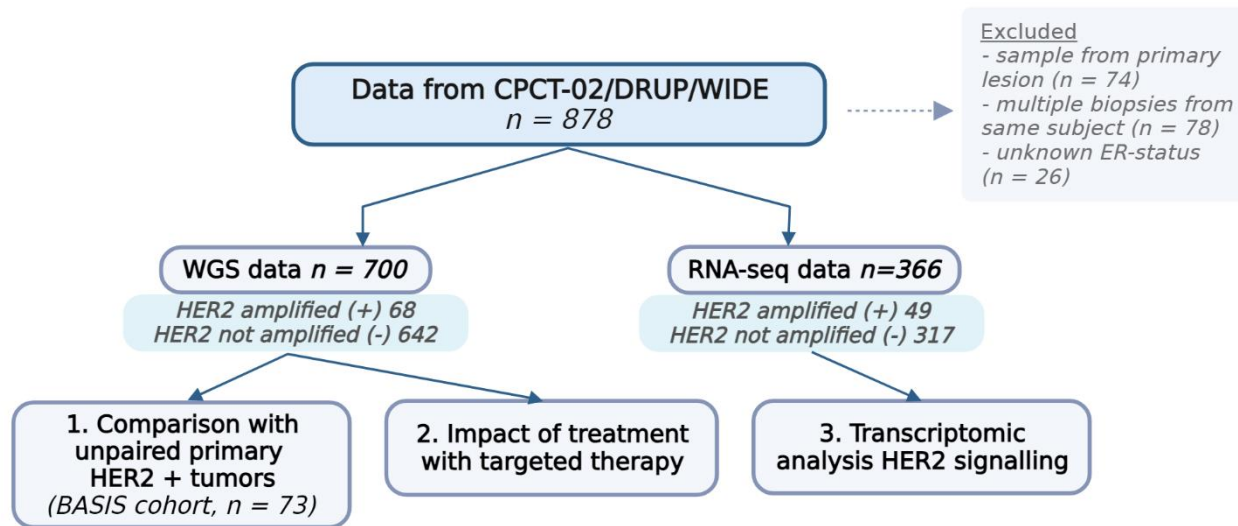
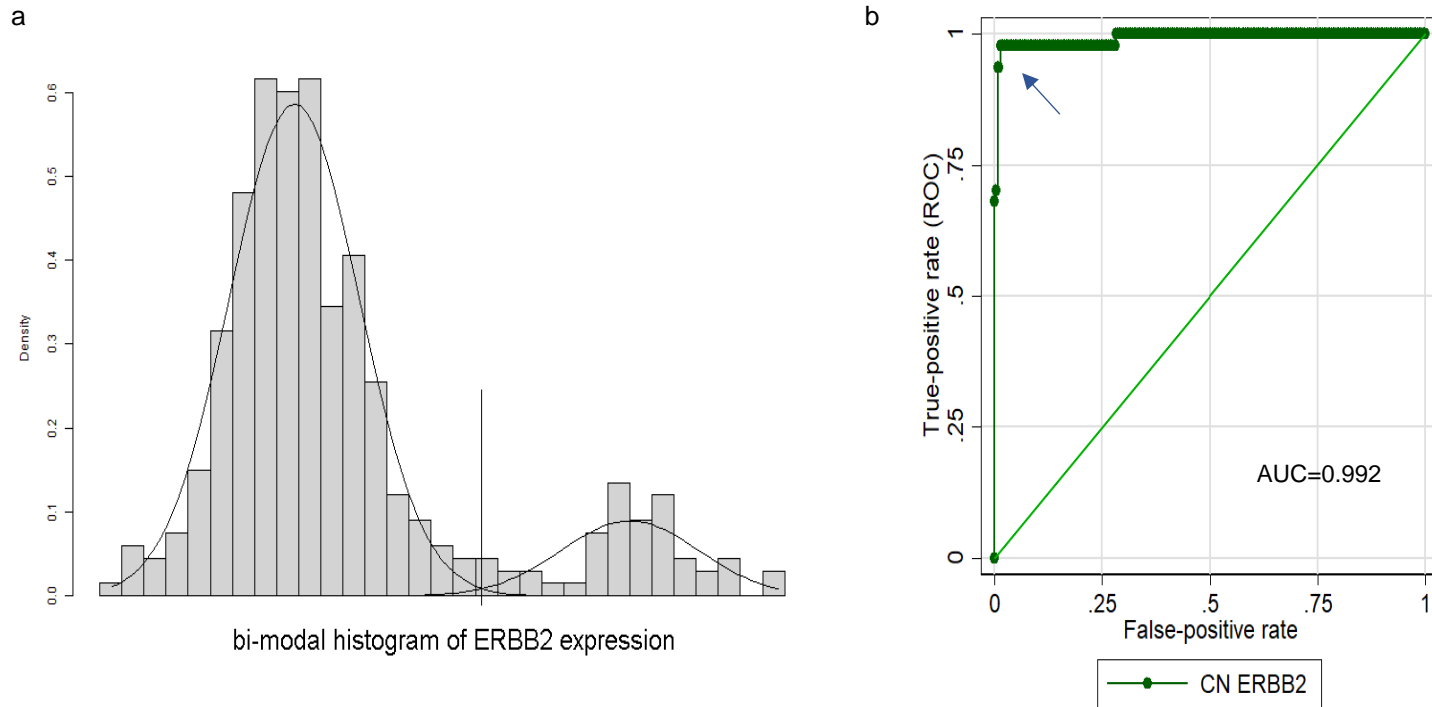


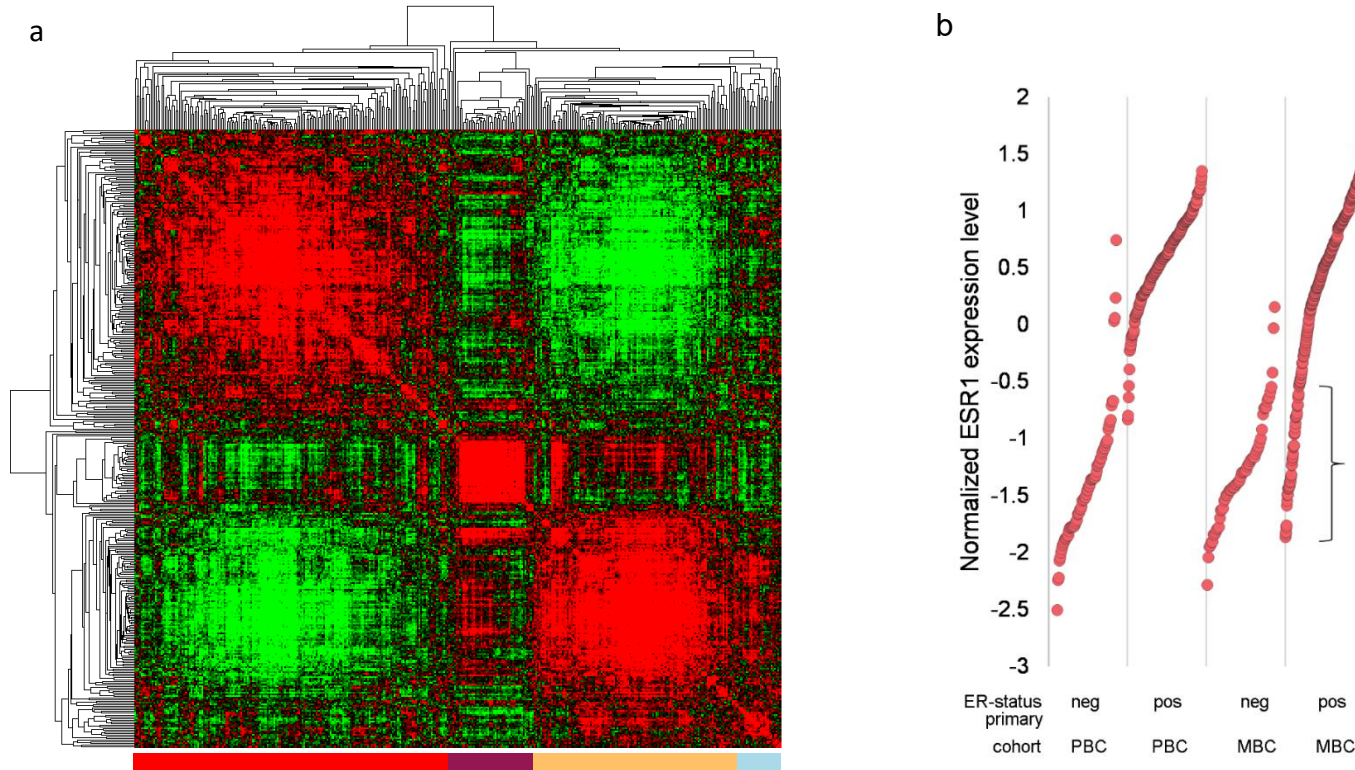
## Supplementary Figures and Tables



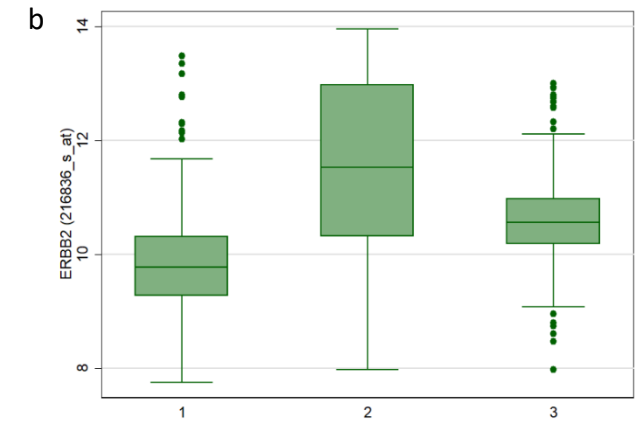
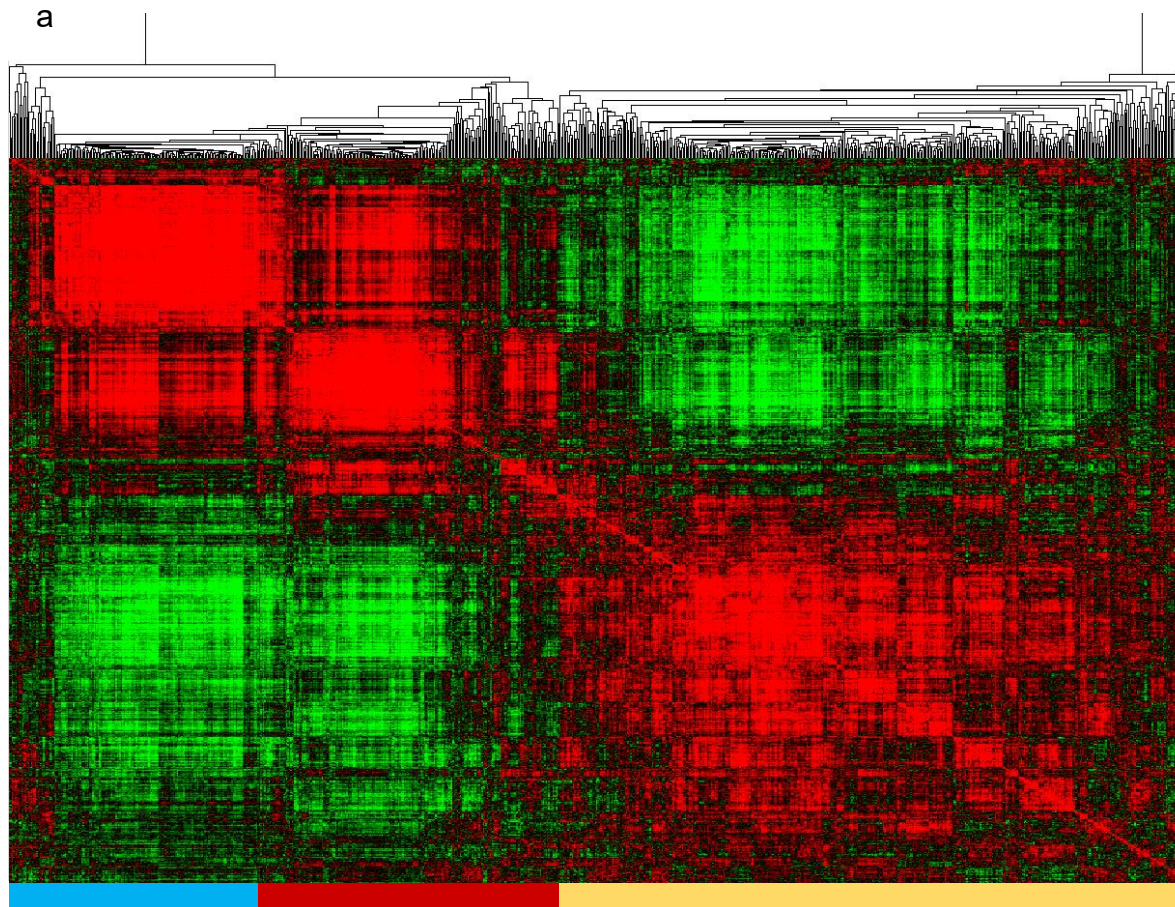
Supplementary Figure 1. Study workflow.



**Supplementary Figure 2. ERBB2 expression and copy number threshold.** a) ERBB2 expression shows a bi-modal distribution. The cross-point of the 2 normal estimation curves (vertical line) was used as threshold. b) ROC curve of ERBB2 CN, grouping samples by expression threshold. The arrow indicates the CN threshold of 9.954 (Youden index 0.965).

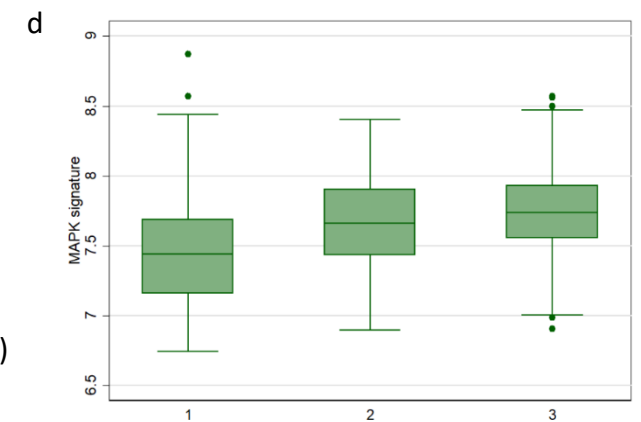


**Supplementary Figure 3. Hierarchical clustering correlation matrix of RNA sequencing data of the 366 MBC samples and *ESR1* expression over cohorts.** a) Hierarchical clustering correlation matrix. Expression levels of 878 genes associated with a HER2 driven expression profile were median centered and used to create a correlation matrix of sample vs sample. This matrix was subsequently used for hierarchical clustering, red and green indicating positive and negative correlation-coefficients, respectively. b) *ESR1* expression by ER-status of primary disease (via pathology reports) and BC groups. To obtain comparable levels, *ESR1* expression levels were z-normalized for PBC/MBC separately (i.e. both PBC and MBC distributions had a mean of 0 and standard deviation of 1). Bracket indicates overlapping area where ER positive cases (by status in primary disease) show expression levels comparable to ER negative cases.



c

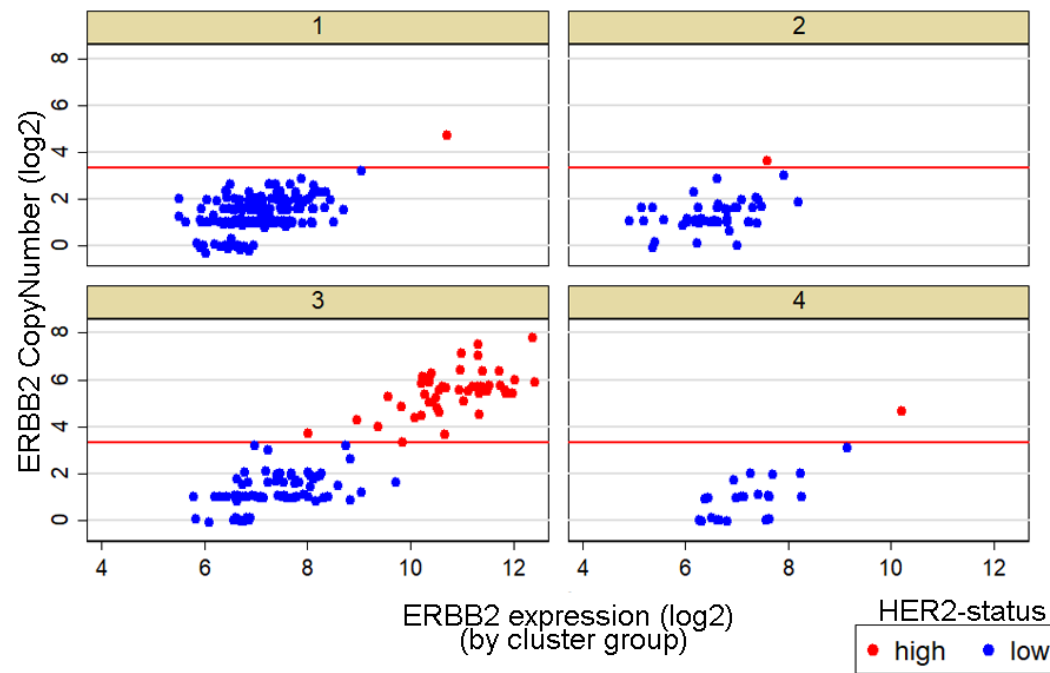
Subtype	cluster			Total
	1	2	3	
Basal	150	43	0	193
Her2	6	102	4	112
LumA	0	15	212	227
LumB	4	22	117	143
Normal	23	38	131	192
<b>Total</b>	<b>183</b>	<b>220</b>	<b>464</b>	<b>867</b>



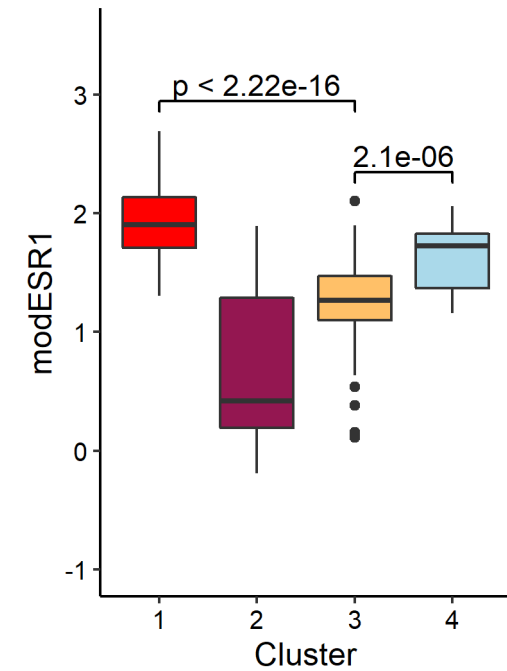
**Supplementary Figure 4. Hierarchical clustering correlation matrix independent public data of PBC.**

a) Expression levels of 878 genes associated with a HER2 driven expression profile were median centered to create a correlation matrix of sample vs sample. This matrix was subsequently used for hierarchical clustering, red and green indicating positive and negative correlation-coefficients, respectively. b) main clusters from (a) versus ERBB2 expression levels. c) versus molecular subtypes. d) versus average expression of MAPK signature genes.

a



b



**Supplementary Figure 5. ERBB2 copy number and expression by cluster group and ESR1 pathway score by cluster group.** a) ERBB2 copy number (log2) and ERBB2 expression by cluster group. Red indicates HER2+ samples. b) ESR1 pathway expression by cluster group. The score on this module was significantly lower than in cluster 1 and 4, which also had a high frequency of ER-positive primary samples.

Supplementary Table 1: Univariable items tested for outcome on AHT

<b>categorical</b>	<b>remark</b>
ER-Status	ER+ as group 1
HER2+ Status	HER2+ as group 1
Nr of prior therapy lines	binary: 0 and 1 line as group 0
TMB_10_5	TMB grouped 0-5,5-10,>10
Whole Genome Duplication	yes/no
Chromotrypsis	yes/no
PIK3CA	mutation yes/no
ERBB2	mutation yes/no
domain	mutation ERBB2 by domain (Extracellular / Tyrosine Kinase Domain)
penp	combination of PIK3CA, ERBB2, NF1, PTEN
TP53	mutation yes/no
PIK3CA	mutation yes/no
MUC16	mutation yes/no
HMCN1	mutation yes/no
RYR2	mutation yes/no
USH2A	mutation yes/no
HYDIN	mutation yes/no
CDK12	mutation yes/no
OBSCN	mutation yes/no
ABCA13	mutation yes/no
CACNA1G	mutation yes/no
CSMD1	mutation yes/no
PKHD1L1	mutation yes/no
RYR1	mutation yes/no
SYNE2	mutation yes/no
ATR	mutation yes/no
CSMD3	mutation yes/no

<b>categorical</b>	<b>remark</b>
LRP1B	mutation yes/no
MED1	mutation yes/no
PLEC	mutation yes/no
VPS13B	mutation yes/no
ZFHX4	mutation yes/no
Amp1	Gistic region yes/no
Amp2	Gistic region yes/no
Amp3	Gistic region yes/no
Amp4	Gistic region yes/no
Amp5	Gistic region yes/no
Amp6	Gistic region yes/no
Amp7	Gistic region yes/no
Amp8	Gistic region yes/no
Amp9	Gistic region yes/no
Amp10	Gistic region yes/no
Amp11	Gistic region yes/no
Amp12	Gistic region yes/no
Amp13	Gistic region yes/no
Amp14	Gistic region yes/no
Amp15	Gistic region yes/no
Amp16	Gistic region yes/no
Del17	Gistic region yes/no
Del18	Gistic region yes/no
Del20	Gistic region yes/no
Del31	Gistic region yes/no



<b>continuous</b>	<b>remark</b>
Nr of prior therapy lines	
Muts.InDel	nr of somatic Insertion/Deletions
Muts.MNV	nr of somatic multinucleotide substitutions
Muts.SNV	nr of somatic singlenucleotide substitutions
TMB	
SV.DEL	nr of structural variant of type deletion
SV.DUP	nr of structural variant of type tandem duplication
SV.INV	nr of structural variant of type inversion
SV.SINGLE	nr of structural variant of type single
SV.TRA	nr of structural variant of type translocation
totalSV	total nr of SVs
genomePloidy	
SBS1	% contribution
SBS2	% contribution
SBS3	% contribution
SBS5	% contribution
SBS8	% contribution
SBS13	% contribution
SBS18	% contribution
SBS39	% contribution
SBS40	% contribution
DBS2	% contribution
DBS3	% contribution
DBS4	% contribution
DBS5	% contribution
DBS6	% contribution
DBS7	% contribution
DBS9	% contribution
DBS11	% contribution

<b>continuous</b>	<b>remark</b>
ID1	% contribution
ID2	% contribution
ID3	% contribution
ID4	% contribution
ID5	% contribution
ID6	% contribution
ID8	% contribution
ID9	% contribution
ID10	% contribution
SV2	% contribution
SV4	% contribution
SV5	% contribution
SV6	% contribution
nr_GISTIC2	Number of CNV regions via GISTIC

Supplementary Table 2: HER2-specific genes

<b>ENSG</b>	<b>NAME</b>	<b>ENSG</b>	<b>NAME</b>	<b>ENSG</b>	<b>NAME</b>
ENSG00000178372	CALML5	ENSG00000187634	SAMD11	ENSG00000117115	PADI2
ENSG00000176887	SOX11	ENSG00000229453	SPINK8	ENSG00000118514	ALDH8A1
ENSG00000198729	PPP1R14C	ENSG00000213420	GPC2	ENSG00000135472	FAIM2
ENSG00000198535	C2CD4A	ENSG00000131015	ULBP2	ENSG00000120875	DUSP4
ENSG00000172551	MUCL1	ENSG00000115850	LCT	ENSG00000159166	LAD1
ENSG00000165125	TRPV6	ENSG00000101846	STS	ENSG00000230601	TEX48
ENSG00000172478	MAB21L4	ENSG00000189377	CXCL17	ENSG00000058335	RASGRF1
ENSG00000163220	S100A9	ENSG00000102970	CCL17	ENSG00000081148	IMPG2
ENSG00000134323	MYCN	ENSG00000249961	TERB1	ENSG00000125898	FAM110A
ENSG00000143546	S100A8	ENSG00000130675	MNX1	ENSG00000258947	TUBB3
ENSG00000179913	B3GNT3	ENSG00000203985	LDLRAD1	ENSG00000101333	PLCB4
ENSG00000137648	TMPRSS4	ENSG00000182782	HCAR2	ENSG00000104941	RSPH6A
ENSG00000163362	INAVA	ENSG00000133962	CATSPERB	ENSG00000188483	IER5L
ENSG00000115221	ITGB6	ENSG00000132746	ALDH3B2	ENSG00000088305	DNMT3B
ENSG00000158089	GALNT14	ENSG00000081985	IL12RB2	ENSG00000183496	MEX3B
ENSG00000107242	PIP5K1B	ENSG00000143512	HHIPL2	ENSG00000071575	TRIB2
ENSG00000261115	TMEM178B	ENSG00000162949	CAPN13	ENSG00000006118	TMEM132A
ENSG00000105523	FAM83E	ENSG00000135698	MPHOSPH6	ENSG00000140832	MARVELD3
ENSG00000069812	HES2	ENSG00000088836	SLC4A11	ENSG00000163993	S100P
ENSG00000177202	SPACA4	ENSG00000088726	TMEM40	ENSG00000184343	SRPK3
ENSG00000166268	MYRFL	ENSG00000128165	ADM2	ENSG00000170684	ZNF296
ENSG00000127249	ATP13A4	ENSG00000099994	SUSD2	ENSG00000223573	TINCR
ENSG00000137975	CLCA2	ENSG00000148377	IDI2	ENSG00000165202	OR1Q1
ENSG00000205502	C2CD4B	ENSG00000102387	TAF7L	ENSG00000171208	NETO2
ENSG00000120471	TP53AIP1	ENSG00000135480	KRT7	ENSG00000151117	TMEM86A
ENSG00000168389	MFSD2A	ENSG00000182308	DCAF4L1	ENSG00000140798	ABCC12
ENSG00000131019	ULBP3	ENSG00000103089	FA2H	ENSG00000160867	FGFR4

<b>ENSG</b>	<b>NAME</b>
ENSG0000063127	SLC6A16
ENSG00000184709	LRRC26
ENSG00000185863	TMEM210
ENSG00000086548	CEACAM6
ENSG00000148215	OR5C1
ENSG00000181649	PHLDA2
ENSG00000188959	C9orf152
ENSG00000135248	FAM71F1
ENSG00000248099	INSL3
ENSG00000106077	ABHD11
ENSG00000186193	SAPCD2
ENSG00000179057	IGSF22
ENSG00000181019	NQO1
ENSG00000105088	OLFM2
ENSG00000187566	NHLRC1
ENSG00000117009	KMO
ENSG00000197119	SLC25A29
ENSG00000100031	GGT1
ENSG00000157613	CREB3L1
ENSG00000188322	SBK1
ENSG00000161911	TREML1
ENSG00000111981	ULBP1
ENSG00000166866	MYO1A
ENSG00000104894	CD37
ENSG00000189030	VHLL
ENSG00000078804	TP53INP2
ENSG00000100290	BIK
ENSG00000151715	TMEM45B

<b>ENSG</b>	<b>NAME</b>
ENSG00000169583	CLIC3
ENSG00000182902	SLC25A18
ENSG00000131379	C3orf20
ENSG00000130783	CCDC62
ENSG00000149506	ZP1
ENSG00000110400	NECTIN1
ENSG00000230054	TEX53
ENSG00000116703	PDC
ENSG00000115339	GALNT3
ENSG00000118557	PMFBP1
ENSG00000160211	G6PD
ENSG00000212747	RTL8B
ENSG00000115884	SDC1
ENSG00000003249	DBNDD1
ENSG00000241484	ARHGAP8
ENSG00000103067	ESRP2
ENSG00000134909	ARHGAP32
ENSG00000198807	PAX9
ENSG00000146386	ABRACL
ENSG00000198753	PLXNB3
ENSG00000167800	TBX10
ENSG00000196639	HRH1
ENSG00000184635	ZNF93
ENSG00000135269	TES
ENSG00000198363	ASPH
ENSG00000197070	ARRDC1
ENSG00000130164	LDLR
ENSG00000197506	SLC28A3

<b>ENSG</b>	<b>NAME</b>
ENSG00000121270	ABCC11
ENSG00000135750	KCNK1
ENSG00000205426	KRT81
ENSG00000106789	CORO2A
ENSG00000181588	MEX3D
ENSG00000203485	INF2
ENSG00000253309	SERPINE3
ENSG00000198369	SPRED2
ENSG00000102554	KLF5
ENSG00000181016	LSMEM1
ENSG00000102996	MMP15
ENSG00000181090	EHMT1
ENSG00000171219	CDC42BPG
ENSG00000131037	EPS8L1
ENSG00000170537	TMC7
ENSG00000185674	LYG2
	PRR5-
ENSG00000248405	ARHGAP8
ENSG00000147689	FAM83A
ENSG00000111644	ACRBP
ENSG00000051620	HEBP2
ENSG00000261609	GAN
ENSG00000144214	LYG1
ENSG00000188050	RNF133
ENSG00000196781	TLE1
ENSG00000135245	HILPDA
ENSG00000139988	RDH12
ENSG00000172183	ISG20
ENSG00000188643	S100A16

<b>ENSG</b>	<b>NAME</b>
ENSG00000112599	GUCA1B
ENSG00000139318	DUSP6
ENSG00000178026	LRRC75B
ENSG00000069399	BCL3
ENSG00000272398	CD24
ENSG00000135643	KCNMB4
ENSG00000177025	C19orf18
ENSG00000125257	ABCC4
ENSG00000183421	RIPK4
ENSG00000124664	SPDEF
ENSG00000165555	NOXRED1
ENSG00000184828	ZBTB7C
ENSG00000156966	B3GNT7
ENSG00000168528	SERINC2
ENSG00000064547	LPAR2
ENSG00000099889	ARVCF
ENSG00000162639	HENMT1
ENSG00000258429	PDF
ENSG00000171786	NHLH1
ENSG00000196411	EPHB4
ENSG00000138074	SLC5A6
ENSG00000071564	TCF3
ENSG00000143061	IGSF3
ENSG00000164049	FBXW12
ENSG00000183762	KREMEN1
ENSG00000102984	ZNF821
ENSG00000196338	NLGN3
ENSG00000104881	PPP1R13L
ENSG00000197442	MAP3K5

<b>ENSG</b>	<b>NAME</b>
ENSG00000197496	SLC2A10
ENSG00000173261	PLAC8L1
ENSG00000240038	AMY2B
ENSG00000103460	TOX3
ENSG00000169758	TMEM266
ENSG00000145555	MYO10
ENSG00000143013	LMO4
ENSG00000102385	DRP2
ENSG00000130529	TRPM4
ENSG00000178409	BEND3
ENSG00000239264	TXNDC5
ENSG00000240849	PEDS1
ENSG00000172780	RAB43
ENSG00000136295	TTYH3
ENSG00000114315	HES1
ENSG00000106089	STX1A
ENSG00000176973	FAM89B
ENSG00000164638	SLC29A4
ENSG00000175567	UCP2
ENSG00000183963	SMTN
ENSG00000133422	MORC2
ENSG00000167508	MVD
ENSG00000198911	SREBF2
ENSG00000074416	MGLL
ENSG00000113758	DBN1
ENSG00000125895	TMEM74B
ENSG00000155714	PDZD9
ENSG00000143507	DUSP10
ENSG00000169925	BRD3

<b>ENSG</b>	<b>NAME</b>
ENSG00000149782	PLCB3
ENSG00000203950	RTL8A
ENSG00000134317	GRHL1
ENSG00000064270	ATP2C2
ENSG00000101255	TRIB3
ENSG00000106003	LFNG
ENSG00000184731	FAM110C
ENSG00000135540	NHSL1
ENSG00000146072	TNFRSF21
ENSG00000077044	DGKD
ENSG00000102898	NUTF2
ENSG00000075218	GTSE1
ENSG00000124766	SOX4
ENSG00000006432	MAP3K9
ENSG00000080845	DLGAP4
ENSG00000185340	GAS2L1
ENSG00000125247	TMTC4
ENSG00000100359	SGSM3
ENSG00000119772	DNMT3A
ENSG00000186187	ZNRF1
ENSG00000112242	E2F3
ENSG00000104866	PPP1R37
ENSG00000275183	LENG9
ENSG00000078237	TIGAR
ENSG00000118263	KLF7
ENSG00000168140	VASN
ENSG00000010818	HIVEP2
ENSG00000112787	FBRSL1
ENSG00000051128	HOMER3

<b>ENSG</b>	<b>NAME</b>
ENSG00000160190	SLC37A1
ENSG00000107130	NCS1
ENSG00000130881	LRP3
ENSG00000160439	RDH13
ENSG00000167535	CACNB3
ENSG00000131149	GSE1
ENSG00000112655	PTK7
ENSG00000173457	PPP1R14B
ENSG00000143995	MEIS1
ENSG00000100266	PACSIN2
ENSG00000204569	PPP1R10
ENSG00000140374	ETFA
ENSG00000188486	H2AX
ENSG00000184545	DUSP8
ENSG00000126214	KLC1
ENSG00000254986	DPP3
ENSG00000126458	RRAS
ENSG00000165389	SPTSSA
ENSG00000167470	MIDN
ENSG00000146904	EPHA1
ENSG00000139722	VPS37B
ENSG00000160883	HK3
ENSG00000175274	TP53I11
ENSG00000148396	SEC16A
ENSG00000165724	ZMYND19
ENSG00000196526	AFAP1
ENSG00000136830	NIBAN2
ENSG00000106799	TGFBR1
ENSG00000187678	SPRY4

<b>ENSG</b>	<b>NAME</b>
ENSG00000149418	ST14
ENSG00000196576	PLXNB2
ENSG00000196123	KIAA0895L
ENSG00000147144	CCDC120
ENSG00000011422	PLAUR
ENSG00000177169	ULK1
ENSG00000125772	GPCPD1
ENSG00000109625	CPZ
ENSG00000215529	EFCAB8
ENSG00000189306	RRP7A
ENSG00000119514	GALNT12
ENSG00000139832	RAB20
ENSG00000103248	MTHFSD
ENSG00000165684	SNAPC4
ENSG00000277443	MARCKS
ENSG00000110047	EHD1
ENSG00000146410	MTFR2
ENSG00000131165	CHMP1A
ENSG00000147166	ITGB1BP2
ENSG00000100403	ZC3H7B
ENSG00000133818	RRAS2
ENSG00000102390	PBDC1
ENSG00000135723	FHOD1
ENSG00000133275	CSNK1G2
ENSG00000130669	PAK4
ENSG00000114423	CBLB
ENSG00000205078	SYCE1L
ENSG00000095383	TBC1D2
ENSG00000103005	USB1

<b>ENSG</b>	<b>NAME</b>
ENSG00000198792	TMEM184B
ENSG00000254440	PBOV1
ENSG00000151883	PARP8
ENSG00000167523	SPATA33
ENSG00000102349	KLF8
ENSG00000140848	CPNE2
ENSG00000102871	TRADD
ENSG00000131061	ZNF341
ENSG00000092820	EZR
ENSG00000081803	CADPS2
ENSG00000188290	HES4
ENSG00000100075	SLC25A1
ENSG00000134590	RTL8C
ENSG00000093010	COMT
ENSG00000005238	FAM214B
ENSG00000257923	CUX1
ENSG00000238227	TMEM250
ENSG00000160796	NBEAL2
ENSG00000160325	CACFD1
ENSG00000125753	VASP
ENSG00000178386	ZNF223
ENSG00000125834	STK35
ENSG00000167657	DAPK3
ENSG00000163872	YEATS2
ENSG00000097007	ABL1
ENSG00000102804	TSC22D1
ENSG00000175220	ARHGAP1
ENSG00000159840	ZYX
ENSG00000075240	GRAMD4

<b>ENSG</b>	<b>NAME</b>
ENSG00000173153	ESRRA
ENSG00000099956	SMARCB1
ENSG00000197081	IGF2R
ENSG00000130787	HIP1R
ENSG00000110697	PITPNM1
ENSG00000072274	TFRC
ENSG00000041982	TNC
ENSG00000188818	ZDHHC11
ENSG00000185467	KPNA7
ENSG00000188566	NDOR1
ENSG00000162645	GBP2
ENSG00000182218	HHIPL1
ENSG00000034510	TMSB10
ENSG00000112137	PHACTR1
ENSG00000100401	RANGAP1
ENSG00000015475	BID
ENSG00000159399	HK2
ENSG00000070010	UFD1
ENSG00000006459	KDM7A
ENSG00000072401	UBE2D1
ENSG00000119682	AREL1
ENSG00000141959	PFKL
ENSG00000103042	SLC38A7
ENSG00000089639	GMIP
ENSG00000145979	TBC1D7
ENSG00000176619	LMNB2
ENSG00000114554	PLXNA1
ENSG00000106348	IMPDH1

<b>ENSG</b>	<b>NAME</b>
ENSG00000160305	DIP2A
ENSG00000095951	HIVEP1
ENSG00000183255	PTTG1P
ENSG00000008083	JARID2
ENSG00000170340	B3GNT2
ENSG00000128298	BAIAP2L2
ENSG00000067955	CBFB
ENSG00000160877	NACC1
ENSG00000103335	PIEZO1
ENSG00000089159	PXN
ENSG00000271303	SRXN1
ENSG00000167173	C15orf39
ENSG00000158470	B4GALT5
ENSG00000160271	RALGDS RP11-
ENSG00000241962	111H13.1
ENSG00000173214	MFSD4B
ENSG00000198373	WWP2
ENSG00000074181	NOTCH3
ENSG00000167378	IRGQ
ENSG00000197136	PCNX3
ENSG00000106683	LIMK1
ENSG00000136378	ADAMTS7
ENSG00000104142	VPS18
ENSG00000160310	PRMT2
ENSG00000137094	DNAJB5
ENSG00000278662	GOLGA6L10
ENSG00000164047	CAMP
ENSG00000105281	SLC1A5

<b>ENSG</b>	<b>NAME</b>
ENSG00000099814	CEP170B
ENSG00000065457	ADAT1
ENSG00000088038	CNOT3
ENSG00000137166	FOXP4
ENSG00000090372	STRN4
ENSG00000119139	TJP2
ENSG00000160285	LSS
ENSG00000130347	RTN4IP1
ENSG00000184792	OSBP2
ENSG00000100156	SLC16A8
ENSG00000101294	HM13
ENSG00000123130	ACOT9
ENSG00000135048	CEMIP2
ENSG00000205336	ADGRG1
ENSG00000164054	SHISA5
ENSG00000130706	ADRM1
ENSG00000103111	MON1B
ENSG00000203883	SOX18
ENSG00000186716	BCR
ENSG00000129566	TEP1
ENSG00000141985	SH3GL1
ENSG00000118960	HS1BP3
ENSG00000198752	CDC42BPB
ENSG00000171443	ZNF524
ENSG00000139209	SLC38A4
ENSG00000196588	MRTFA
ENSG00000116871	MAP7D1
ENSG00000146535	GNA12

<b>ENSG</b>	<b>NAME</b>
ENSG00000157593	SLC35B2
ENSG00000152558	TMEM123
ENSG00000105063	PPP6R1
ENSG00000175463	TBC1D10C
ENSG00000163812	ZDHHC3
ENSG00000188157	AGRN
ENSG00000134882	UBAC2
ENSG00000139793	MBNL2
ENSG00000187605	TET3
ENSG00000050820	BCAR1
ENSG00000119408	NEK6
ENSG00000172757	CFL1
ENSG00000242802	AP5Z1
ENSG00000159720	ATP6V0D1
ENSG00000138835	RGS3
ENSG00000149743	TRPT1
ENSG00000205250	E2F4
ENSG00000101084	RAB5IF
ENSG00000103035	PSMD7
ENSG00000142208	AKT1
ENSG00000103043	VAC14
ENSG00000179820	MYADM
ENSG00000135587	SMPD2
ENSG00000142409	ZNF787
ENSG00000160218	TRAPPC10
ENSG00000167491	GATAD2A
ENSG00000148334	PTGES2
ENSG00000107438	PDLIM1
ENSG00000182154	MRPL41

<b>ENSG</b>	<b>NAME</b>
ENSG00000215193	PEX26
ENSG00000136026	CKAP4
ENSG00000174177	CTU2
ENSG00000124788	ATXN1
ENSG00000123989	CHPF
ENSG00000163170	BOLA3
ENSG00000135636	DYSF
ENSG00000007866	TEAD3
ENSG00000132970	WASF3
ENSG00000115216	NRBP1
ENSG00000198113	TOR4A
ENSG00000104853	CLPTM1
ENSG00000188986	NELFB
ENSG00000198324	PHETA1
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ENSG00000126262	FFAR2
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ENSG00000214160	ALG3
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ENSG00000185825	BCAP31
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ENSG00000196865	NHLRC2
ENSG00000075624	ACTB
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ENSG00000168778	TCTN2
ENSG00000204172	AGAP9
ENSG00000086589	RBM22

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ENSG00000081791	DELE1
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ENSG00000157343	ARMC12
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ENSG00000185875	THNSL1
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ENSG00000122008	POLK
ENSG00000132570	PCBD2
ENSG00000101773	RBBP8
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ENSG00000204219	TCEA3
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ENSG00000197776	KLHDC1
ENSG00000131437	KIF3A

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ENSG00000184271	POU6F1
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ENSG00000141642	ELAC1
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ENSG00000142082	SIRT3
ENSG00000113108	APBB3
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ENSG00000237190	CDKN2AIPNL
ENSG00000164615	CAMLG
ENSG00000144893	MED12L
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ENSG00000196632	WNK3
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ENSG00000104205	SGK3
ENSG00000059588	TARBP1
ENSG00000170099	SERPINA6
ENSG00000154309	DISP1
ENSG00000163749	CCDC158
ENSG00000131507	NDFIP1
ENSG00000144040	SFXN5
ENSG00000174885	NLRP6
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ENSG00000118276	B4GALT6
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ENSG00000043143	JADE2
ENSG00000121753	ADGRB2

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ENSG00000168765	GSTM4
ENSG00000158062	UBXN11
ENSG00000120915	EPHX2
ENSG00000063854	HAGH
ENSG00000258818	RNASE4
ENSG00000169313	P2RY12
ENSG00000176723	ZNF843
ENSG00000167972	ABCA3
ENSG00000109758	HGFAC
ENSG00000187240	DYNC2H1
ENSG00000049769	PPP1R3F
ENSG00000111666	CHPT1
ENSG00000285868	CTB-109A12.2
ENSG00000150593	PDCD4
ENSG00000152086	TUBA3E
ENSG00000134352	IL6ST
ENSG00000112874	NUDT12
ENSG00000036448	MYOM2
ENSG00000145743	FBXL17
ENSG00000070081	NUCB2
ENSG00000171160	MORN4
ENSG00000155850	SLC26A2
ENSG00000173258	ZNF483
ENSG00000171174	RBKS

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ENSG00000103540	CCP110
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ENSG00000144649	GASK1A
ENSG00000105707	HPN
ENSG00000159307	SCUBE1
ENSG00000196177	ACADSB
ENSG00000157303	SUSD3
ENSG00000145882	PCYOX1L
ENSG00000150627	WDR17
ENSG00000164241	C5orf63
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ENSG00000137821	LRRC49
ENSG00000171385	KCND3
ENSG00000239887	C1orf226
ENSG00000241935	HOGA1
ENSG00000055163	CYFIP2
ENSG00000010438	PRSS3
ENSG00000125510	OPRL1
ENSG00000180999	C1orf105
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ENSG00000063180	CA11
ENSG00000162104	ADCY9

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ENSG00000145375	SPATA5
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ENSG00000136059	VILL
ENSG00000183066	WBP2NL
ENSG00000163491	NEK10
ENSG00000140443	IGF1R
ENSG00000132563	REEP2
ENSG00000159374	M1AP
ENSG00000269190	FBXO17
ENSG00000143375	CGN
ENSG00000158813	EDA
ENSG00000204116	CHIC1
ENSG00000102043	MTMR8
ENSG00000179902	C1orf194
ENSG00000159445	THEM4
ENSG00000120729	MYOT
ENSG00000244274	DBNDD2
ENSG00000167371	PRRT2
ENSG00000164742	ADCY1
ENSG00000128596	CCDC136
ENSG00000206181	ELOA2
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ENSG00000088543	C3orf18
ENSG00000135423	GLS2

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ENSG00000285043	2515O10.6
ENSG00000149050	ZNF214
ENSG00000163040	CCDC74A
ENSG00000082175	PGR
ENSG00000159208	CIART
ENSG00000115112	TFCP2L1
ENSG00000151892	GFRA1
ENSG00000171791	BCL2
ENSG00000185739	SRL
ENSG00000116031	CD207
ENSG00000168329	CX3CR1
ENSG00000165953	SERPINA12
ENSG00000160460	SPTBN4
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ENSG00000133256	PDE6B
ENSG00000196372	ASB13
ENSG00000267385	CTB-50L17.14
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ENSG00000164128	NPY1R
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ENSG00000066468	FGFR2

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ENSG00000113739	STC2
ENSG00000206013	IFITM5
ENSG00000175356	SCUBE2
ENSG00000149927	DOC2A
ENSG00000091831	ESR1

Supplementary Table 3: ERBB2 mutations in the RNAseq samples

patient	cluster-nr	Consequence.HGVSp	mutType	AA-Change	domain
p1	3	ENSP00000269571.4:p.D110E	SNV	D110E	ex
p2	3	ENSP00000269571.4:p.R190W	SNV	R190W	ex
p3	3	ENSP00000269571.4:p.D277Y	SNV	D277Y	ex
p4	3	ENSP00000269571.4:p.S310F	SNV	S310F	ex
p5	3	ENSP00000269571.4:p.S310F	SNV	S310F	ex
p6	1	ENSP00000269571.4:p.R678Q	SNV	R678Q	ex
p7	1	ENSP00000269571.4:p.L755S	SNV	L755S	TK
p8	3	ENSP00000269571.4:p.L755S	SNV	L755S	TK
p9	3	ENSP00000269571.4:p.V777L	SNV	V777L	TK
p10	3	ENSP00000269571.4:p.V777L	SNV	V777L	TK
p11	3	ENSP00000269571.4:p.-780_-781insGSP	InDel	780_- 781insGSP	TK
p12	3	ENSP00000269571.4:p.I788F	SNV	I788F	TK
p13	3	ENSP00000269571.4:p.E876K	SNV	E876K	TK
p14	3	ENSP00000269571.4:p.M955I	SNV	M955I	TK
p15	3	ENSP00000269571.4:p.P983S	SNV	P983S	TK
p16	3	ENSP00000269571.4:p.E717D, ENSP00000269571.4:p.L755S	SNV	E717D, L755S	Ex/TK
p17	3	ENSP00000269571.4:p.L755S, ENSP00000269571.4:p.T862A	SNV	L755S, T862A	TK
p18	3	ENSP00000269571.4:p.D769Y, ENSP00000269571.4:p.E1114K	SNV	D769Y, E1114K	TK

*ex: extracellular, TK: Tyrosine Kinase*

Supplementary Table 4: IPA-Upstream Regulators using genes Suppl. Table 1

<b>Upstream Regulator</b>	<b>Molecule Type</b>	<b>Predicted Activation State</b>	<b>Activation z-score</b>	<b>p-value of overlap</b>	<b>Target Molecules in Dataset</b>
ERBB2	kinase	Activated	2.339	2.65E-05	ABCG2,ABL1,ABRACL,ACTB,AKT1,ATF4,BCL2,BCL3,CDC23,CDC42BPG,CEBPB,CX3CR1,DOK1,DUSP6,E2F3,EPHX2,ESR1,FFAR2,GALNT3,HES1,HES2,HGSNAT,HM13,IGF1R,IGF2R,IL6ST,ITGB6,KRT7,KRT81,LAD1,LMO4,LPAR2,LSS,MUCL1,MYCN,MYO10,NAGPA,NOTCH3,NPY1R,NRBP1,NUCB2,OPRL1,P2RY12,P2RY13,PDCD4,PHLDA2,PLAUR,POLK,POLR3GL,PRSS3,PTTG1IP,RETREG1,S100P,SDC1,SLC22A5,SMTN,SOX4,SPDEF,SYCP3,TGFBR1,TMEM132A,TNC,TSC22D1
RAF1	kinase	Activated	2.931	9.57E-05	BCL2,CD37,CDC42EP1,CTSL,DUSP4,DUSP6,ESR1,HNRNPAB,IGF1R,LAD1,MGLL,NQO1,PHLDA2,PLAUR,PPP1R10,PRSS3,SDC1,SLC26A2,TSC22D1,TUBB2A
ERG	transcription regulator	Activated	2.138	0.000156	ABCC4,ADGRG1,ARMC12,BCR,CDC42BPB,COLGALT1,DBN1,DIP2A,IGF1R,MAGI1,MAP3K5,MYCN,MYO10,PLAUR,PXN,RGS3,RRAS,SOX4,SREBF2,WASF3
NRG1	growth factor	Activated	2.154	0.000701	ARPC4,ATF1,ATF4,BCL2,BDNF,CDC42EP1,DUSP4,DUSP6,HES1,HK2,INSL3,LMO4,MARCKS,MGLL,MNX1,PDCD4,PGR,PLAUR,PXN,SOX4,TGFR1
EGF	growth factor	Activated	2.563	0.000944	ABCG2,AKT1,B4GALT5,BCL2,CCL17,CDC42EP1,CEBPB,DGKD,DNMT3B,DUSP4,DUSP6,E2F3,ESR1,EZR,FAM89B,HES1,IGF1R,INSL3,MAP3K5,MNX1,MYCN,PDCD4,PGR,PHLDA2,PIK3R1,PLAUR,S100A9,SDC1,SLC37A1,SOX4,SPRY4,ST3GAL3,SYCP3,TFCP2L1,TNC,TRH,TUBB3,ULK1,VASP
TP73	transcription regulator	Activated	2.231	0.000953	AFAP1,ARVCF,BCAR1,BCL2,BID,CAMLG,DMTF1,EDA,FGFR2,G6PD,GLS2,GRAMD4,GTSE1,HAGH,HES1,HIVEP1,IGF1R,IGSF3,KCNK1,KLF5,LIMK1,MGMT,MYCN,NOTCH3,SHISA5,SPTBN4,TFCP2L1,TP53AIP1,TP53I11,UBE2D1,ULK1,WNK3