Pleiotropic anti-myeloma activity of ITF2357: inhibition of interleukin-6 receptor signaling and repression of *miR-19a* and *miR-19b*

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Online Supplementary Table S1. Functional annotations of the 140 up-regulated genes in ITF2357 treated *versus* untreated KMS18 cell line at 2 h.

Genes are ordered according to the average fold change (FC) in expression level and the probe set with the highest zg score was selected whenever more than one recognized the same gene.

Probe Set ID	Gene Symbol	FC	z_g	Gene Title	Chromosomal Location
227909_at	**MGC39606**	8,08	34,41	hypothetical protein MGC39606	Xq26.3
209795_at	**CD69**	5,92	6,86	CD69 molecule	12p13-p12
213820_s_at	**STARD5**	4,89	22,32	StAR-related lipid transfer (START) domain containing 5	15q26
229603_at	**BBS12**	4,59	19,02	Bardet-Biedl syndrome 12	4q27
206022_at	**NDP**	4,29	5,25	Norrie disease (pseudoglioma)	Xp11.4
202388_at	**RGS2**	4,11	37,06	regulator of G-protein signaling 2, 24kDa	1q31
1562648_at	**CCDC88A**	4,01	13,56	Coiled-coil domain containing 88A	2p16.1
204621_s_at	**NR4A2**	3,92	33,23	nuclear receptor subfamily 4, group A, member 2	2q22-q23
232138_at	**MBNL2**	3,73	18,21	Muscleblind-like 2 (Drosophila)	13q32.1
210280_at	**MPZ**	3,70	17,93	myelin protein zero (Charcot-Marie-Tooth neuropathy 1B)	1q23.3
203395_s_at	**HES1**	3,65	12,86	hairy and enhancer of split 1, (Drosophila)	3q28-q29
230141_at	**ARID4A**	3,55	30,52	AT rich interactive domain 4A (RBP1-like)	14q23.1
220987_s_at	**NUAK2**	3,53	13,01	NUAK family, SNF1-like kinase, 2	1q32.1
217009_at	**PGK2**	3,53	11,78	phosphoglycerate kinase 2	6p12.3
1560199_x_at	**FLJ11903**	3,51	5,26	similar to hypothetical protein MGC40405	5q12.1
218032_at	**SNN**	3,43	10,67	stannin	16p13
204859_s_at	**APAF1**	3,39	12,70	apoptotic peptidase activating factor 1	12q23
202581_at	**HSPA1B**	3,24	9,31	heat shock 70kDa protein 1B	6p21.3
229732_at	**HSZFP36**	3,20	8,89	ZFP-36 for a zinc finger protein	19p13.2
223580_at	**SPSB2**	3,17	10,22	splA/ryanodine receptor domain and SOCS box containing 2	12p13.31
238851_at	**ANKRD13A**	3,15	8,89	ankyrin repeat domain 13A	12q24.11
209681_at	**SLC19A2**	3,03	15,95	solute carrier family 19 (thiamine transporter), member 2	1q23.3
229773_at	**SNAP23**	3,03	6,17	Synaptosomal-associated protein, 23kDa	15q15.1
232881_at	**NESPAS**	2,99	18,77	GNAS1 antisense	20q13.32
213927_at	**MAP3K9**	2,92	16,22	mitogen-activated protein kinase kinase kinase 9	14q24.3-q31
1556203_a_at	**SRGAP2**	2,90	11,97	SLIT-ROBO Rho GTPase activating protein 2	1q32.1
228149_at	**FLJ31818**	2,85	12,47	hypothetical protein FLJ31818	7q31.1
1558844_at	**LOC387790**	2,85	6,86	hypothetical LOC387790	11q13.5
228745_at	**SGTB**	2,82	16,78	small glutamine-rich tetratricopeptide repeat (TPR)-containing, beta	5q12.3
1557091_at	**FLJ36070**	2,81	10,28	likely ortholog of MEF2-activating SAP transcriptional regulator	19q13.33
227572_at	**USP30**	2,80	11,78	ubiquitin specific peptidase 30	12q24.11
1555372_at	**BCL2L11**	2,78	8,77	BCL2-like 11 (apoptosis facilitator)	2q13
242739_at	**C6orf201**	2,77	8,33	Chromosome 6 open reading frame 201	6p25.2
241762_at	**FBXO32**	2,74	13,24	F-box protein 32	8q24.13
238682_at	**CCDC96**	2,72	11,17	coiled-coil domain containing 96	4p16.1
210151_s_at	**DYRK3**	2,70	12,66	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3	1q32.1
219390_at	**FKBP14**	2,68	10,84	FK506 binding protein 14, 22 kDa	7p15.1
211433_x_at	**KIAA1539**	2,67	6,95	KIAA1539	9p13.3
208922_s_at	**NXF1**	2,66	16,47	nuclear RNA export factor 1	11q12-q13
209808_x_at	**ING1**	2,66	11,98	inhibitor of growth family, member 1	13q34

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Online Supplementary Table S2. Functional annotations of the 102 down-regulated genes in ITF2357 treated *versus* untreated KMS18 cell line at 2 h.

Genes are ordered according to the average fold change (FC) in expression level. The zg score is also reported for each gene and the probe set with the highest zg score was selected whenever more than one recognized the same gene

Probe Set ID	Gene Symbol	FC	z_g	Gene Title	Chromosomal Location
236368_at	**KIAA0368**	-4,45	-10,62	KIAA0368	9q31.3
204913_s_at	**SOX11**	-4,30	-19,26	SRY (sex determining region Y)-box 11	2p25
231173_at	**PYROXD1**	-4,30	-7,44	pyridine nucleotide-disulphide oxidoreductase domain 1	12p12.1
241436_at	**SCNN1G**	-4,13	-9,59	sodium channel, nonvoltage-gated 1, gamma	16p12
1552330_at	**MGC16385**	-3,89	-12,34	hypothetical protein MGC16385	16q24.3
225417_at	**EPC1**	-3,85	-17,90	enhancer of polycomb homolog 1 (Drosophila)	10p11
213418_at	**HSPA6**	-3,80	-15,16	heat shock 70kDa protein 6 (HSP70B')	1q23
212921_at	**SMYD2**	-3,79	-10,72	SET and MYND domain containing 2	1q41
232291_at	**MIRH1**	-3,78	-17,79	microRNA host gene (non-protein coding) 1	13q31.3
206683_at	**ZNF165**	-3,74	-8,86	zinc finger protein 165	6p21.3
223467_at	**RASD1**	-3,66	-9,06	RAS, dexamethasone-induced 1	17p11.2
220252_x_at	**CXorf21**	-3,66	-7,31	chromosome X open reading frame 21	Xp21.2
202431_s_at	**MYC**	-3,58	-13,79	v-myc myelocytomatosis viral oncogene homolog (avian)	8q24.21
218242_s_at	**SUV420H1**	-3,50	-23,19	suppressor of variegation 4-20 homolog 1 (Drosophila)	11q13.2
220391_at	**ZBTB3**	-3,39	-7,49	zinc finger and BTB domain containing 3	11q12.3
225816_at	**PHF17**	-3,34	-14,06	PHD finger protein 17	4q26-q27
203654_s_at	**COIL**	-3,28	-10,10	coilin	17q22-q23
1552427_at	**ZNF485**	-3,08	-12,04	zinc finger protein 485	10q11.21
227687_at	**HYLS1**	-3,05	-21,38	hydrolethalus syndrome 1	11q24.2
229551_x_at	**ZNF367**	-3,05	-10,58	zinc finger protein 367	9q22|9q22.32
1558896_at	**C1orf69**	-3,03	-4,57	chromosome 1 open reading frame 69	1q42.13
237086_at	**FOXA1**	-2,94	-9,80	Forkhead box A1	14q12-q13
220590_at	**ITFG2**	-2,88	-8,47	integrin alpha FG-GAP repeat containing 2	12p13.33
214193_s_at	**C1orf107**	-2,84	-14,59	chromosome 1 open reading frame 107	1q32.2
221193_s_at	**ZCCHC10**	-2,83	-8,96	zinc finger, CCHC domain containing 10	5q31.1
242700_at	**PON2**	-2,82	-6,61	paraoxonase 2	7q21.3
1557575_at	**STBD1**	-2,80	-8,85	starch binding domain 1	4q24-q25
1552287_s_at	**AFG3L1**	-2,78	-13,18	AFG3 ATPase family gene 3-like 1 (S. cerevisiae)	16q24.3
230494_at	**SLC20A1**	-2,78	-10,17	Solute carrier family 20 (phosphate transporter), member 1	2q11-q14
236347_at	**MMAA**	-2,77	-7,35	methylmalonic aciduria (cobalamin deficiency) cblA type	4q31.22
213268_at	**CAMTA1**	-2,76	-10,46	calmodulin binding transcription activator 1	1p36.31-p36.23
219990_at	**E2F8**	-2,71	-28,44	E2F transcription factor 8	11p15.1
225838_at	**EPC2**	-2,69	-9,68	enhancer of polycomb homolog 2 (Drosophila)	2q23.1
219253_at	**TMEM185B**	-2,66	-9,35	transmembrane protein 185B	2q14.2
222883_at	**C1orf163**	-2,64	-17,96	chromosome 1 open reading frame 163	1p32.3
203247_s_at	**ZNF24**	-2,59	-11,22	zinc finger protein 24	18q12
228287_at	**ING5**	-2,58	-10,29	inhibitor of growth family, member 5	2q37.3
232613_at	**PBRM1**	-2,57	-11,97	polybromo 1	3p21

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Online Supplementary Table S3. Functional annotations of the 574 up-regulated genes in ITF2357 treated *versus* untreated KMS18 cell line at 6 h.

Genes are ordered according to the average fold change (FC) in expression level. The zg score is also reported for each gene and the probe set with the highest zg score was selected whenever more than one recognized the same gene

Probe Set ID	Gene Symbol	FC	z_g	Gene Title	Chromosomal Location
226213_at	**ERBB3**	27,30	7,94	v-erb-b2 erythroblastic leukemia viral oncogene homolog 3 (avian)	12q13
227449_at	**EPHA4**	26,90	14,44	EPH receptor A4	2q36.1
1556499_s_at	**COL1A1**	22,00	13,00	collagen, type I, alpha 1	17q21.33
225306_s_at	**SLC25A29**	19,20	11,70	solute carrier family 25, member 29	14q32.2
227909_at	**MGC39606**	16,30	43,76	hypothetical protein MGC39606	Xq26.3
232164_s_at	**EPPK1**	16,10	15,61	epiplakin 1	8q24.3
209392_at	**ENPP2**	13,90	13,46	ectonucleotide pyrophosphatase/phosphodiesterase 2 (autotaxin)	8q24.1
211031_s_at	**CLIP2**	13,40	18,53	CAP-GLY domain containing linker protein 2	7q11.23
226436_at	**RASSF4**	12,30	28,03	Ras association (RalGDS/AF-6) domain family 4	10q11.21
214023_x_at	**TUBB2B**	11,60	12,57	tubulin, beta 2B	6p25
205088_at	**MAMLD1**	11,20	8,35	mastermind-like domain containing 1	Xq28
225793_at	**LIX1L**	11,00	11,02	Lix1 homolog (mouse)-like	1q21.1
220331_at	**CYP46A1**	10,80	8,24	cytochrome P450, family 46, subfamily A, polypeptide 1	14q32.1
223276_at	**MST150**	10,70	6,22	MSTP150	5q33.1
226000_at	**CTTNBP2NL**	10,60	13,48	CTTNBP2 N-terminal like	1p13.2
207571_x_at	**C1orf38**	10,40	17,34	chromosome 1 open reading frame 38	1p35.3
203408_s_at	**SATB1**	10,20	22,25	SATB homeobox 1	3p23
218032_at	**SNN**	9,77	57,13	stannin	16p13
229626_at	**LOC387856**	9,31	6,29	similar to expressed sequence AI836003	12q13.11
227812_at	**TNFRSF19**	9,22	11,25	tumor necrosis factor receptor superfamily, member 19	13q12.11-q12.3
201631_s_at	**IER3**	8,71	12,10	immediate early response 3	6p21.3
230104_s_at	**TPPP**	7,91	13,09	tubulin polymerization promoting protein	5p15.3
224609_at	**SLC44A2**	7,55	6,05	solute carrier family 44, member 2	19p13.1
203271_s_at	**UNC119**	7,42	14,48	unc-119 homolog (C. elegans)	17q11.2
204859_s_at	**APAF1**	7,36	12,38	apoptotic peptidase activating factor 1	12q23
200878_at	**EPAS1**	7,13	25,44	endothelial PAS domain protein 1	2p21-p16
228499_at	**PFKFB4**	7,09	14,49	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4	3p22-p21
204165_at	**WASF1**	7,08	21,92	WAS protein family, member 1	6q21-q22
228228_at	**DACT3**	7,00	34,24	dapper, antagonist of beta-catenin, homolog 3 (Xenopus laevis)	19q13.32
236313_at	**CDKN2B**	6,92	54,06	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	9p21
222108_at	**AMIGO2**	6,73	8,96	adhesion molecule with Ig-like domain 2	12q13.11
223391_at	**SGPP1**	6,36	17,00	sphingosine-1-phosphate phosphatase 1	14q23.2
203140_at	**BCL6**	6,33	12,90	B-cell CLL/lymphoma 6 (zinc finger protein 51)	3q27
206907_at	**TNFSF9**	6,24	12,80	tumor necrosis factor (ligand) superfamily, member 9	19p13.3
231991_at	**C20orf160**	6,07	8,62	chromosome 20 open reading frame 160	20q11.2
220974_x_at	**SFXN3**	6,00	10,99	sideroflexin 3	10q24.31

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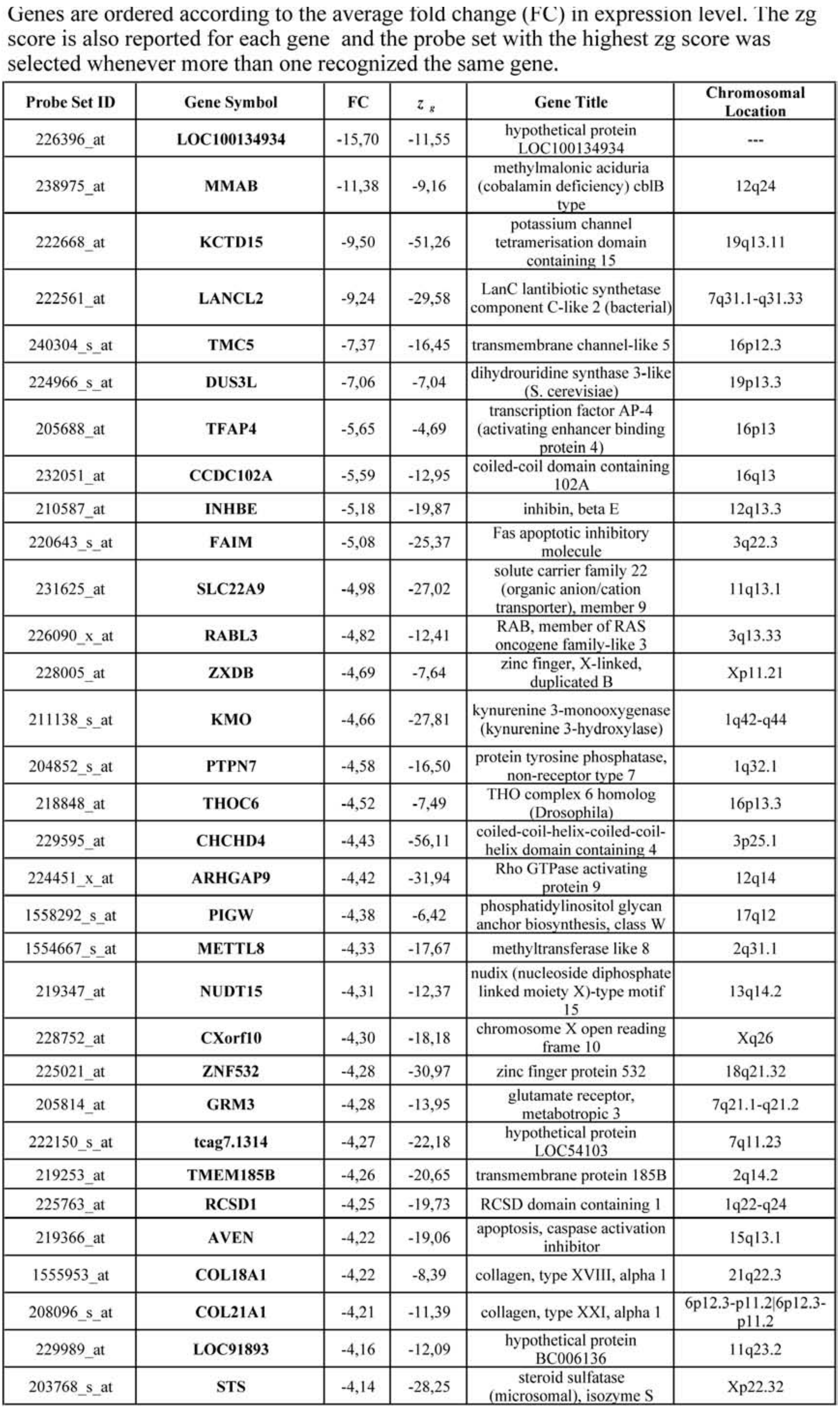
Online Supplementary Table S4. Functional annotations of the 556 down-regulated genes in ITF2357 treated *versus* untreated KMS18 cell line at 6 h.

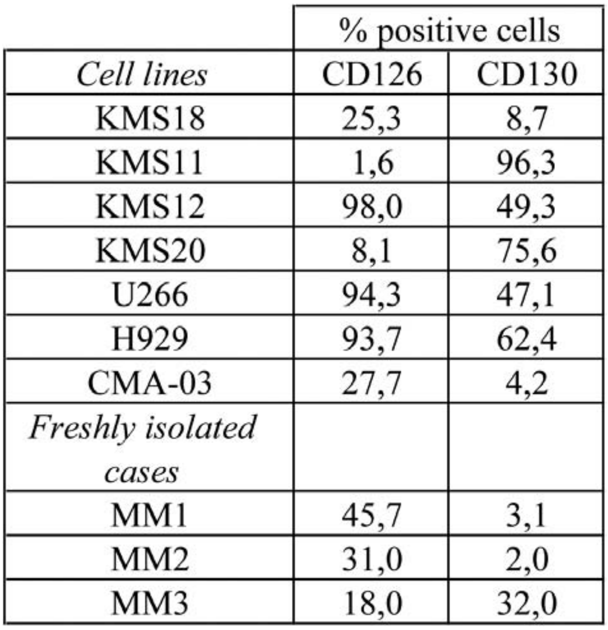


Genes are ordered according to the average fold change (FC) in expression level. The zg score is also reported for each gene and the probe set with the highest zg score was selected whenever more than one recognized the same gene.

Probe Set ID	Gene Symbol	FC	z_g	Gene Title	Chromosomal Location
226396_at	**LOC100134934**	-15,70	-11,55	hypothetical protein LOC100134934	---
238975_at	**MMAB**	-11,38	-9,16	methylmalonic aciduria (cobalamin deficiency) cblB type	12q24
222668_at	**KCTD15**	-9,50	-51,26	potassium channel tetramerisation domain containing 15	19q13.11
222561_at	**LANCL2**	-9,24	-29,58	LanC lantibiotic synthetase component C-like 2 (bacterial)	7q31.1-q31.33
240304_s_at	**TMC5**	-7,37	-16,45	transmembrane channel-like 5	16p12.3
224966_s_at	**DUS3L**	-7,06	-7,04	dihydrouridine synthase 3-like (S. cerevisiae)	19p13.3
205688_at	**TFAP4**	-5,65	-4,69	transcription factor AP-4 (activating enhancer binding protein 4)	16p13
232051_at	**CCDC102A**	-5,59	-12,95	coiled-coil domain containing 102A	16q13
210587_at	**INHBE**	-5,18	-19,87	inhibin, beta E	12q13.3
220643_s_at	**FAIM**	-5,08	-25,37	Fas apoptotic inhibitory molecule	3q22.3
231625_at	**SLC22A9**	-4,98	-27,02	solute carrier family 22 (organic anion/cation transporter), member 9	11q13.1
226090_x_at	**RABL3**	-4,82	-12,41	RAB, member of RAS oncogene family-like 3	3q13.33
228005_at	**ZXDB**	-4,69	-7,64	zinc finger, X-linked, duplicated B	Xp11.21
211138_s_at	**KMO**	-4,66	-27,81	kynurenine 3-monooxygenase (kynurenine 3-hydroxylase)	1q42-q44
204852_s_at	**PTPN7**	-4,58	-16,50	protein tyrosine phosphatase, non-receptor type 7	1q32.1
218848_at	**THOC6**	-4,52	-7,49	THO complex 6 homolog (Drosophila)	16p13.3
229595_at	**CHCHD4**	-4,43	-56,11	coiled-coil-helix-coiled-coil-helix domain containing 4	3p25.1
224451_x_at	**ARHGAP9**	-4,42	-31,94	Rho GTPase activating protein 9	12q14
1558292_s_at	**PIGW**	-4,38	-6,42	phosphatidylinositol glycan anchor biosynthesis, class W	17q12
1554667_s_at	**METTL8**	-4,33	-17,67	methyltransferase like 8	2q31.1
219347_at	**NUDT15**	-4,31	-12,37	nudix (nucleoside diphosphate linked moiety X)-type motif 15	13q14.2
228752_at	**CXorf10**	-4,30	-18,18	chromosome X open reading frame 10	Xq26
225021_at	**ZNF532**	-4,28	-30,97	zinc finger protein 532	18q21.32
205814_at	**GRM3**	-4,28	-13,95	glutamate receptor, metabotropic 3	7q21.1-q21.2
222150_s_at	**tcag7.1314**	-4,27	-22,18	hypothetical protein LOC54103	7q11.23
219253_at	**TMEM185B**	-4,26	-20,65	transmembrane protein 185B	2q14.2
225763_at	**RCSD1**	-4,25	-19,73	RCSD domain containing 1	1q22-q24
219366_at	**AVEN**	-4,22	-19,06	apoptosis, caspase activation inhibitor	15q13.1
1555953_at	**COL18A1**	-4,22	-8,39	collagen, type XVIII, alpha 1	21q22.3
208096_s_at	**COL21A1**	-4,21	-11,39	collagen, type XXI, alpha 1	6p12.3-p11.2|6p12.3-p11.2
229989_at	**LOC91893**	-4,16	-12,09	hypothetical protein BC006136	11q23.2
203768_s_at	**STS**	-4,14	-28,25	steroid sulfatase (microsomal), isozyme S	Xp22.32

refer to the corresponding pdf Todoerti Suppl Table 4 for full table

Online Supplementary Table S5. Expression of CD126 and CD130 in MM cells.



	% positive cells	
Cell lines	CD126	CD130
KMS18	25,3	8,7
KMS11	1,6	96,3
KMS12	98,0	49,3
KMS20	8,1	75,6
U266	94,3	47,1
H929	93,7	62,4
CMA-03	27,7	4,2
Freshly isolated cases		
MM1	45,7	3,1
MM2	31,0	2,0
MM3	18,0	32,0