x10 <sup>-6</sup>	9.596x10 <sup>-4</sup>
IFNG-AS1	ENSG00000255733	-1.835	8.785	5.312x10 <sup>-6</sup>	9.412x10 <sup>-4</sup>
LINC02389	ENSG00000255693	-2.680	3.853	6.172x10 <sup>-6</sup>	9.596x10 <sup>-4</sup>
AL158206.1	ENSG00000260912	-1.689	4.848	5.987x10 <sup>-6</sup>	9.596x10 <sup>-4</sup>
LINC00373	ENSG00000231019	-2.223	2.116	6.589x10 <sup>-6</sup>	9.982x10 <sup>-4</sup>
AC002350.2	ENSG00000278993	1.043	4.097	6.797x10 <sup>-6</sup>	9.982x10 <sup>-4</sup>
AC010680.3	ENSG00000271011	-1.897	2.232	6.813x10 <sup>-6</sup>	9.982x10 <sup>-4</sup>
AP005212.4	ENSG00000283294	-2.081	6.930	6.156x10 <sup>-6</sup>	9.596x10 <sup>-4</sup>

<sup>1</sup> ENSG – Ensembl Gene ID, <sup>2</sup> FC - fold change, <sup>3</sup> AveExpr - average log-expression values.

**Table S5:** Normalized expression levels of significantly deregulated lncRNAs lymphocyte antigen antisense RNA 1 (LY86-AS1) and VIM Antisense RNA 1 (VIM-AS1) in validation phase of the study.

Diagnosis	Sample	LY86-AS1 ( $2^{-\Delta Ct}$ )	VIM-AS1 ( $2^{-\Delta Ct}$ )
MM	1	$5.143 \times 10^{-5}$	$1.185 \times 10^{-3}$
	2	$1.440 \times 10^{-4}$	$1.141 \times 10^{-2}$
	3	$8.461 \times 10^{-3}$	$1.899 \times 10^{-2}$
	4	$3.038 \times 10^{-3}$	$7.941 \times 10^{-3}$
	5	$1.992 \times 10^{-5}$	$6.531 \times 10^{-3}$
	6	$1.636 \times 10^{-4}$	$1.921 \times 10^{-3}$
	7	$1.371 \times 10^{-4}$	$2.107 \times 10^{-3}$
	8	$1.083 \times 10^{-3}$	$1.423 \times 10^{-2}$
	9	$1.358 \times 10^{-3}$	$1.151 \times 10^{-3}$
	10	$2.324 \times 10^{-4}$	$4.604 \times 10^{-3}$
	11	$6.596 \times 10^{-5}$	$2.852 \times 10^{-3}$
	12	$8.806 \times 10^{-6}$	$1.924 \times 10^{-3}$
	13	$2.585 \times 10^{-4}$	$5.676 \times 10^{-3}$
	14	$3.262 \times 10^{-3}$	$1.414 \times 10^{-3}$
	15	$9.312 \times 10^{-5}$	$5.884 \times 10^{-4}$
	16	$2.485 \times 10^{-5}$	$4.208 \times 10^{-3}$
	17	$2.383 \times 10^{-4}$	$1.027 \times 10^{-3}$
	18	$4.481 \times 10^{-4}$	$1.282 \times 10^{-3}$
	19	$6.547 \times 10^{-3}$	$3.235 \times 10^{-3}$
	20	0	$1.717 \times 10^{-3}$
	21	$9.621 \times 10^{-4}$	$1.190 \times 10^{-3}$
	22	$4.261 \times 10^{-4}$	$1.399 \times 10^{-3}$
	23	$8.118 \times 10^{-4}$	$2.557 \times 10^{-3}$
	24	$4.998 \times 10^{-4}$	$5.743 \times 10^{-4}$
	25	$1.130 \times 10^{-3}$	$2.071 \times 10^{-3}$
	26	$1.524 \times 10^{-3}$	$1.798 \times 10^{-3}$
	27	$1.211 \times 10^{-4}$	$9.055 \times 10^{-4}$
	28	$1.136 \times 10^{-3}$	$7.818 \times 10^{-4}$
PCL	1	$6.264 \times 10^{-6}$	$8.823 \times 10^{-4}$
	2	$7.168 \times 10^{-6}$	$7.842 \times 10^{-4}$
	3	0	$3.644 \times 10^{-4}$
	4	$2.259 \times 10^{-5}$	$1.087 \times 10^{-3}$
	5	$3.463 \times 10^{-6}$	$2.650 \times 10^{-3}$
	6	$6.934 \times 10^{-5}$	$2.174 \times 10^{-3}$
	7	$2.530 \times 10^{-4}$	$1.047 \times 10^{-3}$
	8	$4.212 \times 10^{-5}$	$3.985 \times 10^{-4}$
	9	$5.282 \times 10^{-5}$	$9.732 \times 10^{-4}$
	10	$1.990 \times 10^{-6}$	$1.766 \times 10^{-3}$
	11	$3.351 \times 10^{-6}$	$9.059 \times 10^{-3}$
	12	$2.218 \times 10^{-6}$	$7.622 \times 10^{-4}$

MM – multiple myeloma, PCL – plasma cell leukemia



**Figure S1.** Housekeeping gene analysis for normalization using TATAA Reference Gene Panel: (a) GeNorm software analysis. PPIA housekeeping gene with  $M = 0.586$  and (b) NormFinder software analysis. PPIA housekeeping gene with  $SD = 0.0513$ .