

## **A Phase II Study of Arginine Deiminase (ADI-PEG20) in Relapsed/Refractory or Poor-Risk Acute Myeloid Leukemia Patients**

Hui-Jen Tsai<sup>1,2,3</sup>, Shih Sheng Jiang<sup>1</sup>, Wen-Chun Hung<sup>1</sup>, Gautam Borthakur<sup>4</sup>, Sheng-Fung Lin<sup>3</sup>, Naveen Pemmaraju<sup>4</sup>, Elias Jabbour<sup>4</sup>, John S.

Bomalaski<sup>5</sup>, Ya-Ping Chen<sup>2</sup>, Hui-Hua Hsiao<sup>3</sup>, Ming-Chung Wang<sup>6</sup>, Ching-Yuan Kuo<sup>6</sup>, Hung Chang<sup>7</sup>, Su-Peng Yeh<sup>8</sup>, Jorge Cortes<sup>4</sup>, Li-Tzong

Chen<sup>1,2,3,9</sup>, Tsai-Yun Chen<sup>2</sup>

**Supplementary Table 1.** FAB subtype, baseline marrow blast percentage and cytogenetic change of the 21 evaluable patients

CR+SD (N=9)			PD (N=12)				
Cases	FAB subtype	baseline BM blast (%)	cytogenetic abnormality	Cases	FAB subtype	baseline BM blast (%)	cytogenetic abnormality
1	M7	58.2	+8, +21	3	M2	71	normal
2	M2	9.2	normal	4	M0	76.2	del(18), -18
6	M0	70-80	43-47. XX, add(18)	5	M2	58	t(8;21)
9	M4eo	44.6	inv(16)	7	M4	>90	del(15)
12	M0	64.2	+11, +14, +2, +21, add(7)(p22), -12	8	M1	81.5	der(7;12)
14	M0	50.8	del(9)	10	M2	63.6	del(1), -5, -6, -8, -9, add(15, add(16), -18, +21, +6mar(16))
16	N/A*	59	+1. add(1), del(1), add(2), del(3)	11	M1	72.8	del(1), ad(2), del(5), add(16), -17, -18
17	N/A*	34	del(6q)	13	M1	89.6	del(2), del(5), +6, add(6), +8, -18, idem, +20, -7, add(14)
18	N/A*	30	normal	15	N/A*	46	t(1;3), t(1;6), der(3)t(3;10)
				19	N/A*	15	del(13), del(20), +Y
				20	N/A*	14	normal
				21	N/A*	26	inv(16), del(20)

median**		50.8				67.3	
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\*, N/A: not available

\*\* ,  $P= 0.25$  by Wilcoxon Rank Sum Test

## Supplementary Table 2

enriched gene sets in BMMC of Case 1 and Case 2 before ADI-PEG20 versus after ADI-PEG20

Gene set	nominal p-value	FDR q-value	NES*	core genes
ROSS_AML_OF_FAB_M7_TYPE	<0.001	<0.001	-3.08	DLC1, RHAG, RYR3, GATA2, PLOD2, ITGA2B, KEL, LAPTM4B, TFR2, PROS1, PNMT, MINPP1, DNMT3, ANK1, SERPINI1, TAL1, APOE, DNAJC6, PCDH9, PDLIM5, MYH10, ABCC4, NET1, NEO1, FADS2, UROD, GP1BA, BMP2K, KCNH2, NGFRAP1, CMAS, GATA1, TIMP3, KLF1, HLTF, FHL2, ICAM4, DNAJC9, TPM1, SDPR, MYL4, RDX, CTNBL1, PRUNE, PDCD10, PCCB, APOC1, ZMYND8, ALDH1A1
<a href="#">*JAATINEN_HEMATOP_OIETICSTEM_CELL_UP</a>	<0.001	<0.001	-2.58	MEG3, MPL, SCN3A, <a href="#">GATA2</a> , MYCT1, VWDE, OBSL1, DEPTOR, LAPTM4B, KIAA1211, CYTL1, PDZD2, RBPMS, FAM92A1, CPA3, TANC1, FAM69B, ZBTB8A, MAST4,

			ZNF711, KIT, SMARCA1, C11orf95, ZNF521, GNAI1, CBX2, NDN, ANGPT1, SHANK3, SCHIP1, CRISPLD1, TFPI, PTPLA, MAP7, PREX2, CALN1, <a href="#">SEPP1</a> , DPY19L2, HMGA2, TXNRD3, FGD5, FAM171B, CNKSR3, COL24A1, GCSH, LOC100506844, ME3, LIMCH1, SERPING1, FRMD6, KHDRBS3, NKAIN2, ARHGAP22, <a href="#">AKR1C3</a> , <a href="#">SOCS2</a> , ZC3HAV1L, SMAD1, BCAT1, <a href="#">GUCY1A3</a> , CDK6, TRO, <a href="#">CRHBP</a> , GPR126, DDAH1, GATM, RHOBTB1, PDGFC, CD109, <a href="#">NPR3</a> , MEIS1, <a href="#">JUP</a> , ISYNA1, TMEM200A, <a href="#">MEST</a> , ZBED3, FAIM, CD34, PGBD1, MYB, MAP9, PON2, DNMT3B, MBLAC2, TRIP6, PXDN, TMEM5, KDELC1, COL5A1, SLC39A8, PLA2G12A, TRIM24, CHST13, TMEM44, ZNF618, <a href="#">FHL1</a> , HDGFRP3, BEND4, ZNRF1, CCNB1IP1, MYO5C, DPPA4,
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				<p>ALG10B, STMN1, TAF1D, PPM1H, GPR125, KDM5B, ATP2C1, ANKRD28, DPY19L4, SRD5A3, DOCK7, PLEKHA5, FAM115A, RDX, ATP6V0A2, TUSC1, CDK2AP1, SCN9A, BIVM, EBPL, PAIP1, GOLIM4, C11orf54, FAM175A, <u>ALDH1A1</u>, PROM1, DTL, TMEM38B, TSPYL5, PRMT5, F2RL1, ZNF165, SLC39A10, BSPRY, WDR17, PAICS, CDK4, TRIM73, FABP5, HSPD1, WBP5, CPT1A, NT5DC2, ANKRD6, PSMB5, SSBP2, TNFRSF21, WASF1, CMAHP, ZNF512B, HOXA9, IGLL1</p>
YAGI_AML _FAB_MAR KERS	<0.001	0.003	-2.07	<p>MYO16, GABRE, DLC1, FGFR3, GAD1, RHAG, PYR3, GATA2, ADAMTS3, TRPC6, PLOD2, ITGA2B, KEL, PBX1, LAPTM4B, PROS1, CFH, LAMA5, CXADR, MAST4, SERPINI1, CDC42BPA, TRPC1, SERPINE2, HERC2P2, PIR, CD200, MYH10, PKIA, NET1,</p>

				ALDH5A1, TRIB2, GP1BA, ULK2, STAC, PKIG, SERPINH1, MLLT11, UBXN8, BAMBI, CAV1, ELOVL6, TIMP3, CLCN4, LDB1, ZBTB16, CD180, BAG2, SNTA1, HDGFRP3, TPM1, DLEU1, MYL4, RFC3, TNFRSF4, FADS1, TFDP2, ACO1, PAQR3, PDCD10, TGM2, FAM20B, PCCB, DDHD2, NAE1, GP9, ZMYND8, ALDH1A1, TBPL1
<a href="#">SCHURING A_STAT5A TARGETS UP</a>	<0.001	0.005	-2.02	GYPB, RHAG, HBE1, ANK1, CD36, LEPR, XK, KLHL29, PIM1, CISH
<a href="#">REACTOM E_PLATELE T_AGGREG ATION_PLU G_FORMAT ION</a>	0.006	0.133	-1.69	MPL, GP1BB, ADRA2A, ITGA2B, RAPGEF3, GP1BA, GP5, PTK2, VWF, RAPGEF4, FN1, GP9
<a href="#">REACTOM E_FORMAT</a>	0.038	0.197	-1.56	TUBB4A, CCT2, TUBA1C, TUBB2B, TUBB6, TUBA1A, CCT3, TUBA1B,

<a href="#">ION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCTRIC</a>				TUBB2A, CCT4, TCP1, TUBB3, TUBB4B, CCT6A, CCT7, CCT5
HALLMARK_MYC_TARGETS_V2	0.024	0.127	-1.48	MYC, NDUFAF4, RCL1, SORD, BYSL, NPM1, GNL3, PA2G4, CDK4, HSPD1, RABEPK, DCTPP1, PLK4, MCM4, NOLC1, PLK1, PRMT3, MRTO4, IPO4, UNG, NIP7, SLC29A2, TBRG4, PUS1, PPAN, SRM, TFB2M, DDX18, TCOF1, WDR74, TMEM97, RRP9, MYBBP1A, UTP20, AIMP2, CBX3, NOP16, PPRC1, WDR43, MPHOSPH10, NOP2
<a href="#">HALLMARK_MYC_TARGETS_V1</a>	0.068	0.322	-1.23	MYC, IMPDH2, CCT2, APEX1, HSP90AB1, ODC1, NPM1, CCT3, CDC20, HNRNPA1, TFDP1, EIF4E, GNL3, POLD2, GLO1, PA2G4, CDK4, MAD2L1, HSPD1, RAN,



			<p>PRM1, SET, RPS3, ACP1, ILF2, MCM4, NOLC1, IARS, CCT4, EIF2S1, TOMM70A, HNRNPC, CDK2, SMARCC1, YWHAQ, TCP1, GSPT1, YWHAE, ABCE1, RPS6, G3BP1, RPL14, ORC2, NCBP2, POLE3, DEK, GNB2L1, HDGF, SRSF3, HDAC2, ERH, CCT7, SF3B3, EIF4G2, RSL1D1, EIF3J, PPIA, CCT5, MCM7, EIF4A1, RPL22, VDAC3, C1QBP, TRIM28, SRSF7, SYNCRIP, RPS2, PWP1, RPLP0, SNRPG, CCNA2, PSMD14, XPO1, SRM, MRPL9, RFC4, HNRNPR, DHX15, TUFM, EPRS, DDX18, SERBP1, BUB3, CANX, KARS, MCM2, SSB, CAD, PTGES3, RRP9, PSMA1, PABPC4, RPS10, PSMA4, SLC25A3, AIMP2, EXOSC7, SSBP1, PHB2, HNRNPA2B1, DDX21, H2AFZ, TRA2B, PSMB2, CLNS1A, CBX3, EIF3B, PRDX3, EEF1B2, HNRNPU, NME1, NOP16, VDAC1,</p>
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				USP1, EIF4H, PPM1G, UBE2E1
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\*       , the common genes on hematopoietic stem cells

enriched gene sets in BMCC of Case 1 before ADI-PEG20 versus after ADI-PEG20

Gene set	nominal p-value	FDR q-value	NES*	Core genes
<a href="#">ROSS_AML_OF_FAB_M7_TYPE</a>	<0.001	<0.001	-3.21	DLC1, PLOD2, RYR3, LAPTM4B, GATA2, PNMT, ITGA2B, TFR2, RHAG, DNMT3, KEL, STXBP6, PCDH9, PROS1, PDLIM5, SERPINI1, MINPP1, APOE, ANK1, TIMP3, NGFRAP1, NET1, ABCC4, FADS2, TAL1, SLC39A4, DNAJC6, MYH10, GATA1, BMP2K, NEO1, ICAM4, KLF1, KCNH2, CTNBL1, GP1BA, ZMYND8, MYL4, APOC1, SDPR, TPM1, PCCB, HLTF, PTGS1, ARMC8, CMAS, PDCD10, C14orf2, DRAP1, MRPS12, DNAJC9, RDX, UROD, ALDH1A1, PSMD6, PRUNE, SOD1, SQLE
<a href="#">KEGG_RIB</a>	<0.001	<0.001	-2.56	RPL36A, RPL31, RPS3, RPS8,

<a href="#">OSOME</a>				RPS24, RPL9, RPS17, RPS3A, RPL12, RPS4X, RPL22L1, RPL7, RPL36, RPS20, RPS6, RPS5, RPL3, RPL10A, RPS18, RPLP0, RPS21, RPL15, RPL29, RPS23, RPL24, RPL37A, MRPL13, RPL14, RPL7A, RPL5, RPS11, RPS26, RPL8, RPL32, RPS2, RPS12, RPL4, RPL41, RPL22, RPL27A, RPS27A, RPL18A, RPS29, RPL35, RPL13A, RPL37, RPL10, RPS9, RPL18, RPSA, RPS4Y1, RPL30, RPS10, RPL13, RPS7, RPS15, RPL23, RPS25, RPS27, RPL19, RPL26, RPL23A, RPL34, RPL11, RPL35A, RPL28, RPL17, RPS19
<a href="#">REACTOME PEPTIDE CHAIN ELONGATION</a>	<0.001	<0.001	-2.56	RPL36A, RPL31, RPS3, RPS8, RPS24, RPL9, RPS17, RPS3A, RPL12, EEF2, RPS4X, RPL7, RPL36, RPS20, RPS6, RPS5, RPL3, RPL10A, RPS18, RPLP0, RPS21, RPL15, RPL29, RPS23, RPL24, RPL37A, RPL14, RPL7A, RPL5, RPS11, RPS26, RPL8, RPL32, RPS2, RPS12,

				RPL4, RPL41, RPL22, RPL27A, RPS27A, RPL18A, RPS29, RPL35, RPL13A, RPL37, RPL10, RPS14, RPS9, RPL18, RPSA, RPS4Y1, RPL30, RPS10, RPL13, RPS7, RPS15, RPL23, RPS25, RPS27, RPL19, RPL26, EEF1A1, RPL23A, RPSAP9, RPL34, RPL11, RPL35A, RPL28, RPL17, RPL19
REACTOME_3_UTR_MEDIATED_TRANSLATIONAL_REGULATION	<0.001	<0.001	-2.53	RPL36A, RPL31, RPS3, RPS8, RPS24, RPL9, RPS17, RPS3A, RPL12, EIF3E, RPS4X, RPL7, RPL36, RPS20, RPS6, RPS5, RPL3, RPL10A, RPS18, RPLP0, EIF3D, RPS21, RPL15, EIF3C, RPL29, RPS23, RPL24, RPL37A, RPL14, RPL7A, RPL5, RPS11, RPS26, RPL8, RPL32, RPS2, RPS12, RPL4, EIF3H, RPL41, EIF3B, RPL22, RPL27A, RPS27A, RPL18A, RPS29, EIF4G1, RPL35, RPL13A, RPL37, RPL10, RPS14, RPS9, RPL18, EIF1AX, RPSA, EIF3J, RPS4Y1, RPL30,

				RPS10, RPL13, EIF3F, RPS7, RPS15, RPL23, RPS25, RPS27, RPL19, EIF4A1, RPL26, RPL23A, RPSAP9, RPL34, EIF4E, RPL11, RPL35A, RPL28, RPL17, RPS19, RPL6, EIF4B
REACTOME_FORMATION_OF_THE_TERNARY_COMPLEX_AND_SUBSEQUENTLY_THE_43S_COMPLEX	<0.001	<0.001	-2.39	RPS3, RPS8, RPS24, RPS17, RPS3A, EIF3E, RPS4X, RPS20, RPS6, RPS5, RPS18, EIF3D, RPS21, EIF3C, RPS23, RPS11, RPS2, RPS12, EIF3H, EIF3B, RPS27A, RPS29, RPS14, RPS9, EIF1AX, RPSA, EIF3J, RPS4Y1, RPS10, EIF3F, RPS7, RPS15, RPS25, RPS27, RPSAP9
<a href="#">YAGI_AML_FAB_MAR_KERS</a>	<0.001	<0.001	-2.37	MYO16, GABRE, DLC1, TRPC6, PLOD2, RYR3, LAPTM4B, FGFR3, GAD1, GATA2, ITGA2B, ADAMTS3, PBX1, RHAG, CXADR, KEL, CFH, LAMA5, PROS1, MAST4, CDC42BPA, SERPINI1, TOM1L1,

				HERC2P2, PIR, TIMP3, PKIG, NET1, TRPC1, TRIB2, ULK2, SERPINE2, MYH10, PKIA, ALDH5A1, CLCN4, ZBTB16, SNTA1, LDB1, BAMBI, SERPINH1, GP1BA, UBXN8, ZMYND8, MYL4, ELOVL6, MLLT11, TGM2, CSF2RB, TPM1, PLA2G6, TFDP2, PCCB, FADS1, DDHD2, ACO1, CTSW, HDGFRP3, MORF4L2, FAM20B, PAFAH1B3, PDCD10, TM7SF2, TGIF1, ICAM2, BAG2, CAV1, DRAP1
<a href="#">REACTOME TRANSLATION</a>	<0.001	<0.001	-2.33	RPL36A, RPL31, RPS3, RPS8, EIF4EBP1, RPS24, RPL9, RPS17, RPS3A, EEF1G, RPL12, EIF2B4, EEF2, EIF3E, RPS4X, RPL7, RPL36, RPS20, RPS6, RPS5, RPL3, RPL10A, RPS18, EEF1B2, RPLP0, EIF3D, RPS21, RPL15, EIF3C, RPL29, RPS23, RPL24, RPL37A, RPL14, RPL7A, RPL5, RPS11, RPS26, RPL8, RPL32, RPS2, RPS12, RPL4, EIF3H, RPL41, EIF3B, RPL22, RPL27A,

				RPS27A, RPL18A, RPS29, EIF4G1, RPL35, RPL13A, RPL37, RPL10, RPS14, RPS9, RPL18, EIF1AX, RPSA, EIF3J, RPS4Y1, SRP14, RPL30, RPS10, RPL13, EIF3F, RPS7, RPS15, RPL23, RPS25, RPS27, RPL19, EIF4A1, RPL26, EEF1A1, RPL23A, RPSAP9, RPL34, EIF4E, SRPRB, RPL11, RPL35A, EIF5B, ETF1, RPL28, RPL17, DDOST, RPS19
<a href="#">HALLMARK MYC TARGETS V1</a>	<0.001	<0.001	-2.27	MYC, IMPDH2, APEX1, NPM1, CCT2, RPS3, HSP90AB1, NME1, TRIM28, CDK4, POLD2, GNB2L1, HNRNPA1, SMARCC1, GNL3, NOLC1, RPS6, RPS5, C1QBP, ILF2, CCT3, NOP56, HDAC2, TCP1, EEF1B2, RPLP0, EIF3D, PHB, SET, SYNCRIP, CCT5, PABPC4, IARS, ACP1, PA2G4, HSPD1, CCT4, RPL14, RUVBL2, SNRPD1, CAD, LSM7, CCT7, YWHAE, NHP2, NOP16, NCBP2, G3BP1, CSTF2,

				<p>MCM7, SSBP1, AIMP2, PHB2, RPS2, CLNS1A, FBL, ODC1, CDK2, PSMD3, EIF3B, GLO1, RPL22, RAN, SNRPA, LSM2, KPNB1, RSL1D1, TUFM, SNRPD2, RPL18, GSPT1, UBE2E1, EIF1AX, EIF3J, MRPS18B, CYC1, SRSF2, GOT2, TOMM70A, RPS10, SERBP1, SLC25A3, YWHAQ, HDDC2, PRDX4, HNRNPR, MRPL9, PTGES3, MCM2, RANBP1, COPS5, PSMA1, EIF4A1, KARS, ABCE1, RPL34, IFRD1, DDX21, EIF4E, SRSF1, VDAC1, SF3B3, CBX3, SRSF7, SRM, SNRPA1, PWP1, ETF1, SRSF3, DDX18, RNPS1, ORC2, RRP9, PSMA6, EIF4G2, RPL6, SSB, HNRNPC, XPOT, EPRS, PSMD8, TRA2B, MCM4, PPIA, PSMD14, EXOSC7</p>
<a href="#">SCHURING</a> <a href="#">A_STAT5A</a> <a href="#">TARGETS</a>	<0.001	0.001	-2.22	<p>RHAG, ANK1, GYPB, CD36, XK, RAC3, LEPR, MAOA, PIM1, HBE1, TRAF4, CISH</p>



<a href="#">UP</a>				
<a href="#">KEGG_STEROID_HORMONE_BIOSYNTHESIS</a>	0.003	0.015	-1.97	CYP7B1, AKR1C1, AKR1C2, AKR1C3, HSD17B8
<a href="#">SCHUHMA_CHER_MYC_TARGETS_UP</a>	<0.001	0.024	-1.95	MYC, MEST, AK4, PYCR1, IMPDH2, SORD, TARBP1, TMEM97, SLC39A14, FABP5, EBNA1BP2, NME1, FXN, CDK4, RABEPK, POLD2, TFRC, SLC16A1, NOLC1, UCK2, DDX10, TBL3, AHCY, GCSH, PAICS, IARS, PPAT, FKBP4, PEBP1, CAD, DHODH, GRSF1, AIMP2, RRS1, POLR2H, ODC1, FASN, ZNF239, PRDX4, EXOSC2, RANBP1, MRPL3, AUH, ABCE1, DDX21, KIAA0020, RCC1, SRM, BOP1, CTSC, MTHFD1
<a href="#">REACTOME_METABOLISM_OF_R</a>	<0.001	0.032	-1.9	RPL36A, EXOSC4, RPL31, RPS3, RPS8, RPS24, MAPK11, RPL9, RPS17, PRMT5, RPS3A, ZFP36L1,

<a href="#">NA</a>			PSMB5, RPL12, CNOT7, NUP43, RPS4X, RPL7, RPL36, TNKS1BP1, RPS20, PAIP1, RPS6, RPS5, GEMIN6, RPL3, RPL10A, RPS18, RPLP0, PSMD6, RPS21, RPL15, NUP35, RPL29, EXOSC6, SEH1L, RPS23, LSM1, RPL24, RPL37A, RPL14, SNUPN, RPL7A, AAAS, RPL5, SNRPD1, RPS11, RPS26, NCBP2, RPL8, RPL32, PSMC2, KHSRP, RPS2, CLNS1A, RPS12, RPL4, PSMD3, RPL41, SNRPE, RPL22, RPL27A, RPS27A, RPL18A, RPS29, EIF4G1, PPP2R2A, RPL35, LSM2, RPL13A, RPL37, RPL10, RPS14, SNRPD2, RPS9, RPL18, UPF3A, RPSA, GEMIN2, NUP153, RPS4Y1, RPL30, RPS10, GEMIN5, SNRPF, RPL13, RQCD1, DCP1B, CNOT10, SMG9, RPS7, RPS15, RPL23, EXOSC2, SMN1, TGS1, RPS25, RPS27, RPL19, PSMA1, EIF4A1, AKT1, NUP62, RPL26,
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				RPL23A, GEMIN4, NUP93, RPSAP9, RPL34, LSM5, PSMB6, EIF4E, SNRNPB, RPL11, RPL35A, PPP2R1A, ETF1, PSMB7, RPL28, RNPS1, RPL17, UPF3B, HSPB1, RPS19, PSMA6, PHAX, CNOT8, PSME4, RPL6, EIF4B, DDX20, PSMD4, EXOSC3, EXOSC8, PSMD10, PSMD8, EIF4A3, WDR77
<a href="#">HALLMARK MYC TARGETS V2</a>	<0.001	0.004	-1.87	MYC, SORD, TMEM97, NPM1, DCTPP1, RCL1, CDK4, PPAN, RABEPK, BYSL, GNL3, NOLC1, NOP56, NDUFAF4, PHB, PES1, UNG, MRTO4, PA2G4, HSPD1, WDR74, FARSA, PUS1, TBRG4, PRMT3, NOP16, IPO4, AIMP2, WDR43, TCOF1, IMP4, GRWD1, MYBBP1A, SLC29A2, PPRC1, TFB2M, NOP2, CBX3, SRM, DDX18, RRP9
<a href="#">REACTOME FORMAT</a>	0.009	0.046	-1.83	TUBB4A, TUBB6, CCT2, TUBA1A, TUBA1C, TUBB2B, CCT3, TCP1,

<a href="#">ION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCTRIC</a>				TUBB2A, CCT5, CCT4, CCT7, CCT8, CCT6A, TUBB3
<a href="#">REACTOME_PLATELET_AGGREGATION_PATHWAY</a>	0.004	0.123	-1.67	MPL, GP1BB, ADRA2A, ITGA2B, RAPGEF4, GP1BA, PTK2
<a href="#">PID_MYC_ACTIVATION_PATHWAY</a>	<0.001	0.126	-1.66	MYCT1, SERPINI1, MYC, BCAT1, FOSL1, PIM1, POLR3D, NPM1, NME1, CDK4, PDCD10, TP53, TFRC, CCND2, HMGA1, MINA, TAF9, SMAD3, NME2, MTA1, MAX, KAT2A, HSPD1, RUVBL1, BMI1, RUVBL2, TAF4B, CAD, SNAI1, ODC1, SLC2A1, EIF4G1, NBN, ACTL6A, EIF4A1, HSPA4, PMAIP1, EIF4E, PTMA, NCL, RCC1, RPL11,

				HSP90AA1, DDX18
<a href="#">HALLMAR K_HEME_M ETABOLIS M</a>	<0.001	0.135	-1.42	RHAG, KEL, MINPP1, ANK1, GYPB, SLC7A11, SELENBP1, GYPE, XK, TAL1, CLIC2, GATA1, BMP2K, NFE2, ICAM4, SPTA1, KLF1, RAP1GAP, HBD, BCAM, ADD2, MYL4, TRIM58, MBOAT2, SMOX, ABCB6, CA1, MOCOS, FECH, FN3K, TFDP2, UBAC1, MPP1, RCL1, HBQ1
<a href="#">HALLMAR K_FATTY ACID_MET ABOLISM</a>	0.018	0.16	-1.35	ACSM3, AADAT, CD36, CEL, BPHL, LTC4S, APEX1, MAOA, ACOT2, MIF, NTHL1, REEP6, CPT1A, EHHADH, GSTZ1, BCKDHB, ALDH3A1, PCBD1, CA2, UROD, ALDH1A1, GRHPR, UGDH, ADSL, CRAT, PPARA, HIBCH, DECR1, ACAA2, ODC1, EPHX1, ECI2, FASN, PRDX6, ELOVL5, HADH, ALAD, SMS, PTPRG, GLUL, NBN, HMGCL, SETD8, ADIPOR2, GCDH, OSTC, AUH, ECHS1, DLST,

				ACADM, ACADS, HSP90AA1, ECH1, GPD2, HMGCS1, CPT2
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enriched gene sets in BMMC of Case 1 in relapsed status versus after ADI-PEG20 in complete remission status

Gene set	nominal p-value	FDR q-value	NES*	Core genes
<a href="#">ROSS_AML_OF_FAB_M7_TYPE</a>	<0.001	<0.001	3.01	DLC1, LAPTM4B, RYR3, ITGA2B, PLOD2, RHAG, TFR2, GATA2, APOE, PROS1, STXBP6, MINPP1, SERPINI1, PNMT, KEL, APOC1, NEO1, TIMP3
<a href="#">YAGI_AML_FAB_MAR_KERS</a>	<0.001	<0.001	2.5	MYO16, GABRE, DLC1, ADAMTS3, TOM1L1, LAPTM4B, RYR3, ITGA2B, PLOD2, FGFR3, GAD1, RHAG, CXADR, GATA2, PROS1, CFH, CDC42BPA, PBX1, SERPINI1, KEL, TRPC1, TRIB2, HERC2P2, PIR, UBXN8, TIMP3, NET1, TUSC3, SERPINE2, TRPC6, ALDH5A1, CLCN4, PKIG, MYH10, PLA2G6, ELOVL6, MLLT11, PKIA, PCCB, LDB1, PAQR3, LAMA5, BAG2,

				ULK2, NLRP3, CD200, CSF2RB, ILF2, ALDH1A1, MORF4L2, PDCD10, ACO1, TGM2, NAE1, SERPINH1, ZMYND8, CTSW, FAM20B, RFC3, FADS1
<a href="#">HALLMAR K MYC TA RGETS V1</a>	<0.001	<0.001	2.19	MYC, IMPDH2, NPM1, C1QBP, CCT2, APEX1, HSPD1, MAD2L1, EEF1B2, GLO1, SNRPD1, SNRPG, CLNS1A, NME1, CDK4, HNRNPA1, PSMC6, ILF2, HSP90AB1, NDUFAB1, ERH, GNL3, TCP1, ABCE1, TOMM70A, CCT4, VBP1, MRPL9, CCT3, IARS, RSL1D1, EIF4E, AIMP2, CCT5, HDAC2, KPNA2, PSMA2, RPL14, DDX18, RPL34, YWHAQ, EIF3D, EIF1AX, NCBP2, MRPS18B, PSMD14, PSMD8, PWP1, DUT, EPRS, PSMA6, G3BP1, EIF2S1, PPIA, UBE2E1, SRSF1, RAN, SNRPB2, SNRPD2, PHB, LSM7, PRDX3, KARS, UBA2, SET, VDAC3, RPS5, PSMA4, NOLC1, PA2G4, MCM4, SRSF7,

				SSBP1, RPL22, CYL1, RPLP0, SMARCC1, GNB2L1, CCNA2, XPOT, CBX3, HSPE1, COPS5, RUVBL2, PPM1G, HDDC2, SERBP1, AP3S1, XRCC6, CDK2, MCM2, POLD2, NOP56, PHB2, SSB, PCNA, DHX15, GSPT1, RRM1, VDAC1, PSMD7, SNRPD3, EIF3B, PRDX4, SLC25A3, PSMA7, CNBP, RPS6, ACP1, DDX21, CANX, SF3B3, EIF2S2, XPO1, ORC2, RFC4, PABPC4, YWHAE, EIF4A1, POLE3, HNRNPC, BUB3, HNRNPR, PSMC4, TRA2B, SRSF2, PSMA1, MCM7, ODC1, STARD7, PSMD1, PSMD3, SRSF3, RAD23B, COX5A, DEK, ETF1, H2AFZ
<a href="#">SEKI INFLAMMATOR Y RESPONSE LPS UP</a>	<0.001	0.013	2.04	FAM84A, CCL3, CXCL2, IER3, ADAMTS7, CXCL10, EXOC3L4, CSF1, NFKBIZ, NFKBIA, EREG, MAFF, TSLP, CCRL2, RIPK2, SOD2, GBP1



<a href="#">WONG MIT OCHONDRI A_GENE_M ODULE</a>	<0.001	0.017	2	SLC9A2, SLC40A1, MAOA, TRIM45, MRPS33, GCAT, NT5M, MRPL36, MRPL13, COQ3, PCCB, ABCB6, MRPL42, MRPL45, ACAT1, AGMAT, UNG, NDUFS4, SOD2, HSCB, DCTN6, NDUFB4, NDUFAF1, NDUFAB1, MTHFD2, NDUFB1, TOMM70A, ALDH6A1, COX6C, PDHX, MRPL40, PDHB, MRPS30, MRPS36, DECR1, TFAM, UQCRB, MRPS18B, ATP5F1, FH, NIPSNAP1, MTRR, MCCC2, NDUFA7, DLD, DUT, SLC25A32, UQCRQ, SCO1, MRPS17, NME4, MRPL32, KARS, CRYZ, VDAC3, COX7B, MRPL3, ATP5C1, NDUFV2, MRPS28, ATOX1, CYC1, PDK3, ATP5J, CRYZL1, TIMM10, NQO1, MRPL18, NDUFA4, TIMM23, TIMM13, NDUFS3, SEC61G, CPT1A, WARS2, TOMM7, NDUFA5, NDUFA12, COX18, NDUFB6, ECHS1, NDUFA8, MRPL11, MCAT,
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				ATP6V1E1, ATP5G2, GPX4, COX7A2, COX7C, DAP3, NDUFB3, UQCRFS1, ATP6V1C1, ATP5B, ATP5O, ATP6V1G1, MRPL49, NDUFS8, NDUFB8, NDUFB10, NDUFA6, ATP5I, MRPS15, NDUFB5, NDUFS5, MRPL27, ATP5L, NDUFV1, UQCR10, HSD17B10, PTRH2, VDAC2, COX5A, COX6A1, ATP13A3, AUH, COX7A2L, ATP6V1D, UQCR11, IDH2, SDHB
<a href="#">VANASSE BCL2 TAR GETS UP</a>	<0.001	0.044	1.85	RELN, RYR2, SLC16A9, MACC1, SERPING1, LIFR
<a href="#">HALLMAR K_TNFA_SI GNALING VIA_NFKB</a>	<0.001	0.041	1.66	IL1B, SERPINE1, CXCL2, CXCL3, IER3, CXCL10, EDN1, CSF1, F3, MYC, CCL4, PTGS2, LAMB3, NFKBIA, BCL2A1, DNAJB4, DUSP1, ETS2, G0S2, MAFF, PDLIM5, ZBTB10, TNFAIP6, BTG3, CCRL2, YRDC, RIPK2, KYNU, IL18, SOD2, CXCL11, TNF, CD83,

				STAT5A, PTGER4, SERPINB2, CD69, EGR1, KLF9, ATF3, NAMPT, SGK1, MSC, TRIP10, MARCKS, CCL2
<a href="#">HALLMARK_MYC_TARGETS_V2</a>	0.012	0.024	1.62	MYC, NDUFAF4, SORD, NPM1, HSPD1, TMEM97, RABEPK, UNG, CDK4, WDR74, GNL3, AIMP2, IMP4, NIP7, DDX18, FARSA, MPHOSPH10, PHB, RCL1, WDR43, NOLC1, PA2G4, MCM4, MRTO4, CBX3, HSPE1, DCTPP1
<a href="#">HALLMARK_INFLAMMATORY_RESPONSE</a>	<0.001	0.031	1.56	IL1B, SERPINE1, SLC1A2, KCNJ2, DCBLD2, CXCL9, CXCL10, EDN1, CSF1, F3, MYC, ADORA2B, MMP14, ICAM4, NFKBIA, EREG, ITGB8, FFAR2, CALCRL, TNFAIP6, AQP9, CCRL2, MSR1, TLR3, RIPK2, TIMP1, NLRP3, IL18, AHR, RNF144B, ATP2C1, CXCL11, IL10, LAMP3, NM1, PTGER4
<a href="#">HALLMARK_FATTY</a>	0.005	0.033	1.54	AADAT, BMPR1B, CEL, MAOA, LTC4S, ACSM3, CD36, G0S2, OSTC,

<a href="#">ACID_MET ABOLISM</a>				MIF, APEX1, CCDC58, BPHL, PTPRG, UROD, ACOT2, INMT, NBN, NTHL1, EHHADH, ALDH1A1, CA2, HIBCH, PCBD1, PTS, PDHB, DECR1, MDH1, ECI2, FH, ADSL, HMGCS1, DLD, SDHD, HPGD, GRHPR, SMS, CPT2, ACAA2, CRYZ, ACADM, HADHB
<a href="#">HALLMAR K_E2F_TAR GETS</a>	0.005	0.072	1.44	DSCC1, MYC, LYAR, GINS1, CKS2, WEE1, MAD2L1, PAICS, UNG, NBN, TFRC, NME1, CDK4, HMGB3, CDKN2A, ASF1A, MTHFD2, EXOSC8, NUDT21, RFC3, NUP107, KPNA2, ORC6, HN1, DCK, DUT, POP7, UBE2T, EIF2S1, RFC2, SRSF1, RAN, ZW10, DLGAP5, PPP1R8, CSE1L, CCNB2, DEPDC1, NOLC1, CKS1B, PA2G4, MCM4, NUP205, RAD21, MCM3, DCTPP1, RACGAP1, XRCC6, MCM2, ING3, POLD2, PRKDC, NAA38, NOP56, RPA2, PCNA, STMN1, GSPT1, BUB1B, RPA3, PHF5A, CDK1, SLBP,

				HMMR, PRDX4, SMC6, UBE2S, CDKN3, KIF2C, PLK4, HMGA1, XPO1, RQCD1, BRCA2, ORC2, PTTG1, CDKN2C, IPO7, TRA2B, ANP32E, SRSF2, PNN, MCM7, SSRP1, RAD51AP1, NUP153, RBBP7, TOP2A, CHEK1, MLH1, DEK, H2AFZ, SMC4, TP53, AURKA
<a href="#">HALLMAR K_IL6_JAK _STAT3_SIG NALING</a>	0.031	0.075	1.42	IL1B, CXCL3, CXCL9, CXCL10, CSF1, IL7, PDGFC, CD36, LEPR, TNFRSF12A, IL1R2, PIM1, SOCS1, CSF2RB, CD38, CXCL11, A2M, TNF
<a href="#">HALLMAR K_HEME_M ETABOLIS M</a>	0.005	0.088	1.39	RHAG, MINPP1, KEL, CLIC2, XK, SELENBP1, SLC7A11, ANK1, ICAM4, TAL1, KLF1, SPTA1, BMP2K, NFE2, CA1, MBOAT2, ABCB6, FECH, BCAM, UROD, GATA1, TFRC, GYPA, RAP1GAP, TSPO2, GMPS, CA2, MPP1, RHCE, ALDH6A1, ABCG2, HBD, TCEA1, GCLC, TMCC2, GYPB, TRIM58, LMO2, UBAC1, CAT, TRAK2, RCL1,

				BPGM, SMO
<a href="#">HALLMARK_XENOBIOTIC_METABOLISM</a>	0.049	0.158	1.3	SERPINE1, GAD1, PROS1, AKR1C2, MAOA, G6PC, BCAT1, CASP6, ACOX2, CD36, ETS2, CROT, PDLIM5, AQP9, BPHL, TMEM97, KYNU, AKR1C3, RAP1GAP, ADH5, PYCR1, TPST1, CA2, ENPEP, GSS, JUP, PTS, GCLC

enriched gene sets in BMMC of Case 2 before ADI-PEG20 versus after ADI-PEG20

Gene set	nominal p-value	FDR q-value	NES*	Core genes
<a href="#">PID_SYNDROME_CAN_1_PATHWAY</a>	0.013	0.141	-1.74	COL4A1, COL16A1, COL5A2, COL8A1, COL12A1, COL14A1, COL1A2, COL3A1, MET, COL6A3, COL5A1, COL7A1, COL4A4, COL8A2
<a href="#">NABA_COLLAGENS</a>	0.011	0.154	-1.73	COL4A1, COL16A1, COL5A2, COL8A1, COL12A1, COL14A1, COL6A5, COL1A2, COL6A6, COL28A1, COL3A1, COL4A2, COL6A3, COL5A1, COL7A1,

				COL4A4, COL8A2, COL19A1, COL4A3, COL26A1, COL24A1
<a href="#">VALK AML CLUSTER 8</a>	0.015	0.267	-1.73	GYPA, RHCE, RHD, GYPB, SNCA, ABCG2, TNS1, TAL1, CDH1, ANK1, TSPAN5, PBX1, TRAK2, SELENBP1, ARHGEF12
<a href="#">NAKAYAM A FGF2 TA RGETS</a>	0.021	0.362	-1.69	COL4A1, GPT, COL5A2, COL8A1, IGF1, OLFML3, CXCL12, PDGFRB, MSMO1
<a href="#">REACTOM E COLLAG EN FORMA TION</a>	0.021	0.265	-1.65	COL4A1, COL16A1, COL5A2, ADAMTS2, COL8A1, COL12A1, COL14A1, COL1A2, COL28A1, COL3A1, ADAMTS3, COL4A2, TLL1, COL6A3, COL5A1, COL7A1, PCOLCE, COL4A4, PLOD2, COL8A2, COL19A1, LEPREL1, SERPINH1
<a href="#">HALLMAR K HEME M ETABOLIS M</a>	0.015	0.346	-1.35	CTSE, GYPE, GYPB, RHCE, RHD, GYPB, TSPO2, ACSL6, CA1, AHSP, RHAG, KEL, SNCA, ABCG2, EPB42, TNS1, SPTB, SPTA1, SLC6A9, TAL1, RAP1GAP, MINPP1, ADD2, CPOX,

			<p>TRIM58, PDZK1IP1, ANK1, CA2, ABCB6, HBB, TMCC2, TSPAN5, IGSF3, SLC2A1, HMBS, HBQ1, HBD, TRAK2, SELENBP1, PC, ERMAP, UROD, TFRC, SLC25A37, ARHGEF12, BPGM, ENDOD1, PPOX, HBBP1, DAAM1, PIGQ, ISCA1, SLC11A2, GLRX5, XPO7, HEBP1, GCLC, SLC30A1, ALAD, FAM46C, MARCH8, AGPAT4, EIF2AK1, MFHAS1, EPB41, AQP3, RNF123, RANBP10, BMP2K, E2F2, HBZ, CLCN3, RCL1, HIST1H4C, MGST3, BTRC, BNIP3L, UCP2, ASNS, UBAC1, GYPC, DCUN1D1, CROCCP2, KAT2B, UROS, NUDT4, NFE2, MXI1, NCOA4, OPTN, BTG2, SLC7A11, SLC25A38, HDGF, TCEA1, CAT, CTNS, ALDH6A1, BLVRA, KLF3</p>
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\*NES: Normalized enrichment score



**Supplementary Table 3.**

enriched gene sets in BMCC of Case 1 and Case 2 before ADI-PEG20 (BMCC1B and BMCC2B) versus 3 non-responders

Gene set	nominal p-value	FDR q-value	NES*	Core genes
<a href="#">ROSS AML OF FAB M7 TYP E</a>	<0.001	<0.001	2.68	RYR3, RHAG, PCDH9, ANK1, KEL, TFR2, ITGA2B, TAL1, KCNH2, NEO1, PROS1, DLC1, ALDH1A1, MYH10, GP1BA, DNAJC6, KLF1, GATA1, MINPP1, SERPINI1, PNMT, FHL2, APOC1, DNM3, TPM1, PDLIM5, UROD, SDPR, PLOD2, TIMP3, BMP2K, STXBP6, CMAS, ABCC4
<a href="#">YAGI AML FAB MARKERS</a>	<0.001	0.01	1.98	RYR3, RHAG, ADAMTS3, PBX1, KEL, GAD1, PIR, ITGA2B, PROS1, DLC1, CXADR, ALDH1A1, LAMA5, MYH10, GP1BA, SERPINI1, CLCN4, PKIA, CDC42BPA, GP9, TPM1, CAV1, TRIB2, SNTA1, ULK2, TRPC1, PLOD2, ELOVL6,

				HDGFRP3, NTRK1, CPM, TIMP3, PKIG, CACNA2D2, NR4A2, TGM2, CFH, NCAM1, LAPTM4B, NET1, HERC2P2, CSF2RB, UBXN8, MAST4, RRAS2, LDB1, GATA2, ATXN1, ELL2, SERPINE2, STAT4, FGFR3, TBPL1, RFC3, PDCD10, ANXA5, MED21, F2R, CAST, CD164, DLEU1, ELOVL5, NAE1
<a href="#">OLSSON_E2F3_TARGETS_UP</a>	0.004	0.029	1.86	PTGER3, C1orf198, ELF3, AKR1C2, DAG1, ECE1, PVRL1
<a href="#">SCHURINGA_S_TAT5A_TARGETS_UP</a>	0.007	0.055	1.76	RHAG, ANK1, XK, CD36, LEPR, VEGFA
<a href="#">REACTOME_PLATELET_AGGREGATION_PLUG_FORMATION</a>	0.006	0.118	1.72	GP1BB, ITGA2B, PTK2, GP1BA, GP9, ADRA2A, GP5, FN1, VWF, RASGRP1
<a href="#">PID_WNT_NON_CANONICAL_PATHWAY</a>	0.013	0.211	1.63	ROR2, MAPK10, FZD6, DAAM1, FZD5, FZD7

<a href="#">HALLMARK_T NFA_SIGNALIN G_VIA_NFKB</a>	0.013	0.12	1.36	G0S2, CCND1, LAMB3, BMP2, EGR2, TUBB2A, CSF1, CYR61, EGR3, PDLIM5, PPAP2B, PPAP2B, CXCL10, FOSL1, INHBA, CD80, GPR183, TNFRSF9, EGR1, CD83, BIRC3, MARCKS, NR4A2, NR4A1, CLCF1, KYNU, DUSP4, TRIP10, MAFF, SMAD3, VEGFA, BTG1, PTGS2, TNFAIP6, SERPINE1, IFIT2, SLC2A3, PANX1, SOD2, BTG2, RHOB, DUSP2, NAMPT, DNAJB4, CD69, HBEGF, SGK1, IRS2, ID2, YRDC, NR4A3, IL1B
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enriched gene sets in pre-ADI-PEG20 BMMC of 3 non-responders versus 2 responders

Gene set	nominal p-value	FDR q-value	NES*	core genes
<a href="#">SCHURING A_STAT5A</a>	<0.001	0.019	-1.96	MPO, CEBPA, ELANE, CTSG, TYROBP, CD44, PECAM1

<a href="#"><u>TARGETS_DN</u></a>				
<a href="#"><u>VALK_AML_CLUSTER_10</u></a>	<0.001	0.019	-1.93	AZU1, MN1, CFD, CHRDL1, SETBP1, LPHN1, RNASE2, RBPMS, SPON1, PPP1R16B, NPDC1, SPTBN1, FLNB, F2RL1, CRIM1, PRKD2, CD22
<a href="#"><u>KAMIKUBO_MYELOID_CEBPA_NETWORK</u></a>	<0.001	0.018	-1.92	PRTN3, CEBPA, EMR1, RAB31, LGALS1, CSF2RA, HP, CYBB, IL18
<a href="#"><u>VILIMAS_NOTCH1_TARGETS_DN</u></a>	0.011	0.123	-1.73	MPO, VPREB1, CTSG, CSF2RA, LRRC25, GFI1, CSF3R
<a href="#"><u>CREIGHTON_AKT1_SIGNALING_VIA_MTOR_UP</u></a>	0.004	0.135	-1.7	ARHGEF16, BIK, CYB561, CLDN3, SLC37A1, DDR1, DUSP10, NEU1, TJP3, PRKCD, UBE2M, LASP1, CLSTN1

<a href="#"><u>VALK_AML_WITH_FLT3_ITD</u></a>	0.015	0.18	-1.66	HOXB6, HOXA9, HOXB3, APP, BAHCC1, IL2RA, MMP2, LCT, LGALS3BP, QPRT, TRPC2, MAP1A, TRIM16, GOLGA8A, IL1RAP, PBX3
<a href="#"><u>WEIGEL_OXIDATIVE_STRESS_RESPONSE</u></a>	0.019	0.228	-1.61	CDH3, APP, COMT, CASK, POLD1, BAX, IGFBP2, ARHGDIA, ZNF91, NF2, XIAP, DAPK1, ITGA5, CUX1, GNAS, CAPNS1
<a href="#"><u>GENTLES_LEUKEMIC_STEM_CELL_DN</u></a>	0.03	0.226	-1.6	CCNA1, STAR, RNASE3, RNASE2, MS4A3, CSTA

NES\*, Normalized enrichment score

