

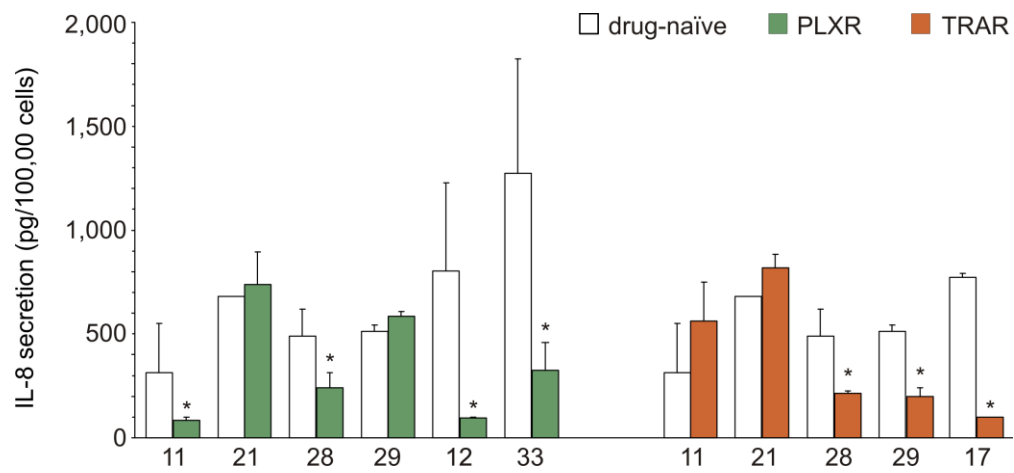


Figure S1. IL-8 levels in the culture media were assessed after 24 hours by using ELISA. Bars represent mean values of 3 biological replicates $\pm$ SD, except for 12_PLXR cells (n=2). Differences are considered significant at * $p < 0.05$.

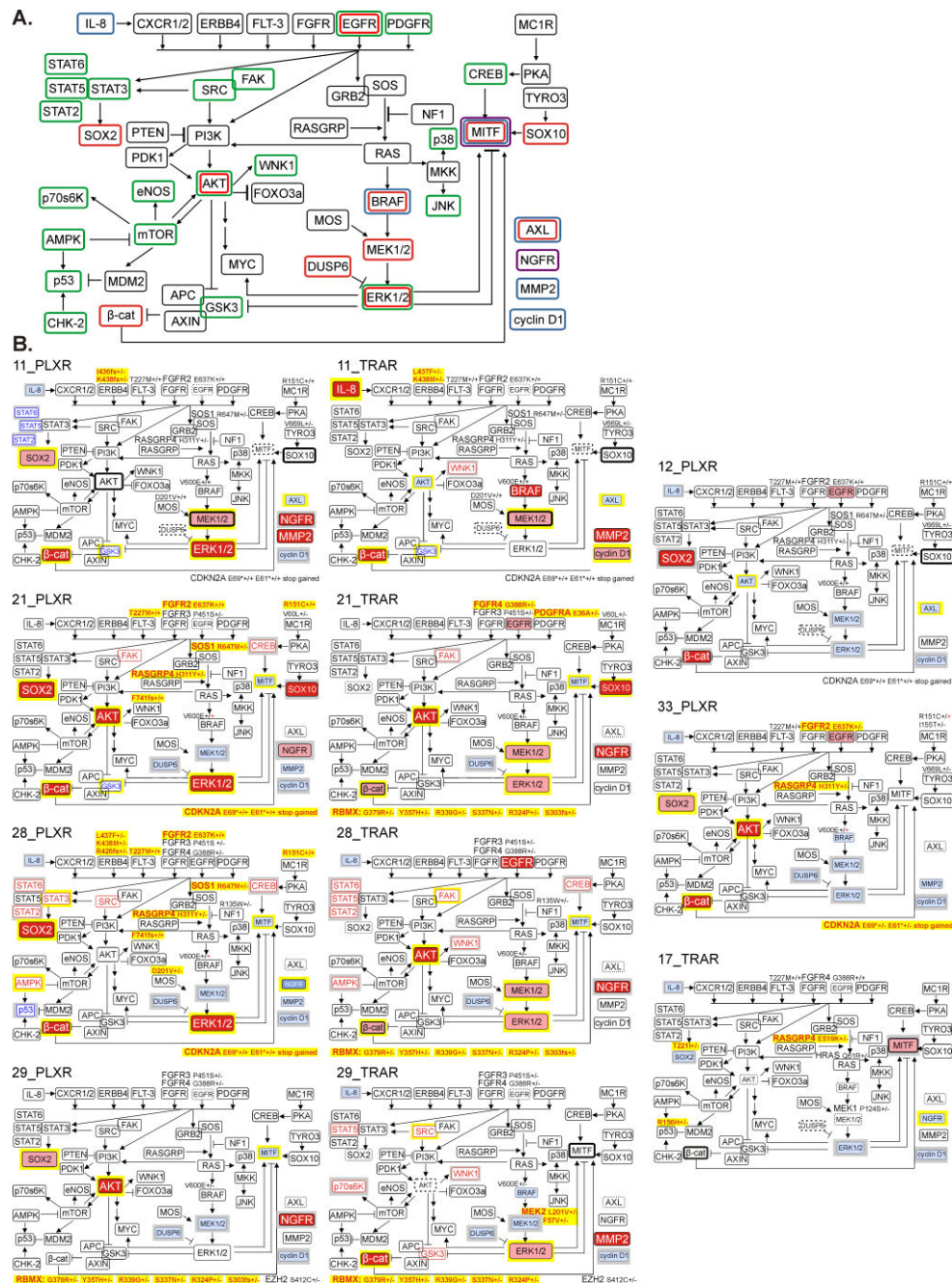


Figure S2. Diverse patterns of resistance showing patient- and drug-specific differences between drug-naïve and drug-resistant melanoma cells. **(A)** Schematic overview of signaling pathways investigated in this study with indicated method of data acquisition. Green frame, phospho-profiling; red frame, Western blotting; blue frame, qRT-PCR; violet frame, flow cytometry; black frame, not analyzed for expression or activity. In addition, all genes encoding proteins shown in the scheme were checked for the potential mutations. **(B)** Color coded overview comparing all tested cell lines in terms of differences between drug-naïve and drug-resistant cells (enlarged panels are shown in Figure 7 for selected cell lines). Red/pink, strong/weak enhancement; blue, inhibition; red/blue frame and font, enhancement/inhibition shown only in phospho-profiling; dotted frame smaller in size, weak level/activity in drug-naïve cells; bold frame, high level/activity in drug-naïve cells; mutations acquired by resistant cells are marked in red, and those already present in drug-naïve cells are marked in black. Changes, which were already induced during immediate response to drugs are in the grey background, whereas changes unique for resistant cells (including mutations) are in the yellow background.

Table S1. Mutation status of genes associated with the regulation of signaling pathways, including MAPK, PI3K/AKT and cell cycle based on the KEGG PATHWAY databases, as well as receptors and transcription factors involved in the execution of cell programs essential for melanoma progression and response to drugs. References for mutations previously implicated in resistance to MAPK inhibition are indicated in upper indices. Only non-synonymous mutations and indels are included, and shown for drug-naïve (DN), vemurafenib-resistant (PLXR) and trametinib-resistant (TRAR) cell lines. Mutations are marked as homozygous (+/+) or heterozygous (+/-). Prediction of functional effects of amino acid substitutions were assessed by using Polyphen-2 software, and were classified as benign (scores 0.000-0.449), possibly damaging (scores 0.450-0.959) and probably damaging (scores 0.960-1.000). Name of protein is given in the brackets if it differs from gene name. R, resistant cells.

gene		11_PLXR	21_PLXR	28_PLXR	29_PLXR	12_PLXR	33_PLXR
<i>ABL1</i>							
<i>ACTG1</i>							
<i>AK1</i> ¹							
<i>AKT1</i> ²							
<i>AKT2</i> ³							
<i>AKT3</i> ²							
<i>ALK</i>	DN	I1461V +/+ benign 0.000		I1461V +/+ benign 0.000	I1461V +/+ benign 0.000	I1461V +/+ benign 0.000	I1461V +/- benign 0.000
	R		I1461V +/+ benign 0.000				I1461V +/+ benign 0.000
<i>AMER1</i>							
<i>ANKRD11</i> ¹	DN		D2376E +/+ benign 0.010	D2376E +/+ benign 0.010	D2376E +/+ benign 0.010		D2376E +/+ benign 0.010
	R						
<i>APC</i>	DN		V1822D +/- benign 0.000	V1822D +/- benign 0.000	V1822D +/- benign 0.000		V1822D +/- benign 0.000
	R						
<i>ARAF</i>							
<i>ARF1</i>							
<i>ARID1A</i> ¹							
<i>ARID1B</i> ¹	DN		Y1427* +/- stop gained			Y1427* +/- stop gained	Y1427* +/- stop gained
	R						
<i>ARID2</i> ⁴							
<i>ARID4A</i> ¹	DN	N724S +/+ benign 0.003		N724S +/+ benign 0.003		N724S +/+ benign 0.003	
	R		N724S +/+ benign 0.003				N724S +/+ benign 0.003
	DN	T779A +/+ benign 0.000		T779A +/+ benign 0.000		T779A +/+ benign 0.000	T779A +/- benign 0.000
	R		T779A +/+ benign 0.000				T779A +/+ benign 0.000
<i>ARID4B</i> ¹							

<i>ARID5B</i> ¹							
<i>ASXL1</i>	DN	G704R +/- probably damaging .986				G704R +/- probably damaging 0.986	
	R		G704R +/- probably damaging 0.986	G704R +/- probably damaging 0.986			G704R +/- probably damaging 0.986
	DN	L815P +/- benign 0.000	L815P +/- benign 0.000	L815P +/- benign 0.000	L815P +/- benign 0.000	L815P +/- benign 0.000	L815P +/- benign 0.000
	R						
<i>ASXL2</i> ¹							
<i>ATM</i>	DN	N1938S +/- benign 0.000	N1938S +/- benign 0.000	N1938S +/- benign 0.000	N1938S +/- benign 0.000	N1938S +/- benign 0.000	N1938S +/- benign 0.000
	R						
<i>ATR</i> ^{1,4}	DN	R2425Q +/- benign 0.000				R2425Q +/- benign 0.000	
	R		R2425Q +/- benign 0.000	R2425Q +/- benign 0.000			R2425Q +/- benign 0.000
	DN	M211T +/- benign 0.000	M211T +/- benign 0.000	M211T +/- benign 0.000	M211T +/- benign 0.000	M211T +/- benign 0.000	M211T +/- benign 0.000
	R		M211T +/- benign 0.000	M211T +/- benign 0.000			
	DN	N1668fs +/- frameshift variant					
	R			N1668fs +/- frameshift variant			
<i>ATRX</i> ¹							
<i>ATXN2</i> ¹	DN	Q188 +/- disruptive inframe deletion	Q188 +/- disruptive inframe deletion	Q188 +/- disruptive inframe deletion	Q188 +/- disruptive inframe deletion	Q188 +/- disruptive inframe deletion	Q188 +/- disruptive inframe deletion
	R						
	DN	L107V +/- benign 0.000	L107V +/- benign 0.000	L107V +/- benign 0.000	L107V +/- benign 0.000	L107V +/- benign 0.000	L107V +/- benign 0.000
	R		L107V +/- benign 0.000	L107V +/- benign 0.000			
<i>AXIN1</i>							
<i>AXIN2</i>	DN	P50S +/- benign 0.000		P50S +/- benign 0.000	P50S +/- benign 0.000	P50S +/- benign 0.000	P50S +/- benign 0.000
	R						
<i>AXL</i>	DN	N266D +/- benign 0.000	N266D +/- benign 0.000	N266D +/- benign 0.000	N266D +/- benign 0.000	N266D +/- benign 0.000	N266D +/- benign 0.000
	R						
<i>B2M</i> ¹							
<i>BACH2</i>							
<i>BAP1</i>							
<i>BCL2L11</i> (BIM) ¹							
<i>BCL10</i> ¹							
<i>BCL11B</i>	DN	V690M +/- benign 0.082					
	R		V690M +/-	V690M +/-		V690M +/-	V690M +/-

			benign 0.082	benign 0.082		benign 0.082	benign 0.082
<i>BCOR</i>							
<i>BCORL1</i> ¹	DN	F111L +/- benign 0.000	F111L +/- benign 0.000	F111L +/- benign 0.000	F111L +/- benign 0.000	F111L +/- benign 0.000	F111L +/- benign 0.000
	R						
<i>BLM</i> ¹							
<i>BMPR1A</i> ¹	DN						P2T +/- benign 0.000
	R						
<i>BOP1</i>							
<i>BRAF</i> ^{2, 5, 6}	DN	V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971
	R		V600E +/- probably damaging 0.971	V600E +/- probably damaging 0.971			V600E +/- probably damaging 0.971
<i>BRCA1</i> ¹	DN	S1634G +/- benign 0.002				S1634G +/- benign 0.002	S1634G +/- benign 0.002
	R		S1634G +/- benign 0.002	S1634G +/- benign 0.002			
	DN	K1183R +/- benign 0.000				K1183R +/- benign 0.000	K1183R +/- benign 0.000
	R		K1183R +/- benign 0.000	K1183R +/- benign 0.000			
	DN	E1038G +/- benign 0.012				E1038G +/- benign 0.012	E1038G +/- benign 0.012
	R		E1038G +/- benign 0.012	E1038G +/- benign 0.012			
	DN	P871L +/- benign 0.000				P871L +/- benign 0.000	P871L +/- benign 0.000
	R		P871L +/- benign 0.000	P871L +/- benign 0.000			
<i>BRCA2</i>	DN	V2466A +/- benign 0.000	V2466A +/- benign 0.000	V2466A +/- benign 0.000	V2466A +/- benign 0.000	V2466A +/- benign 0.000	V2466A +/- benign 0.000
	R						
	DN		T1915M +/- benign 0.000	T1915M +/- benign 0.000	T1915M +/- benign 0.000		T1915M +/- benign 0.000
	R				T1915M +/- benign 0.000		
<i>BRIP1</i> ¹	DN	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000
	R		S919P +/- benign 0.000				S919P +/- benign 0.000
<i>CALR</i> ¹							
<i>CARD11</i>							
<i>CBL</i>							
<i>CCNA1</i> (cyclin A1)							
<i>CCNA2</i> (cyclin A2)	DN	I163V +/-	I163V +/-	I163V +/-	I163V +/-	I163V +/-	I163V +/-

[illegible]

	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000	l471V +/- benign 0.000
CHEK2 (Chk-2)							
CIC ¹							
CIITA	DN	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000
	R						
	DN	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001
	R						
	DN		G501A +/- benign 0.001	G501A +/- benign 0.001	G501A +/- benign 0.001		
	R						
CRBN							
CREB							
CREBBP ¹	DN	V1650G +/- benign 0.183					
	R						
CRLF2							
CTCF ⁴							
CTLA4	DN		T17A +/- benign 0.015	T17A +/- benign 0.015	T17A +/- benign 0.015		
	R						T17A +/- benign 0.015
CTNNB1 (β-catenin)							
CTR9	DN						
	R		S477* +/- stop gained			S477* +/- stop gained	S477* +/- stop gained
CUX1 ¹	DN						
	R	A448T +/- benign 0.127	A448T +/- benign 0.127	A448T +/- benign 0.127	A448T +/- benign 0.127	A448T +/- benign 0.127	A448T +/- benign 0.127
CXCL8 (IL-8)							
CXCR1							
CXCR2							
DAXX ¹							
DDX3X ¹							
DDX53	DN	M381I +/- probably damaging 1.000	M381I +/- probably damaging 1.000			M381I +/- probably damaging 1.000	
	R		M381I +/- probably damaging 1.000	M381I +/- probably damaging 1.000			M381I +/- probably damaging 1.000
	DN	R391M +/- benign 0.000	R391M +/- benign 0.000			R391M +/- benign 0.000	
	R		R391M +/-	R391M +/-			R391M +/-

			benign 0.000	benign 0.000			benign 0.000
DEK	DN		S681P +/-		S681P +/-		S681P +/-
	R		benign 0.000		benign 0.000		benign 0.000
DICER1 ^{1,4}							
DNMT3A							
DUSP1 (MKP1)							
DUSP4 (MKP2) ⁸							
DUSP6 (MKP3)	DN	V114L +/-	V114L +/-	V114L +/-	V114L +/-	V114L +/-	
	R	benign 0.075	benign 0.075	benign 0.075	benign 0.075	benign 0.075	V114L +/-
	DN						S144A +/-
	R						benign 0.000
DUSP7 (MKPX)							
DUSP10 (MKP5)							
DUSP14 (MKP6)							
DUSP16 (MKP7)	DN						
	R	V366M +/-	V366M +/-	V366M +/-		V366M +/-	V366M +/-
		benign 0.005	benign 0.005	benign 0.005		benign 0.005	benign 0.005
DUSP22							
E2F1							
E2F3	DN	D148N +/-				D148N +/-	
	R	possibly damaging 0.915 D389N +/- benign 0.017	D148N +/- possibly damaging 0.915	D389N +/- benign 0.017		possibly damaging 0.915 D389N +/- benign 0.017	
ECT2L	DN	K676fs +/-				K676fs +/-	
	R	frameshift variant	K676fs +/- frameshift variant	K676fs +/- frameshift variant		frameshift variant	K676fs +/- frameshift variant
EED							
EIF1AX ¹							
ELF3							
ELK1							
EGFR	DN	R521K +/-	R521K +/-	R521K +/-	R521K +/-	R521K +/-	
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000	R521K +/- benign 0.000
EP300 ¹	DN	I997V +/-				I997V +/-	
	R	benign 0.000	I997V +/- benign 0.000	I997V +/- benign 0.000		benign 0.000	I997V +/- benign 0.000
	DN	Q2223P +/-				Q2223P +/-	
	R	benign 0.000	Q2223P +/- benign 0.000	Q2223P +/- benign 0.000		benign 0.000	Q2223P +/- benign 0.000

	DN				N2209 +/- disruptive inframe deletion		
	R						
EP400 ¹	DN		A574V +/- possibly damaging 0.854	A574V +/- possibly damaging 0.854	A574V +/- possibly damaging 0.854		
	R						
	DN		A3094T +/- benign 0.001	A3094T +/- benign 0.001	A3094T +/- benign 0.001		
	R						
	DN		Q2742 +/- disruptive inframe insertion	Q2742 +/- disruptive inframe insertion	Q2742 +/- disruptive inframe insertion		
	R						
EPHA3 ¹	DN						
	R	W924R +/- benign 0.000	W924R +/- benign 0.000	W924R +/- benign 0.000	W924R +/- benign 0.000	W924R +/- benign 0.000	W924R +/- benign 0.000
EPHA7 ¹							
EPHB1 ¹							
ERBB2	DN		P8T +/- benign 0.000	P8T +/- benign 0.000	P8T +/- benign 0.000		
	R						
	DN	P1170A +/- possibly damaging 0.953	P1170A +/- possibly damaging 0.953	P1170A +/- possibly damaging 0.953	P1170A +/- possibly damaging 0.953	P1170A +/- possibly damaging 0.953	P1170A +/- possibly damaging 0.953
	R						
ERBB3	DN						P30L +/- benign 0.007
	R						
ERBB4	DN						
	R	I436fs +/- frameshift variant K438fs +/- frameshift variant		L437F +/- possibly damaging 0.928 K438M +/- possibly damaging 0.894 R426 +/- disruptive inframe insertion			
ERCC2	DN		D312N +/- benign 0.065	D312N +/- benign 0.065	D312N +/- benign 0.065		D312N +/- benign 0.065
	R	D312N +/- benign 0.065					
	DN		K751Q +/- benign 0.000	K751Q +/- benign 0.000	K751Q +/- benign 0.000		K751Q +/- benign 0.000
	R						
ERF							
ERRFI1							
ESCO2 ¹							
ETS2 ³	DN	A19T +/- ?				A19T +/- ?	
	R						

ETV6							
EZH2	DN				S412C +/- probably damaging 1.000		
	R						
FAM58A ¹	DN	A18G +/- frameshift variant	A18G +/- frameshift variant	A18G +/- frameshift variant		A18G +/- frameshift variant	A18G +/- frameshift variant
	R						
	DN	A6G +/- frameshift variant		A6G +/- frameshift variant			A6G +/- frameshift variant
	R				A6G +/- frameshift variant		
FANCA ¹	DN	T266A +/- benign 0.000				T266A +/- benign 0.000	T266A +/- benign 0.000
	R		T266A +/- benign 0.000	T266A +/- benign 0.000			
FANCD2 ¹	DN	N405S +/- benign 0.022	N405S +/- benign 0.022	N405S +/- benign 0.022	N405S +/- benign 0.022	N405S +/- benign 0.022	
	R						N405S +/- benign 0.022
FAS ¹							
FAT1 ¹	DN	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000
	R						
	DN	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000
	R						
	DN	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000
	R						R1064G +/- benign 0.000
	DN	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000
	R						V862L +/- benign 0.000
	DN	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000
	R						F614L +/- benign 0.000
	DN	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032
	R						S404R +/- benign 0.032
	DN	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009
	R						V482I +/- benign 0.009
	DN	H1273R +/-				H1273R +/-	H1273R +/-

		benign 0.000				benign 0.000	benign 0.000
	R		H1273R +/- benign 0.000	H1273R +/- benign 0.000			H1273R +/- benign 0.000
<i>FBXO11</i>							
<i>FBXW7</i> ¹	DN	V418M +/- possibly damaging 0.801	V418M +/- possibly damaging 0.801	V418M +/- possibly damaging 0.801		V418M +/- possibly damaging 0.801	V418M +/- possibly damaging 0.801
	R						
<i>FGFR1</i>							
<i>FGFR2</i>	DN	E637K +/- probably damaging 0.970	E637K +/- probably damaging 0.970	E637K +/- probably damaging 0.970		E637K +/- probably damaging 0.970	E637K +/- probably damaging 0.970
	R						
<i>FGFR3</i>	DN		P451S +/- possibly damaging 0.902	P451S +/- possibly damaging 0.902	P451S +/- possibly damaging 0.902		
	R						
<i>FGFR4</i>	DN	V10I +/- benign 0.000	V10I +/- benign 0.000	V10I +/- benign 0.000		V10I +/- benign 0.000	V10I +/- benign 0.000
	R						
	DN	P136L +/- benign 0.000	P136L +/- benign 0.000	P136L +/- benign 0.000 G388R +/- probably damaging 0.998	P136L +/- benign 0.000 G388R +/- probably damaging 0.998	P136L +/- benign 0.000	P136L +/- benign 0.000
	R						
<i>FH</i>							
<i>FLT3</i>	DN	T227M +/- probably damaging 0.999	T227M +/- probably damaging 0.999	T227M +/- probably damaging 0.999		T227M +/- probably damaging 0.999	T227M +/- probably damaging 0.999
	R						
<i>FOXA1</i>							
<i>FOXM1</i>	DN						
	R				S681P +/- benign 0.000		
<i>FOXO3A</i>							
<i>FOXP1</i> ¹							
<i>GADD45A</i>							
<i>GADD45B</i>							
<i>GADD45G</i>							
<i>GNA11</i>							
<i>GNAS</i> ^{1, 4}	DN					P459R +/- benign 0.005	
	R		P459R +/- benign 0.005	P459R +/- benign 0.005			

	DN	A436D +/- benign 0.001	A436D +/- benign 0.001	A436D +/- benign 0.001		A436D +/- benign 0.001	A436D +/- benign 0.001
	R						
<i>GNB1</i> ¹							
<i>GRB2</i>							
<i>GRIN2A</i> ^{1,4}							
<i>GSK3A</i>							
<i>GSK3B</i>							
<i>HDAC4</i>							
<i>HIST1H2BC</i> ¹							
<i>HIST1H3H</i> ¹							
<i>HLA-A</i> ¹							
<i>HLA-B</i>							
<i>HNF1A</i>	DN	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000
	R						
	DN		I27L +/- benign 0.002	I27L +/- benign 0.002	I27L +/- benign 0.002		
	R						
	DN		S487N +/- benign 0.000	S487N +/- benign 0.000	S487N +/- benign 0.000		
	R						
<i>HOXD8</i> ⁹							
<i>HRAS</i>							
<i>IDH1</i> ⁴							
<i>IDH2</i> ⁴							
<i>IGF1R</i>							
<i>IGFBP7</i>	DN	L11F +/- benign 0.005	L11F +/- benign 0.005	L11F +/- benign 0.005		L11F +/- benign 0.005	L11F +/- benign 0.005
	R						
<i>INPP4B</i>							
<i>INPPL1</i>	DN	L632I +/- probably damaging 0.990	L632I +/- probably damaging 0.990	L632I +/- probably damaging 0.990		L632I +/- probably damaging 0.990	L632I +/- probably damaging 0.990
	R						
	DN	A1083G +/- benign 0.000	A1083G +/- benign 0.000	A1083G +/- benign 0.000		A1083G +/- benign 0.000	A1083G +/- benign 0.000
	R						
<i>IRF8</i> ¹							
<i>JAK1</i> ¹							
<i>JAK2</i>							
<i>JARID2</i> ¹							

KDM5C							
KDM6A	DN	T778K +/- benign 0.000				T778K +/- benign 0.000	
	R						
KDR (VEGFR2) ⁴	DN		Q472H +/- benign 0.003	Q472H +/- benign 0.003	Q472H +/- benign 0.003		Q472H +/- benign 0.003
	R						
	DN		V297I +/-	V297I +/-	V297I +/-		
	R		probably damaging 1.000	probably damaging 1.000	probably damaging 1.000		
KEAP1							
KIT							
KMT2A ¹	DN		A30G +/- possibly damaging 0.953	A30G +/- possibly damaging 0.953	A30G +/- possibly damaging 0.953		
	R						
KMT2B ¹	DN	G296S +/- probably damaging 1.000				G296S +/- probably damaging 1.000	
	R		G296S +/- probably damaging 1.000	G296S +/- probably damaging 1.000			G296S +/- probably damaging 1.000
	DN	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000
	R						
	DN	R1021fs +/- frameshift variant	R1021fs +/- frameshift variant	R1021fs +/- frameshift variant	R1021fs +/- frameshift variant	R1021fs +/- frameshift variant	R1021fs +/- frameshift variant
	R						
	DN						P1829L +/- benign 0.006
	R						
KMT2C ^{1,4}	DN						
	R	C988F +/- probably damaging 0.999	C988F +/- probably damaging 0.999	C988F +/- probably damaging 0.999	C988F +/- probably damaging 0.999	C988F +/- probably damaging 0.999	C988F +/- probably damaging 0.999
	DN						
	R	T316S +/- possibly damaging 0.684	T316S +/- possibly damaging 0.684	T316S +/- possibly damaging 0.684	T316S +/- possibly damaging 0.684	T316S +/- possibly damaging 0.684	T316S +/- possibly damaging 0.684
	DN						
	R	L291F +/- probably damaging 1.000	L291F +/- probably damaging 1.000	L291F +/- probably damaging 1.000	L291F +/- probably damaging 1.000	L291F +/- probably damaging 1.000	L291F +/- probably damaging 1.000
	DN						
	R	Y816X +/- frameshift variant	Y816X +/- frameshift variant	Y816X +/- frameshift variant	Y816X +/- frameshift variant	Y816X +/- frameshift variant	Y816X +/- frameshift variant
	DN						
	R			G838S +/- probably damaging			

				1.000			
	DN						
	R				S772L +/- possibly damaging 0.546		
	DN						
	R				R284Q +/- probably damaging 0.984		
	DN						
	R				N729D +/- benign 0.094		
<i>KMT2D</i> ^{1, 4}	DN	V4305I +/- benign 0.039				V4305I +/- benign 0.039	
	R						
	DN		P813L +/- benign 0.000	P813L +/- benign 0.000	P813L +/- benign 0.000		
	R						
<i>KNSTRN</i>	DN						
	R	N279Y +/- probably damaging 0.965	N279Y +/- probably damaging 0.965	N279Y +/- probably damaging 0.965		N279Y +/- probably damaging 0.965	N279Y +/- probably damaging 0.965
<i>KRAS</i> ^{2, 3, 10}							
<i>LAMTOR1</i> (MP1)							
<i>LATS1</i> ¹							
<i>MAP2K1</i> (MEK1) ^{9, 11-13}							
<i>MAP2K2</i> (MEK2) ^{3, 9, 14}							
<i>MAP2K4</i> ¹							
<i>MAPK3</i> (ERK1)							
<i>MAPK1</i> (ERK2)							
<i>MAPK8</i> (JNK1)							
<i>MAPK9</i> (JNK2)							
<i>MAPK10</i> (JNK3)							
<i>MAPK14</i> (p38)							
<i>MC1R</i>	DN						R151C +/- probably damaging 1.000
	R	R151C +/- probably damaging 1.000	R151C +/- probably damaging 1.000	R151C +/- probably damaging 1.000		R151C +/- probably damaging 1.000	R151C +/- probably damaging 1.000

	DN		V60L +/- probably damaging 0.988				I155T +/- probably damaging 0.986
	R						
MDM2							
MDM4							
MED12 ¹	DN	H2116 +/- disruptive inframe insertion				H2116 +/- disruptive inframe insertion	
	R		H2116 +/- disruptive inframe insertion	H2116 +/- disruptive inframe insertion		H2116 +/- disruptive inframe insertion	H2116 +/- disruptive inframe insertion
MEN1 ⁴	DN	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000
	R						
MET							
MGA ¹	DN	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000
	R						
	DN		P1523A +/- possibly damaging 0.657	P1523A +/- possibly damaging 0.657	P1523A +/- possibly damaging 0.657		
	R						
MITF ⁹							
MKI67 (Ki67)	DN	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008	
	R		I2101T +/- benign 0.008	I2101T +/- benign 0.008			
	DN	N104S +/- probably damaging 0.982	N104S +/- probably damaging 0.982	N104S +/- probably damaging 0.982	N104S +/- probably damaging 0.982	N104S +/- probably damaging 0.982	
	R		T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/-	T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/-	T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/-	T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/-	R2786Q +/- probably damaging 0.991 T3150S +/- benign 0.000 N2363S +/- benign 0.000

			benign 0.000 G1042S +/- benign 0.401	benign 0.000 G1042S +/- benign 0.401	benign 0.000 G1042S +/- benign 0.401		
<i>MLH1</i> ¹	DN		I219V +/- benign 0.018				I219V +/- benign 0.018
	R						
<i>MMP2</i>							
<i>MOS</i>	DN	D201V +/- probably damaging 1.000		D201V +/- probably damaging 1.000			
	R						
<i>MPL</i> ¹							
<i>MRE11A</i> ¹							
<i>MSH2</i>							
<i>MSH3</i> ¹	DN	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000	
	R						Q949R +/- benign 0.000
	DN	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075	
	R						A1045T +/- benign 0.075
	DN	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion
	R						
	DN						P72S +/- benign 0.028
	R						
<i>MSH6</i> ¹	DN		G39E +/- benign 0.000	G39E +/- benign 0.000	G39E +/- benign 0.000		
	R						
<i>MTOR</i>	DN	R2152C +/- benign 0.050				R2152C +/- benign 0.050	
	R		R2152C +/- benign 0.050	R2152C +/- benign 0.050			
<i>MUTYH</i> ¹	DN	Q338H +/- benign 0.343	Q338H +/- benign 0.343	Q338H +/- benign 0.343	Q338H +/- benign 0.343		Q338H +/- benign 0.343
	R					Q338H +/- benign 0.343	
<i>MYC</i>							
<i>MYD88</i> ¹							
<i>MYT1</i>	DN		T782S +/- benign 0.035	T782S +/- benign 0.035	T782S +/- benign 0.035		
	R						
<i>NBN</i> ¹	DN	E185Q +/- benign 0.001				E185Q +/- benign 0.001	
	R		E185Q +/- benign 0.001	E185Q +/- benign 0.001			E185Q +/- benign 0.001
<i>NCOR1</i> ¹							

NF1 ¹⁵	DN			R135W +/- probably damaging 1.000			
	R						
NF2 ¹							
NFKBIA							
NGFR							
NOS3 (eNOS)	DN	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000
	R		D298E +/- benign 0.000	D298E +/- benign 0.000			D298E +/- benign 0.000
NOTCH1 ¹							
NOTCH2 ¹	DN	F1209V +/- possibly damaging 0.939				F1209V +/- possibly damaging 0.939	
	R		F1209V +/- possibly damaging 0.939	F1209V +/- possibly damaging 0.939			F1209V +/- possibly damaging 0.939
	DN						N2002S +/- probably damaging .999
	R						
	DN						
	R	N46S +/- benign 0.010	N46S +/- benign 0.010	N46S +/- benign 0.010	N46S +/- benign 0.010	N46S +/- benign 0.010	N46S +/- benign 0.010
	DN						
	R	E38K +/- benign 0.044	E38K +/- benign 0.044	E38K +/- benign 0.044	E38K +/- benign 0.044	E38K +/- benign 0.044	E38K +/- benign 0.044
	DN						
	R	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001
	DN						
	R				A21T +/- benign 0.000		
NOTCH3	DN	C1826F +/- possibly damaging 0.829				C1826F +/- possibly damaging 0.829	
	R		C1826F +/- possibly damaging 0.829	C1826F +/- possibly damaging 0.829			C1826F +/- possibly damaging 0.829
	DN	A2223V +/- benign 0.001	A2223V +/- benign 0.001		A2223V +/- benign 0.001	A2223V +/- benign 0.001	A2223V +/- benign 0.001
	R						
NOTCH4 ⁴							
NRAS ^{2, 12}							
NSD1 ¹							
NTRK1							
NTRK2							
NTRK3							
PAK5 ¹							

<i>PALB2</i> ¹							
<i>PARK2</i> ¹							
<i>PARP1</i> ¹							
<i>PAX5</i> ¹	DN	G266E +/- benign 0.000				G266E +/- benign 0.000	
	R		G266E +/- benign 0.000	G266E +/- benign 0.000			G266E +/- benign 0.000
	DN		T293I +/- benign 0.000	T293I +/- benign 0.000	T293I +/- benign 0.000		T293I +/- benign 0.000
	R						
<i>PBRM1</i> ^{1,4}							
<i>PDGFRA</i>							
<i>PDGFRB</i>							
<i>PDPK1</i> (PDK1)							
<i>PHLPP1</i> ²							
<i>PIGA</i> ¹							
<i>PIK3CA</i> ²							
<i>PIK3CB</i>	DN						R981L +/- possibly damaging 0.601
	R						
<i>PIK3CG</i> ²							
<i>PIK3R1</i>							
<i>PIK3R2</i> ²	DN	S313P +/- benign 0.000 S234R +/- benign 0.000	S313P +/- benign 0.000 S234R +/- benign 0.000	S313P +/- benign 0.000 S234R +/- benign 0.000	S313P +/- benign 0.000 S234R +/- benign 0.000	S313P +/- benign 0.000 S234R +/- benign 0.000	S313P +/- benign 0.000 S234R +/- benign 0.000
	R						
<i>PIK3R3</i>	DN	N283K +/- benign 0.000	N283K +/- benign 0.000 M295X +/- frameshift variant	N283K +/- benign 0.000	N283K +/- benign 0.000	N283K +/- benign 0.000 M295X +/- frameshift variant	N283K +/- benign 0.000
	R						
<i>PMS1</i> ¹							
<i>PMS2</i> ¹	DN	K541E +/- benign 0.000	K541E +/- benign 0.000	K541E +/- benign 0.000	K541E +/- benign 0.000	K541E +/- benign 0.000	K541E +/- benign 0.000
	R						
	DN	P470S +/- benign 0.018	P470S +/- benign 0.018	P470S +/- benign 0.018		P470S +/- benign 0.018	P470S +/- benign 0.018
	R						
<i>POT1</i>							
<i>PPP2R1A</i>	DN						
	R		E332D +/- benign 0.000			E332D +/- benign 0.000	E332D +/- benign 0.000
<i>PPP6C</i> ¹							
<i>PRDM1</i> ¹	DN	G74S +/-				G74S +/-	

	R	benign 0.016	G74S +/- benign 0.016	G74S +/- benign 0.016		benign 0.016	G74S +/- benign 0.016
<i>PRKAA1 (AMPK1)</i>							
<i>PRKAA2 (AMPK2)</i>							
<i>PRKACA (PKA)</i>							
<i>PRKACB (PKA)</i>							
<i>PTCH1</i>	DN		P1315L +/- possibly damaging 0.944	P1315L +/- possibly damaging 0.944	P1315L +/- possibly damaging 0.944		
	R						
<i>PTEN</i> ²							
<i>PTK2 (FAK)</i>							
<i>PTPN1</i>							
<i>PTPN11</i>							
<i>PTPRD</i> ^{1, 4}	DN	G272R +/- probably damaging 0.977				G272R +/- probably damaging 0.977	
	R		G272R +/- probably damaging 0.977	G272R +/- probably damaging 0.977			G272R +/- probably damaging 0.977
	DN						
	R		T781A +/- benign 0.007	T781A +/- benign 0.007	T781A +/- benign 0.007		
<i>PTPRS</i>	DN	C1457R +/- benign 0.000	C1457R +/- benign 0.000	C1457R +/- benign 0.000	C1457R +/- benign 0.000	C1457R +/- benign 0.000	C1457R +/- benign 0.000
	R						
<i>PTPRT</i> ⁴	DN	A29P +/- benign 0.014	A29P +/- benign 0.014	A29P +/- benign 0.014	A29P +/- benign 0.014		
	R						
<i>RAC1</i> ^{9, 16}							
<i>RAD50</i> ¹							
<i>RAD51</i>							
<i>RAF1 (CRAF)</i>							
<i>RASA2</i>							
<i>RASGRF1</i>							
<i>RASGRF2</i>	DN	S753P +/- benign 0.002				S753P +/- benign 0.002	
	R		S753P +/- benign 0.002	S753P +/- benign 0.002			S753P +/- benign 0.002
<i>RASGRP1</i>							
<i>RASGRP2</i>							
<i>RASGRP3</i>	DN	T393A +/- benign 0.131	T393A +/- benign 0.131				
	R						T393A +/- benign 0.131
<i>RASGRP4</i>	DN	H311Y +/-				H311Y +/-	

	R	probably damaging 0.993	H311Y +/- probably damaging 0.993	H311Y +/- probably damaging 0.9		probably damaging 0.993	H311Y +/- probably damaging 0.993
	DN	G165R +/- benign 0.001 I18T +/- benign 0.000					I18T +/- benign 0.000
	R			G165R +/- benign 0.001 I18T +/- benign 0.000			
<i>RASSF2</i>							
<i>RB1</i>							
<i>RBM10</i> ¹⁷							
<i>RBMX</i> ¹⁷	DN						
	R				G379R +/- probably damaging 1.000 Y357H +/- probably damaging 0.995 R339G +/- possibly damaging 0.995 S337N +/- probably damaging 0.981 R324P +/- probably damaging 0.996 S303fs +/- frameshift variant P301L +/- benign 0.269		
<i>RECQL</i> ¹							
<i>RET</i>	DN	G691S +/- benign 0.062				G691S +/- benign 0.062	
	R		G691S +/- benign 0.062				G691S +/- benign 0.062
<i>RHEB</i>							
<i>RICTOR</i>	DN		S837F +/- benign 0.002	S837F +/- benign 0.002	S837F +/- benign 0.002		S837F +/- benign 0.002
	R						R907C +/- possibly damaging 0.915
<i>RIT1</i>							
<i>RNF43</i> ⁴	DN	P231L +/-				P231L +/-	

	R	benign 0.056	P231L +/- benign 0.056	P231L +/- benign 0.056		benign 0.056	P231L +/- benign 0.056
	DN		I47V +/- benign 0.002	I47V +/- benign 0.002	I47V +/- benign 0.002		
	R						
	DN		L418M +/- probably damaging 0.969	L418M +/- probably damaging 0.969	L418M +/- probably damaging 0.969		
	R						
	DN		R343H +/- benign 0.002	R343H +/- benign 0.002	R343H +/- benign 0.002		R343H +/- benign 0.002
	R				R343H +/- benign 0.002		
	DN						P686R +/- benign 0.001
	R						
ROS1	DN	D2213N +/- benign 0.009	D2213N +/- benign 0.009	D2213N +/- benign 0.009	D2213N +/- benign 0.009	D2213N +/- benign 0.009	
	R						D2213N +/- benign 0.009
	DN	S2229C +/- benign 0.000 K2228Q +/- benign 0.000	S2229C +/- benign 0.000 K2228Q +/- benign 0.000	S2229C +/- benign 0.000 K2228Q +/- benign 0.000	S2229C +/- benign 0.000 K2228Q +/- benign 0.000	S2229C +/- benign 0.000 K2228Q +/- benign 0.000	
	R						
RPS6KA1 (RSK1)	DN	K344T +/- benign 0.088				K344T +/- benign 0.088	
	R		K344T +/- benign 0.088	K344T +/- benign 0.088			K344T +/- benign 0.088
RPS6KA2 (RSK3)	DN	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000 I10S +/- benign 0.000
	R						
RPS6KA3 (RSK2)	DN						I38S +/- benign 0.000
	R						
RPS6KA4 (MSK2)	DN	S758A +/- benign 0.000	S758A +/- benign 0.000	S758A +/- benign 0.000	S758A +/- benign 0.000	S758A +/- benign 0.000	S758A +/- benign 0.000
	R	S758A +/- benign 0.000					
RPS6KA5 (MSK1)							
RPS6KB1 (p70S6K)							
RPTOR							
RTEL1	DN	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000		Q1042H +/- benign 0.000
	R					Q1042H +/- benign 0.000	

<i>SAMD4B</i> ³							
<i>SDHA</i> ¹							
<i>SDHB</i> ⁴							
<i>SDHC</i> ¹							
<i>SDHD</i>							
<i>SETD2</i> ^{1,4}	DN		P1962L +/- benign 0.001			P1962L +/- benign 0.001	P1962L +/- benign 0.001
	R						
<i>SF3B1</i> ⁴							
<i>SH2D1A</i>							
<i>SHQ1</i>	DN		S489N +/- benign 0.000	S489N +/- benign 0.000			
	R	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000
	DN						
	R	F72C +/- probably damaging 0.971	F72C +/- probably damaging 0.971	F72C +/- probably damaging 0.971		F72C +/- probably damaging 0.971	F72C +/- probably damaging 0.971
<i>SLX4</i>							
<i>SMAD3</i>							
<i>SMAD4</i> ¹							
<i>SMARCA4</i> (BRG1) ¹							
<i>SOS1</i>	DN	R647M +/- probably damaging 0.998				R647M +/- probably damaging 0.998	
	R		R647M +/- probably damaging 0.998	R647M +/- probably damaging 0.998			
	DN						
	R				S1318C +/- benign 0.145		
<i>SOS2</i>	DN						A208T +/- possibly damaging 0.937
	R						
<i>SOX2</i>							
<i>SOX9</i>							
<i>SOX10</i>							
<i>SPEN</i> ¹	DN	A970V +/- benign 0.006				A970V +/- benign 0.006	
	R						
	DN	L1091P +/- benign 0.000				L1091P +/- benign 0.000	L1091P +/- benign 0.000
	R						

	DN	N2360D +/- benign 0.000				N2360D +/- benign 0.000	N2360D +/- benign 0.000
	R						
	DN						
	R						D2007E +/- benign 0.001
	DN						
	R	L2650 +/- disruptive inframe deletion	L2650 +/- disruptive inframe deletion	L2650 +/- disruptive inframe deletion		L2650 +/- disruptive inframe deletion	L2650 +/- disruptive inframe deletion
SPOP ¹							
SPRED1							
SRC							
STAG2 ¹							
STAT3							
STAT5A							
STAT5B							
STK11							
STK19							
SUFU							
SYK							
TBX2							
TCF3 ¹							
TCF7L2 ¹							
TERT							
TET1	DN	V128F +/- possibly damaging 0.845				V128F +/- possibly damaging 0.845	
	R		V128F +/- possibly damaging 0.845	V128F +/- possibly damaging 0.845			V128F +/- possibly damaging 0.845
	DN		D162G +/- benign 0.295	D162G +/- benign 0.295	D162G +/- benign 0.295		D162G +/- benign 0.295
	R						
	DN	I1123M +/- benign 0.070	I1123M +/- benign 0.070	I1123M +/- benign 0.070	I1123M +/- benign 0.070	I1123M +/- benign 0.070	I1123M +/- benign 0.070
	R						
	DN						S193T +/- benign 0.107
	R						
TET2 ⁴	DN	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001
	R		I1762V +/- benign 0.001	I1762V +/- benign 0.001			I1762V +/- benign 0.001
TGFBR2							
TMEM127 ¹							
TOP1	DN	H81Y +/-				H81Y +/-	

	R	benign 0.273	H81Y +/- benign 0.273	H81Y +/- benign 0.273		benign 0.273	H81Y +/- benign 0.273
TP53	DN	P72R +/- benign 0.083	P72R +/- benign 0.083	P72R +/- benign 0.083	P72R +/- benign 0.083		P72R +/- benign 0.083
	R						
TP53BP1 ¹	DN	K1141Q +/- benign 0.000	K1141Q +/- benign 0.000	K1141Q +/- benign 0.000		K1141Q +/- benign 0.000	K1141Q +/- benign 0.000
	R						
	DN	G417S +/- benign 0.000	G417S +/- benign 0.000	G417S +/- benign 0.000		G417S +/- benign 0.000	G417S +/- benign 0.000
	R						
	DN	D358E +/- benign 0.000	D358E +/- benign 0.000	D358E +/- benign 0.000		D358E +/- benign 0.000	D358E +/- benign 0.000
	R						
TP63 ⁴							
TSC1	DN		M322T +/- benign 0.000	M322T +/- benign 0.000	M322T +/- benign 0.000		
	R						
TSC2							
TYRO3	DN	I346N +/- benign 0.408	I346N +/- benign 0.408	I346N +/- benign 0.408		I346N +/- benign 0.408	I346N +/- benign 0.408
	R						
	DN	V669L +/- probably damaging 1.000				V669L +/- probably damaging 1.000	V669L +/- probably damaging 1.000
	R						
VHL							
WEE1	DN						G210C +/- possibly damaging 0.903
	R						
WNK1	DN		F741fs +/- frameshift variant	F741fs +/- frameshift variant			
	R						
	DN	T1316P +/- benign 0.000 C1766S +/- benign 0.000	T1316P +/- benign 0.000 C1766S +/- benign 0.000 M2068I +/- benign 0.000	T1316P +/- benign 0.000 C1766S +/- benign 0.000 M2068I +/- benign 0.000	T1316P +/- benign 0.000 C1766S +/- benign 0.000 M2068I +/- benign 0.000	T1316P +/- benign 0.000 C1766S +/- benign 0.000	T1316P +/- benign 0.000 C1766S +/- benign 0.000 M2068I +/- benign 0.000
	R						
WT1							
XRCC2 ¹							
ZFHX3 ¹	DN						
	R	S72A +/- benign 0.002	S72A +/- benign 0.002	S72A +/- benign 0.002		S72A +/- benign 0.002	S72A +/- benign 0.002
	DN	V777A +/-	V777A +/-	V777A +/-	V777A +/-	V777A +/-	V777A +/-

	R	benign 0.006	benign 0.006	benign 0.006	benign 0.006	benign 0.006	benign 0.006
	DN		S3513G +/- benign 0.000	S3513G +/- benign 0.000	S3513G +/- benign 0.000		
	R						
	DN			G3527dup +/- disruptive inframe insertion	G3527dup +/- disruptive inframe insertion		
	R						

gene		11_TRAR	21_TRAR	28_TRAR	29_TRAR	17_TRAR
ABL1						
ACTG1						
AK1 ¹						
AKT1 ²						
AKT2 ³	DN					A382T +/- benign 0.001
	R					
AKT3 ²						
ALK	DN	I1461V +/- benign 0.000		I1461V +/- benign 0.000	I1461V +/- benign 0.000	
	R		I1461V +/- benign 0.000			I1461V +/- benign 0.000
AMER1	DN					T625A +/- benign 0.000
	R					
ANKRD11 ¹	DN		D2376E +/- benign 0.010	D2376E +/- benign 0.010	D2376E +/- benign 0.010	
	R					
	DN					P2263S +/- benign 0.002
	R					
	DN					A2023P +/- benign 0.451
	R					
APC	DN		V1822D +/- benign 0.000	V1822D +/- benign 0.000	V1822D +/- benign 0.000	V1822D +/- benign 0.000
	R					
ARAF						
ARF1						
ARID1A ¹						
ARID1B ¹						
ARID2 ⁴						
ARID4A ¹	DN	N724S +/- benign 0.003				N724S +/- benign 0.003
	R					
	DN	T779A +/-				T779A +/-

	R	benign 0.000				benign 0.000
<i>ARID4B</i> ¹						
<i>ARID5B</i> ¹						
<i>ASXL1</i>	DN	G704R +/-				
	R	probably damaging 0.986				
	DN	L815P +/-	L815P +/-	L815P +/-	L815P +/-	L815P +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>ASXL2</i> ¹	DN					K127R +/-
	R					benign 0.003
<i>ATM</i>	DN	N1938S +/-	N1938S +/-	N1938S +/-	N1938S +/-	N1938S +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>ATR</i> ^{1,4}	DN	R2425Q +/-				
	R	benign 0.000				
	DN	M211T +/-	M211T +/-	M211T +/-	M211T +/-	M211T +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
	DN	N1668fs +/-				
	R	frameshift variant				
<i>ATRX</i> ¹						
<i>ATXN2</i> ¹	DN	Q188 +/-	Q188 +/-	Q188 +/-	Q188 +/-	Q188 +/-
	R	disruptive inframe deletion	disruptive inframe deletion	disruptive inframe deletion	disruptive inframe deletion	disruptive inframe deletion
	DN	L107V +/-	L107V +/-	L107V +/-	L107V +/-	L107V +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>AXIN1</i>						
<i>AXIN2</i>	DN	P50S +/-		P50S +/-	P50S +/-	P50S +/-
	R	benign 0.000		benign 0.000	benign 0.000	benign 0.000
<i>AXL</i>	DN	N266D +/-	N266D +/-	N266D +/-	N266D +/-	N266D +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>B2M</i> ¹						
<i>BACH2</i>						
<i>BAP1</i>						
<i>BCL2L11</i> (BIM) ¹						
<i>BCL10</i> ¹						
<i>BCL11B</i>	DN	V690M +/-				
	R	benign 0.082				
<i>BCOR</i>						
<i>BCORL1</i> ¹	DN	F111L +/-	F111L +/-	F111L +/-	F111L +/-	F111L +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>BLM</i> ¹						

<i>BMPR1A</i> ¹	DN					P2T +/+ benign 0.000
	R					
<i>BOP1</i>						
<i>BRAF</i> ^{2,5,6}	DN	V600E +/+	V600E +/-	V600E +/-	V600E +/-	
	R	probably damaging 0.971	probably damaging 0.971	probably damaging 0.971	probably damaging 0.971	
<i>BRCA1</i> ¹	DN	S1634G +/- benign 0.002				S1634G +/- benign 0.002
	R					
	DN	K1183R +/- benign 0.000				K1183R +/- benign 0.000
	R					
	DN	E1038G +/- benign 0.012				E1038G +/- benign 0.012
	R					
<i>BRCA2</i>	DN	P871L +/- benign 0.000				P871L +/- benign 0.000
	R					
	DN	V2466A +/+ benign 0.000	V2466A +/+ benign 0.000	V2466A +/+ benign 0.000	V2466A +/+ benign 0.000	V2466A +/+ benign 0.000
	R					
	DN		T1915M +/- benign 0.000	T1915M +/- benign 0.000	T1915M +/- benign 0.000	
	R		T1915M +/- benign 0.000			
<i>BRIP1</i> ¹	DN	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000	S919P +/- benign 0.000
	R		S919P +/- benign 0.000			
<i>CALR</i> ¹						
<i>CARD11</i>						
<i>CBL</i>						
<i>CCNA1</i> (cyclin A1)						
<i>CCNA2</i> (cyclin A2)	DN	I163V +/- benign 0.000	I163V +/- benign 0.000	I163V +/- benign 0.000	I163V +/- benign 0.000	I163V +/- benign 0.000
	R					
<i>CCNB1</i> (cyclin B1)						
<i>CCNB2</i> (cyclin B2)						
<i>CCND1</i> (cyclin D1) ⁷						
<i>CCND2</i> (cyclin D2)						
<i>CCND3</i> (cyclin D3)	DN	S259A +/- benign 0.000				S259A +/- benign 0.000
	R					
<i>CCNE1</i> (cyclin E1)						

<i>CCNE2</i> (cyclin E2)						
<i>CCNH</i> (cyclin H)	DN		V270A +/- probably damaging 0.965	V270A +/- probably damaging 0.965	V270A +/- probably damaging 0.965	
	R					
<i>CDC25A</i>						
<i>CDC25B</i>						
<i>CDC73</i> ^{1,4}						
<i>CD79B</i>						
<i>CDH1</i> ¹						
<i>CDK1</i>						
<i>CDK2</i>						
<i>CDK4</i>						
<i>CDK6</i>						
<i>CDK7</i>						
<i>CDK12</i> ¹	DN					
	R	K804 +/- inframe deletion				
<i>CDKN1A</i> (p21)						
<i>CDKN1B</i> (p27)	DN	V109G +/- benign 0.047				V109G +/- benign 0.047
	R					
<i>CDKN2A</i> (p16) ²	DN	E69* +/- stop gained E61* +/- stop gained				
	R					
<i>CDKN2B</i> (p15)						
<i>CDKN2C</i> (p18)						
<i>CDKN2D</i> (p19)						
<i>CENPA</i> ¹						
<i>CHEK1</i> (Chk-1) ¹	DN	I471V +/- benign 0.000	I471V +/- benign 0.000	I471V +/- benign 0.000	I471V +/- benign 0.000	I471V +/- benign 0.000
	R					
<i>CHEK2</i> (Chk-2)						
<i>CIC</i> ¹						
<i>CIITA</i>	DN	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000	R175G +/- benign 0.000
	R					
	DN	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001	Q901R +/- benign 0.001
	R					
	DN		G501A +/- benign 0.001	G501A +/- benign 0.001	G501A +/- benign 0.001	
	R					
<i>CRBN</i>						
<i>CREB</i>						

CREBBP ¹	DN	V1650G +/- benign 0.183				
	R					
CRLF2						
CTCF ⁴						
CTLA4	DN		T17A +/- benign 0.015	T17A +/- benign 0.015	T17A +/- benign 0.015	T17A +/- benign 0.015
	R					
CTNNB1 (β-catenin)						
CTR9						
CUX1 ¹						
CXCL8 (IL-8)						
CXCR1						
CXCR2						
DAXX ¹						
DDX3X ¹						
DDX53	DN	M381I +/- probably damaging 1.000	M381I +/- probably damaging 1.000			
	R					
	DN	R391M +/- benign 0.000	R391M +/- benign 0.000			
	R					
DEK	DN		S681P +/- benign 0.000		S681P +/- benign 0.000	
	R					
DICER1 ^{1,4}						
DNMT3A						
DUSP1 (MKP1)						
DUSP4 (MKP2) ⁸						
DUSP6 (MKP3)	DN	V114L +/- benign 0.075	V114L +/- benign 0.075	V114L +/- benign 0.075	V114L +/- benign 0.075	V114L +/- benign 0.075
	R					
DUSP7 (MKPX)						
DUSP10 (MKP5)						
DUSP14 (MKP6)						
DUSP16 (MKP7)	DN	V366M +/- benign 0.005				
	R					
DUSP22						
E2F1	DN					G393S +/- benign 0.022
	R					
E2F3	DN	D148N +/- possibly damaging 0.915 D389N +/-				
	R					

		benign 0.017				
<i>ECT2L</i>	DN	K676fs +/-				
	R	frameshift variant				
	DN					E527K +/-
	R					benign 0.002
<i>EED</i>						
<i>EGFR</i>	DN	R521K +/-	R521K +/-	R521K +/-	R521K +/-	R521K +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
<i>EIF1AX</i> ¹						
<i>ELF3</i>	DN					D91N +/-
	R					probably damaging 1.000
<i>ELK1</i>						
<i>EP300</i> ¹	DN	I997V +/-				I997V +/-
	R	benign 0.000				benign 0.000
	DN	Q2223P +/-				
	R	benign 0.000				
<i>EP400</i> ¹	DN		A574V +/-	A574V +/-	A574V +/-	
	R		possibly damaging 0.854	possibly damaging 0.854	possibly damaging 0.854	
	DN		A3094T +/-	A3094T +/-	A3094T +/-	
	R		benign 0.001	benign 0.001	benign 0.001	
	DN		Q2742 +/-	Q2742 +/-	Q2742 +/-	
	R		disruptive inframe insertion	disruptive inframe insertion	disruptive inframe insertion	
<i>EPHA3</i> ¹	DN	W924R +/-	W924R +/-		W924R +/-	W924R +/-
	R	benign 0.000	benign 0.000	W924R +/-	benign 0.000	benign 0.000
			benign 0.000			
<i>EPHA7</i> ¹						
<i>EPHB1</i> ¹						
<i>ERBB2</i>	DN		P8T +/-	P8T +/-	P8T +/-	
	R		benign 0.000	benign 0.000	benign 0.000	
			P8T +/-			
	R		benign 0.000			
	DN					
	R					I655V +/-
						benign 0.406
	DN	P1170A +/-	P1170A +/-	P1170A +/-	P1170A +/-	P1170A +/-
	R	possibly damaging 0.953	possibly damaging 0.953	possibly damaging 0.953	possibly damaging 0.953	possibly damaging 0.953
<i>ERBB3</i>						

ERBB4	DN					
	R	L437F +/- possibly damaging 0.928 K438M +/- possibly damaging 0.894				
ERCC2	DN		D312N +/- benign 0.065	D312N +/- benign 0.065	D312N +/- benign 0.065	
	R					
	DN		K751Q +/- benign 0.000	K751Q +/- benign 0.000	K751Q +/- benign 0.000	
	R					
ERF						
ERRFI1						
ESCO2 ¹						
ETS2 ³	DN	A19T +/- ?				
	R					
ETV6						
EZH2	DN				S412C +/- probably damaging 1.000	
	R					
FAM58A ¹	DN	A18G +/- frameshift variant				
	R					
	DN	A6G +/- frameshift variant				
	R					
FANCA ¹	DN	T266A +/- benign 0.000				T266A +/- benign 0.000
	R					
	DN					G809D +/- benign 0.000
	R					
	DN					G501S +/- benign 0.000
	R					
FANCD2 ¹	DN	N405S +/- benign 0.022	N405S +/- benign 0.022	N405S +/- benign 0.022	N405S +/- benign 0.022	
	R					
FAS ¹						
FAT1 ¹	DN	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000	K4059N +/- benign 0.000
	R					
	DN	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000	Q2933P +/- benign 0.000
	R					
	DN	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000	R1064G +/- benign 0.000
	R					
	DN	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000	V862L +/- benign 0.000
	R					

	DN	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000	F614L +/- benign 0.000
	R					
	DN	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032	S404R +/- benign 0.032
	R					
	DN	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009	V482I +/- benign 0.009
	R					
	DN	H1273R +/- benign 0.000				H1273R +/- benign 0.000
	R					
FBXO11						
FBXW7 ¹	DN	V418M +/-				
	R	possibly damaging 0.801				
FGFR1						
FGFR2	DN	E637K +/-				
	R	probably damaging 0.970				
FGFR3	DN		P451S +/- possibly damaging 0.902	P451S +/- possibly damaging 0.902	P451S +/- possibly damaging 0.902	
	R					
FGFR4	DN					
	R		G388R +/- probably damaging 0.998	G388R +/- probably damaging 0.998	G388R +/- probably damaging 0.998	G388R +/- probably damaging 0.998
	DN	P136L +/- benign 0.000	P136L +/- benign 0.000	P136L +/- benign 0.000	P136L +/- benign 0.000	P136L +/- benign 0.000
	R	V10I +/- benign 0.000				V10I +/- benign 0.000
FH						
FLT3	DN					
	R					D7G +/- benign 0.000
	DN	T227M +/-				T227M +/-
	R	probably damaging 0.999				probably damaging 0.999
FOXA1	DN					S448N +/- benign 0.001
	R					S448N +/- benign 0.001
FOXM1	DN					
	R		S681P +/- benign 0.000	S681P +/- benign 0.000	S681P +/- benign 0.000	
FOXO3A						
FOXP1 ¹						
GADD45A						

<i>GADD45B</i>						
<i>GADD45G</i>						
<i>GNA11</i>						
<i>GNAS</i> ^{1,4}	DN	A436D +/- benign 0.001				
	R					
	DN					
	R					
<i>GNB1</i> ¹						
<i>GRB2</i>						
<i>GRIN2A</i> ^{1,4}						
<i>GSK3A</i>						
<i>GSK3B</i>						
<i>HDAC4</i>						
<i>HIST1H2BC</i> ¹						
<i>HIST1H3H</i> ¹						
<i>HLA-A</i> ¹						
<i>HLA-B</i>						
<i>HNF1A</i>	DN	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000	S574G +/- benign 0.000
	R					
	DN		I27L +/- benign 0.002	I27L +/- benign 0.002	I27L +/- benign 0.002	
	R					
	DN		S487N +/- benign 0.000	S487N +/- benign 0.000	S487N +/- benign 0.000	
	R					
	DN					A98V +/- benign 0.209
	R					
<i>HOXD8</i> ⁹						
<i>HRAS</i>	DN					Q61R +/- benign 0.008
	R					
<i>IDH1</i> ⁴						
<i>IDH2</i> ⁴						
<i>IGF1R</i>						
<i>IGFBP7</i>	DN	L11F +/- benign 0.005	L11F +/- benign 0.005		L11F +/- benign 0.005	
	R					
<i>INPP4B</i>						
<i>INPPL1</i>	DN	L632I +/- probably damaging 0.990				
	R					
	DN	A1083G +/-				

	R	benign 0.000				
<i>IRF8</i> ¹						
<i>JAK1</i> ¹						
<i>JAK2</i>						
<i>JARID2</i> ¹						
<i>KDM5C</i>						
<i>KDM6A</i>	DN	T778K +/- benign 0.000				T778K +/- benign 0.000
	R					
<i>KDR</i> (VEGFR2) ⁴	DN		Q472H +/- benign 0.003	Q472H +/- benign 0.003	Q472H +/- benign 0.003	
	R					
	DN		V297I +/-	V297I +/-	V297I +/-	
	R		probably damaging 1.000	probably damaging 1.000	probably damaging 1.000	
<i>KEAP1</i>						
<i>KIT</i>						
<i>KMT2A</i> ¹	DN		A30G +/-	A30G +/-	A30G +/-	
	R		possibly damaging 0.953	possibly damaging 0.953	possibly damaging 0.953	
	DN					R2191* +/- stop gained
	R					
<i>KMT2B</i> ¹	DN	G296S +/- probably damaging 1.000				
	R		G296S +/- probably damaging 1.000	G296S +/- probably damaging 1.000		
	DN	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000	D2364G +/- benign 0.000
	R					
	DN	R1021fs +/- frameshift variant	R1021fs +/-	R1021fs +/-	R1021fs +/-	R1021fs +/- frameshift variant
	R		frameshift variant	frameshift variant	frameshift variant	
	DN					P1829L +/- benign 0.006
	R					
<i>KMT2C</i> ^{1,4}						
<i>KMT2D</i> ^{1, 4}	DN	V4305I +/- benign 0.039				
	R					
	DN		P813L +/- benign 0.000	P813L +/- benign 0.000	P813L +/- benign 0.000	
	R					
<i>KNSTRN</i>	DN	N279Y +/- probably damaging 0.965				
	R					
<i>KRAS</i> ^{2, 3, 10}						
<i>LAMTOR1</i> (MP1)						
<i>LATS1</i> ¹						
<i>MAP2K1</i> (MEK1) ^{9, 11-13}	DN					P124S +/-

	R					probably damaging 0.999
MAP2K2 (MEK2) ^{3, 9, 14}	DN					L201V +/- probably damaging 1.000 F57V +/- probably damaging 0.991
	R					
MAP2K4 ¹						
MAPK3 (ERK1)						
MAPK1 (ERK2)						
MAPK8 (JNK1)						
MAPK9 (JNK2)						
MAPK10 (JNK3)						
MAPK14 (p38)						
MC1R	DN	R151C +/- probably damaging 1.000				
	R					
	DN		V60L +/- probably damaging 0.988			
	R					
	DN					R163Q +/- benign 0.004
	R					
MDM2						
MDM4						
MED12 ¹	DN	H2116 +/- disruptive inframe insertion				
	R					
MEN1 ⁴	DN	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000	T546A +/- benign 0.000
	R					
MET						
MGA ¹	DN	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000	T716S +/- benign 0.000
	R					
	DN		P1523A +/- possibly damaging 0.657	P1523A +/- possibly damaging 0.657	P1523A +/- possibly damaging 0.657	
	R					
MITF ⁹						
MKI67 (Ki67)	DN	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008	I2101T +/- benign 0.008
	R		I2101T +/- benign 0.008			I2101T +/- benign 0.008

	DN	N104S +/- probably damaging 0.982	N104S +/- probably damaging 0.982 T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/- benign 0.000 G1042S +/- benign 0.401	N104S +/- probably damaging 0.982 T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/- benign 0.000 G1042S +/- benign 0.401	N104S +/- probably damaging 0.982 T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/- benign 0.000 G1042S +/- benign 0.401	N104S +/- probably damaging 0.982 T2868S +/- probably damaging 0.999 R2786Q +/- probably damaging 0.991 E1403V +/- probably damaging 0.997 K3217E +/- benign 0.000 T3150S +/- benign 0.000 N2363S +/- benign 0.000 G1042S +/- benign 0.401
<i>MLH1</i> ¹	DN		I219V +/- benign 0.018			
	R					
<i>MMP2</i>						
<i>MOS</i>	DN	D201V +/- probably damaging 1.000				
	R					
<i>MPL</i> ¹						
<i>MRE11A</i> ¹						
<i>MSH2</i>						
<i>MSH3</i> ¹	DN	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000	Q949R +/- benign 0.000
	R					
	DN	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075	A1045T +/- benign 0.075
	R					
	DN	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion	A61-P63dup +/- inframe insertion
	R					
	DN					I79V +/- benign 0.000
	R					
<i>MSH6</i> ¹	DN		G39E +/- benign 0.000	G39E +/- benign 0.000	G39E +/- benign 0.000	G39E +/- benign 0.000
	R					
<i>MTOR</i>	DN	R2152C +/- benign 0.050				
	R					
<i>MUTYH</i> ¹	DN	Q338H +/- benign 0.343	Q338H +/- benign 0.343	Q338H +/- benign 0.343	Q338H +/- benign 0.343	
	R					
	DN					V22M +/-

	R					benign 0.185
MYC						
MYD88 ¹						
MYT1	DN		T782S +/- benign 0.035	T782S +/- benign 0.035	T782S +/- benign 0.035	
	R					
NBN ¹	DN	E185Q +/- benign 0.001				
	R					
NCOR1 ¹						
NF1 ¹⁵	DN			R135W +/- probably damaging 1.000		
	R					
NF2 ¹						
NFKBIA						
NGFR						
NOS3 (eNOS)	DN	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000	D298E +/- benign 0.000
	R					
NOTCH1 ¹						
NOTCH2 ¹	DN	F1209V +/- possibly damaging 0.939				
	R					
	DN					
	R	N46S +/- benign 0.010		N46S +/- benign 0.010		N46S +/- benign 0.010
	DN					
	R	E38K +/- benign 0.044		E38K +/- benign 0.044		E38K +/- benign 0.044
	DN					
	R	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001	C19W +/- benign 0.001
	DN					
	R	P6fs +/- frameshift variant	P6fs +/- frameshift variant	P6fs +/- frameshift variant	P6fs +/- frameshift variant	P6fs +/- frameshift variant
	DN					
	R		A21T +/- benign 0.000	A21T +/- benign 0.000		
NOTCH3	DN	C1826F +/- possibly damaging 0.829				
	R					
	DN	A2223V +/- benign 0.001	A2223V +/- benign 0.001	A2223V +/- benign 0.001	A2223V +/- benign 0.001	A2223V +/- benign 0.001
	R					
NOTCH4 ⁴						

<i>NRAS</i> ^{2, 12}						
<i>NSD1</i> ¹	DN					S726P +/-
	R					probably damaging 0.999
	DN					V614L +/-
	R					benign 0.002
<i>NTRK1</i>						
<i>NTRK2</i>						
<i>NTRK3</i>						
<i>PAK5</i> ¹						
<i>PALB2</i> ¹						
<i>PARK2</i> ¹						
<i>PARP1</i> ¹						
<i>PAX5</i> ¹	DN	G266E +/- benign 0.000				
	R					
	DN		T293I +/- benign 0.000	T293I +/- benign 0.000	T293I +/- benign 0.000	T293I +/- benign 0.000
	R					
<i>PBRM1</i> ^{1, 4}						
<i>PDGFRA</i>	DN					
	R		E36A +/- probably damaging 1.000			
<i>PDGFRB</i>						
<i>PDPK1</i> (PDK1)						
<i>PHLPP1</i> ²						
<i>PIGA</i> ¹						
<i>PIK3CA</i> ²	DN					
	R		G1049R +/- benign 0.300			
<i>PIK3CB</i>						
<i>PIK3CG</i> ²						
<i>PIK3R1</i>						
<i>PIK3R2</i> ²	DN	S313P +/- benign 0.000	S313P +/- benign 0.000	S313P +/- benign 0.000	S313P +/- benign 0.000	S313P +/- benign 0.000
	R	S234R +/- benign 0.000	S234R +/- benign 0.000	S234R +/- benign 0.000	S234R +/- benign 0.000	S234R +/- benign 0.000
<i>PIK3R3</i>	DN					
	R	N283K +/- benign 0.000	N283K +/- benign 0.000	N283K +/- benign 0.000	N283K +/- benign 0.000	N283K +/- benign 0.000
<i>PMS1</i> ¹						
<i>PMS2</i> ¹	DN	K541E +/-	K541E +/-	K541E +/-	K541E +/-	K541E +/-

	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
	DN	P470S +/-				
	R	benign 0.018				
	DN					R20Q +/-
	R					possibly damaging 0.857
POT1						
PPP2R1A						
PPP6C ¹						
PRDM1 ¹	DN	G74S +/-				
	R	benign 0.016				
	DN					I117M +/-
	R					possibly damaging 0.950
	DN					D203E +/-
	R					possibly damaging 0.660
PRKAA1 (AMPK1)						
PRKAA2 (AMPK2)						
PRKACA (PKA)						
PRKACB (PKA)						
PTCH1	DN		P1315L +/-	P1315L +/-	P1315L +/-	
	R		possibly damaging 0.944	possibly damaging 0.944	possibly damaging 0.944	
PTEN ²						
PTK2 (FAK)						
PTPN1						
PTPN11						
PTPRD ^{1,4}	DN	G272R +/-				
	R	probably damaging 0.977				
	DN		T781A +/-	T781A +/-	T781A +/-	
	R		benign 0.007	benign 0.007	benign 0.007	
PTPRS	DN	C1457R +/-	C1457R +/-	C1457R +/-	C1457R +/-	C1457R +/-
	R	benign 0.000	benign 0.000	benign 0.000	benign 0.000	benign 0.000
PTPRT ⁴	DN					A29P +/-
	R					benign 0.014
RAC1 ^{9,16}						
RAD50 ¹						
RAD51						
RAF1 (CRAF)						
RASA2						

RASGRF1	DN					S752N +/- benign 0.001
	R					
RASGRF2	DN	S753P +/- benign 0.002				
	R					
RASGRP1						
RASGRP2						
RASGRP3	DN	T393A +/- benign 0.131				
	R					
RASGRP4	DN	H311Y +/- probably damaging 0.993 G165R +/- benign 0.001 I18T +/- benign 0.000				E519K +/- probably damaging 0.997
	R					
RASSF2						
RB1						
RBM10 ¹⁷	DN					R149Q +/- possibly damaging 0.928
	R					
RBMX ¹⁷	DN					
	R		G379R +/- probably damaging 1.000 Y357H +/- probably damaging 0.995 R339G +/- possibly damaging 0.995 S337N +/- probably damaging 0.981 R324P +/- probably damaging 0.996 S303fs +/- frameshift variant P301L +/- benign 0.269	G379R +/- probably damaging 1.000 Y357H +/- probably damaging 0.995 R339G +/- possibly damaging 0.995 S337N +/- probably damaging 0.981 R324P +/- probably damaging 0.996 S303fs +/- frameshift variant P301L +/- benign 0.269	G379R +/- probably damaging 1.000 Y357H +/- probably damaging 0.995 R339G +/- possibly damaging 0.995 S337N +/- probably damaging 0.981 R324P +/- probably damaging 0.996	
RECQL ¹	DN					D481fs +/- frameshift variant
	R					
RET	DN	G691S +/- benign 0.062				
	R					
RHEB						
RICTOR	DN		S837F +/- benign 0.002	S837F +/- benign 0.002	S837F +/- benign 0.002	S837F +/- benign 0.002
	R					

<i>RIT1</i>						
<i>RNF43</i> ⁴	DN	P231L +/- benign 0.056				
	R					
	DN		I47V +/- benign 0.002	I47V +/- benign 0.002	I47V +/- benign 0.002	I47V +/- benign 0.002
	R					
	DN		L418M +/- probably damaging 0.969	L418M +/- probably damaging 0.969	L418M +/- probably damaging 0.969	L418M +/- probably damaging 0.969
	R					
	DN		R343H +/- benign 0.002	R343H +/- benign 0.002	R343H +/- benign 0.002	R343H +/- benign 0.002
	R					
	DN					
	R					
<i>ROS1</i>	DN	D2213N +/- benign 0.009 S2229C +/- benign 0.000 K2228Q +/- benign 0.000	D2213N +/- benign 0.009 S2229C +/- benign 0.000 K2228Q +/- benign 0.000	D2213N +/- benign 0.009 S2229C +/- benign 0.000 K2228Q +/- benign 0.000	D2213N +/- benign 0.009 S2229C +/- benign 0.000 K2228Q +/- benign 0.000	D2213N +/- benign 0.009 S2229C +/- benign 0.000 K2228Q +/- benign 0.000 S1109L +/- benign 0.014
	R					
<i>RPS6KA1</i> (RSK1)	DN	K344T +/- benign 0.088				
	R	K344T +/- benign 0.088				
<i>RPS6KA2</i> (RSK3)	DN	T34A +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000	T34A +/- benign 0.000 E32G +/- benign 0.000
	R	E32G +/- benign 0.000				
<i>RPS6KA3</i> (RSK2)						
<i>RPS6KA4</i> (MSK2)	DN	S758A +/- benign 0.000	S758A +/- benign 0.000	S758A +/- benign 0.000		S758A +/- benign 0.000
	R					
<i>RPS6KA5</i> (MSK1)						
<i>RPS6KB1</i> (p70S6K)						
<i>RPTOR</i>	DN					A523V +/- possibly damaging 0.745
	R					
<i>RTEL1</i>	DN	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000	Q1042H +/- benign 0.000
	R					
<i>SAMD4B</i> ³						
<i>SDHA</i> ¹						
<i>SDHB</i> ⁴						
<i>SDHC</i> ¹						

SDHD	DN					G12S +/- benign 0.005
	R					
SETD2 ^{1,4}	DN		P1962L +/- benign 0.001			P1962L +/- benign 0.001
	R					
SF3B1 ⁴						
SH2D1A						
SHQ1	DN	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000	S489N +/- benign 0.000	
	R					
	DN	F72C +/- probably damaging 0.971				
	R					
SLX4	DN					R204C +/- probably damaging 1.000
	R					
	DN					E248K +/- possibly damaging 0.798
	R					
	DN					M386V +/- benign 0.000
	R					
	DN					N457K +/- benign 0.000
	R					
	DN					L671S +/- benign 0.000
	R					
	DN					A952T +/- benign 0.056
	R					
	DN					A952V +/- possibly damaging 0.926
	R					
	DN					P1122L +/- benign 0.003
	R					
	DN					A1221V +/- benign 0.019
	R					
SMAD3						
SMAD4 ¹						
SMARCA4 (BRG1) ¹						
SOS1	DN	R647M +/- probably damaging 0.998				
	R					
SOS2						
SOX2	DN					
	R					T222I +/-

						possibly damaging 0.804
SOX9						
SOX10						
SPEN ¹	DN	A970V +/- benign 0.006				
	R					
	DN	L1091P +/- benign 0.000				L1091P +/- benign 0.000
	R					
	DN	N2360D +/- benign 0.000				N2360D +/- benign 0.000
	R					
SPOP ¹						
SPRED1						
SRC						
STAG2 ¹						
STAT3						
STAT5A						
STAT5B						
STK11						
STK19						
SUFU						
SYK						
TBX2						
TCF3 ¹						
TCF7L2 ¹						
TERT						
TET1	DN	V128F +/- possibly damaging 0.845				
	R					
	DN					
	R					
	DN	I1123M +/- benign 0.070				I1123M +/- benign 0.070
	R					
	DN					S193T +/- benign 0.107
	R					
TET2 ⁴	DN	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001	I1762V +/- benign 0.001
	R					
	DN					L34F +/- benign 0.246
	R					
	DN					V218M +/-

	R					benign 0.000
	DN					M1701I +/- benign 0.001
	R					
	DN					H1778R +/- probably damaging 0.994
	R					
TGFBR2						
TMEM127 ¹						
TOP1	DN	H81Y +/- benign 0.273				
	R					
TP53	DN	P72R +/- benign 0.083	P72R +/- benign 0.083	P72R +/- benign 0.083	P72R +/- benign 0.083	P72R +/- benign 0.083
	R		P72R +/- benign 0.083			P72R +/- benign 0.083
	DN					
	R					R156H +/- probably damaging 1.000
TP53BP1 ¹	DN	K1141Q +/- benign 0.000				K1141Q +/- benign 0.000
	R					
	DN	G417S +/- benign 0.000				G417S +/- benign 0.000
	R					
	DN	D358E +/- benign 0.000				D358E +/- benign 0.000
	R					
TP63 ⁴						
TSC1	DN		M322T +/- benign 0.000	M322T +/- benign 0.000	M322T +/- benign 0.000	
	R					
TSC2	DN					
	R			D1004Y +/- probably damaging 1.000		
TYRO3	DN	I346N +/- benign 0.408				I346N +/- benign 0.408
	R	V669L +/- probably damaging 1.000				
VHL						
WEE1						
WNK1	DN	T1316P +/- benign 0.000	T1316P +/- benign 0.000	T1316P +/- benign 0.000	T1316P +/- benign 0.000	T1316P +/- benign 0.000
	R	C1766S +/- benign 0.000	C1766S +/- benign 0.000	C1766S +/- benign 0.000	C1766S +/- benign 0.000	C1766S +/- benign 0.000
			M2068I +/- benign 0.000	M2068I +/- benign 0.000	M2068I +/- benign 0.000	

WT1						
XRCC2 ¹						
ZFX3 ¹	DN	S72A +/- benign 0.002				
	R					
	DN	V777A +/- benign 0.006				V777A +/- benign 0.006
	R		V777A +/- benign 0.006	V777A +/- benign 0.006		
	DN					G3527dup +/- disruptive inframe insertion
	R					
	DN					A62V +/- benign 0.147
	R					A997S +/- probably damaging 0.999

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STAG2 E28Kfs*43; **TCF3** Q361Rfs*33; **TCF7L2** C486Vfs*8; **TMEM127** Q231*; **TP53BP1** Q644*; **TP53BP1** P766Qfs*3; **XRCC2** L117Wfs*17; **ZFH3** P3569Qfs*13; **ZFH3** R1309*)

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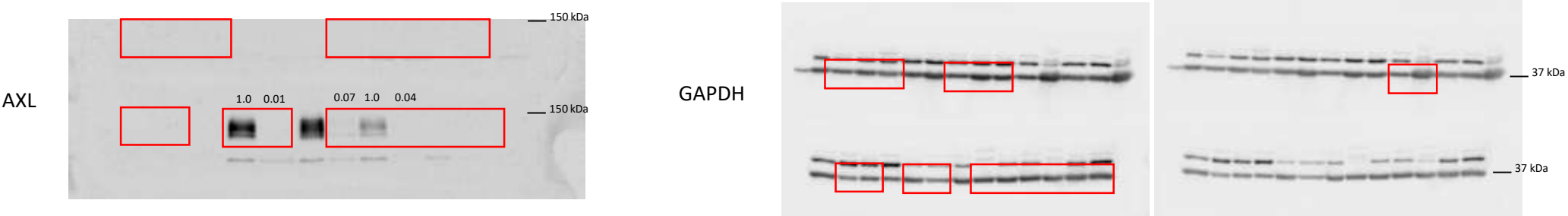
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Table S2. Average library size and final coverage of whole-exome sequencing of genomic DNA samples extracted from vemurafenib- (PLXR) or trametinib-resistant (TRAR) cell lines.

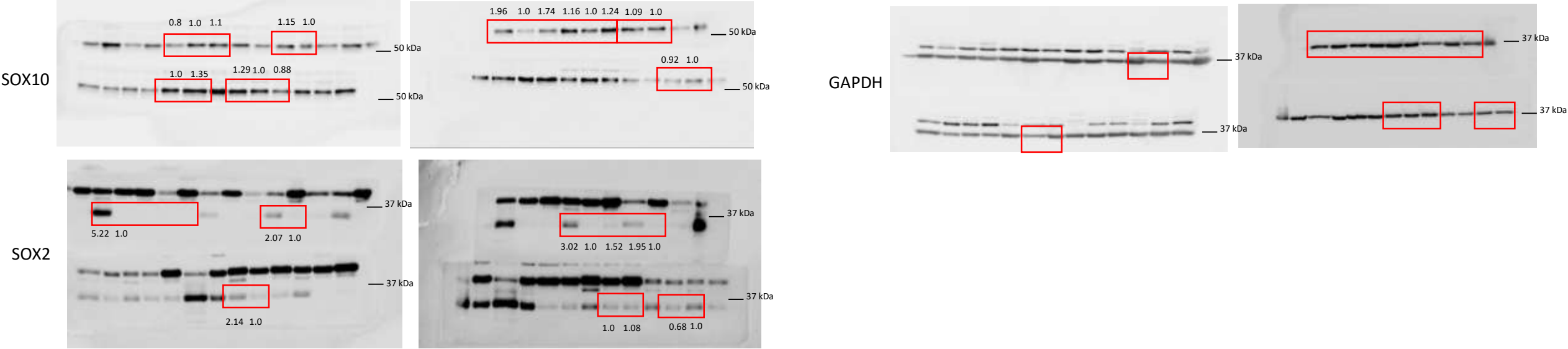
Cell population	Library size (average)	Average throughput depth of target regions
11_PLXR	329 bp	109x
11_TRAR	335 bp	106x
21_PLXR	359 bp	137x
21_TRAR	354 bp	142x
28_PLXR	350 bp	173x
28_TRAR	346 bp	115x
29_PLXR	340 bp	126x
29_TRAR	334 bp	120x
12_PLXR	338 bp	122x
17_TRAR	337 bp	102x

The original immunoblots. Cropped bands are shown in frames. Protein levels were normalized to GAPDH or β -actin based on densitometry analysis, and relative protein levels are shown.

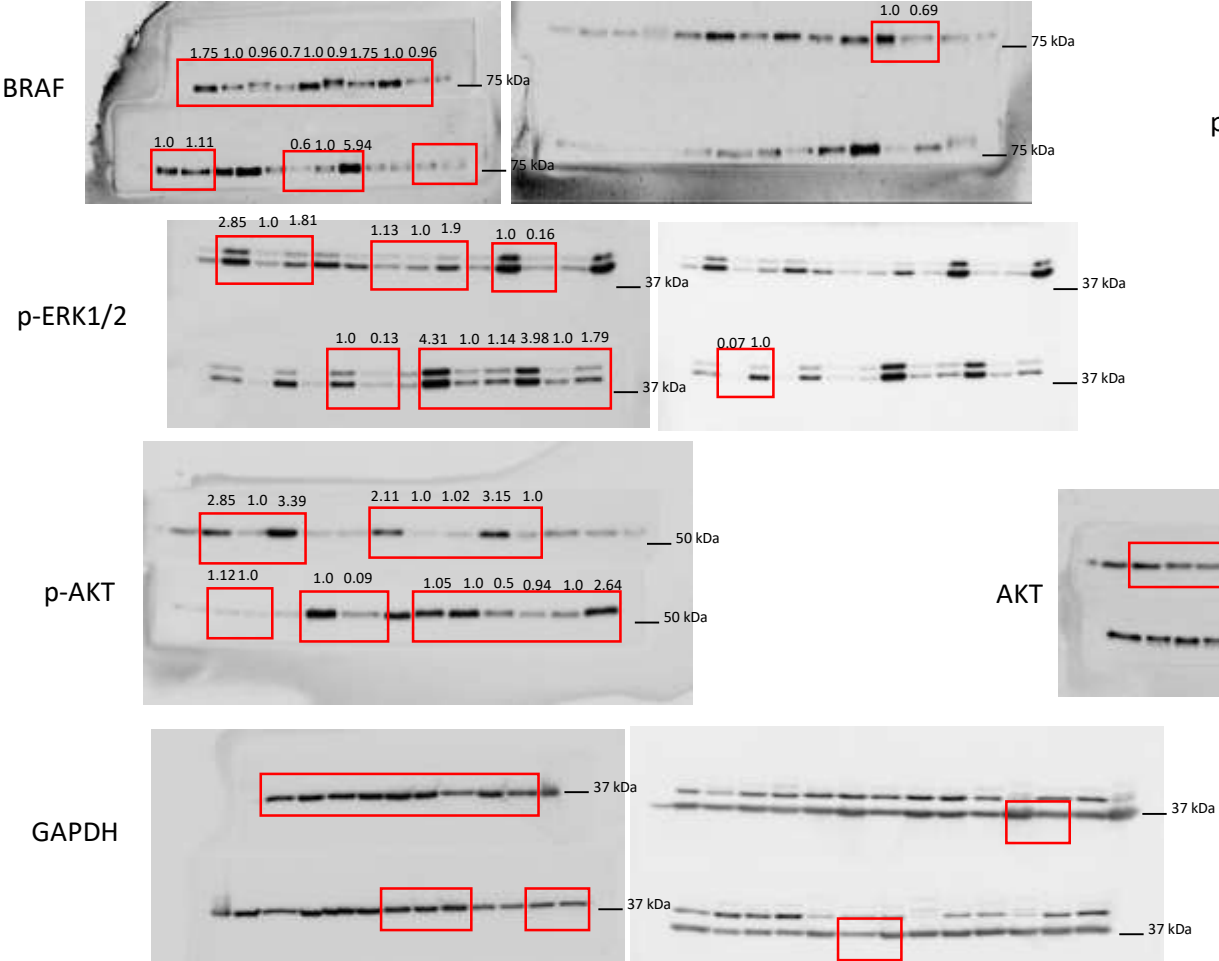
Corresponding to Figure 1E



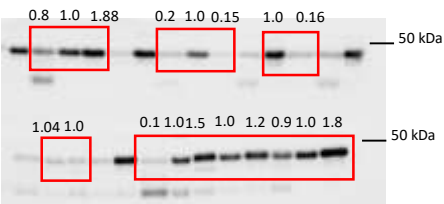
Corresponding to Figure 2C



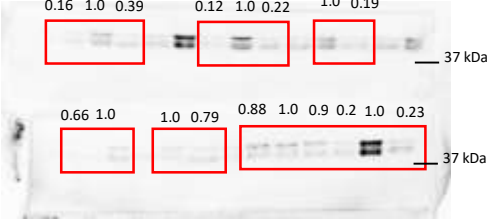
Corresponding to Figure 3B



p-MEK1/2



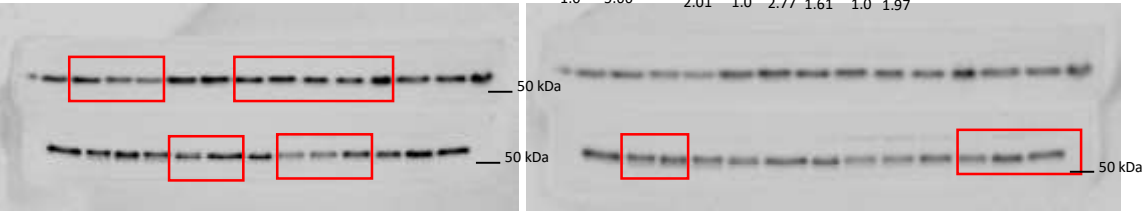
DUSP6



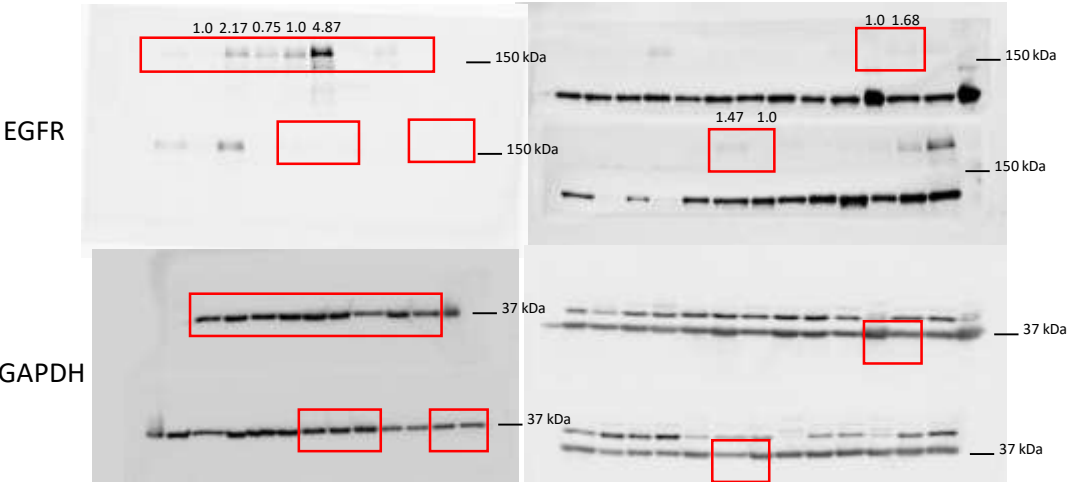
active
b-catenin



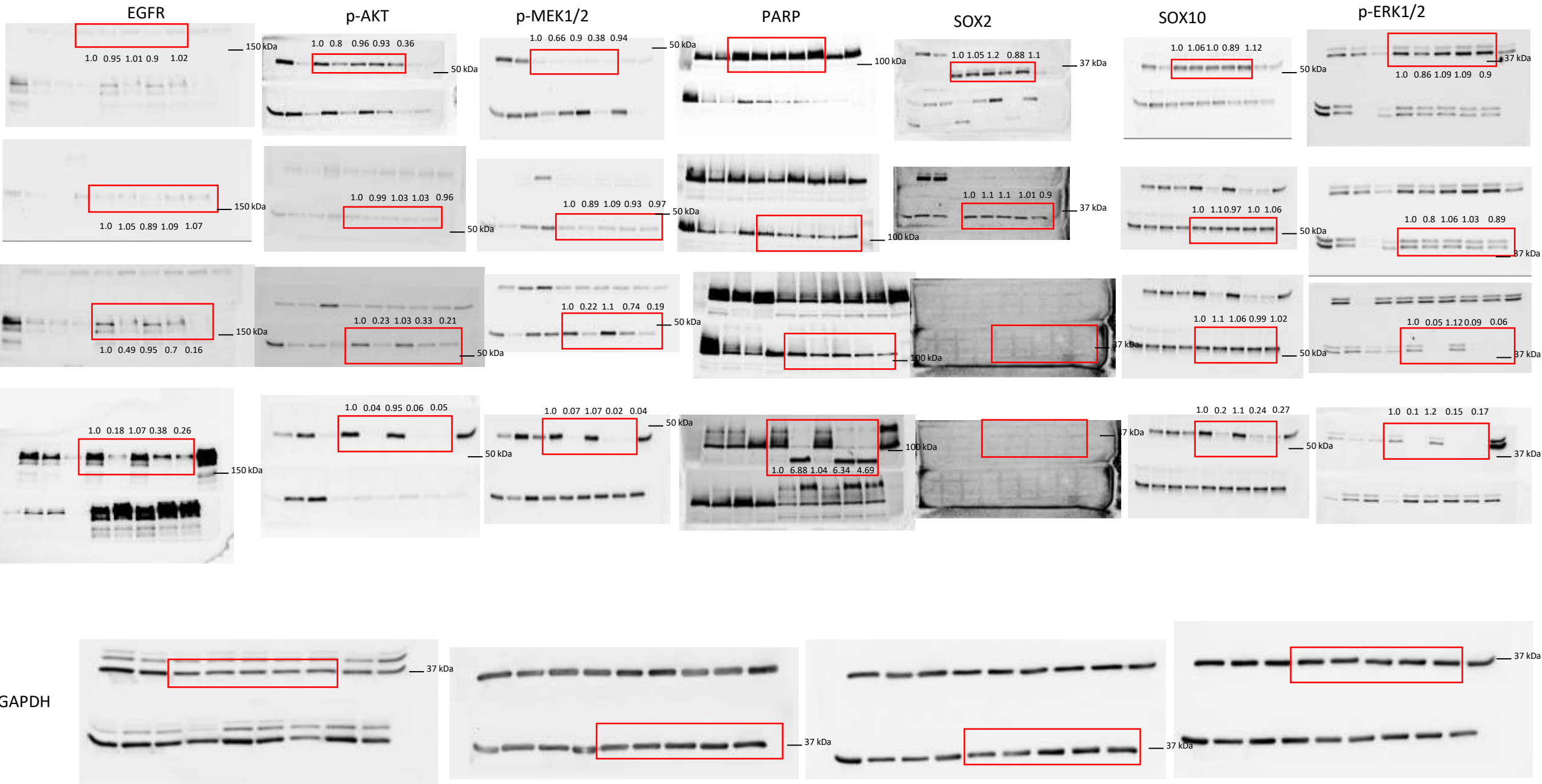
AKT



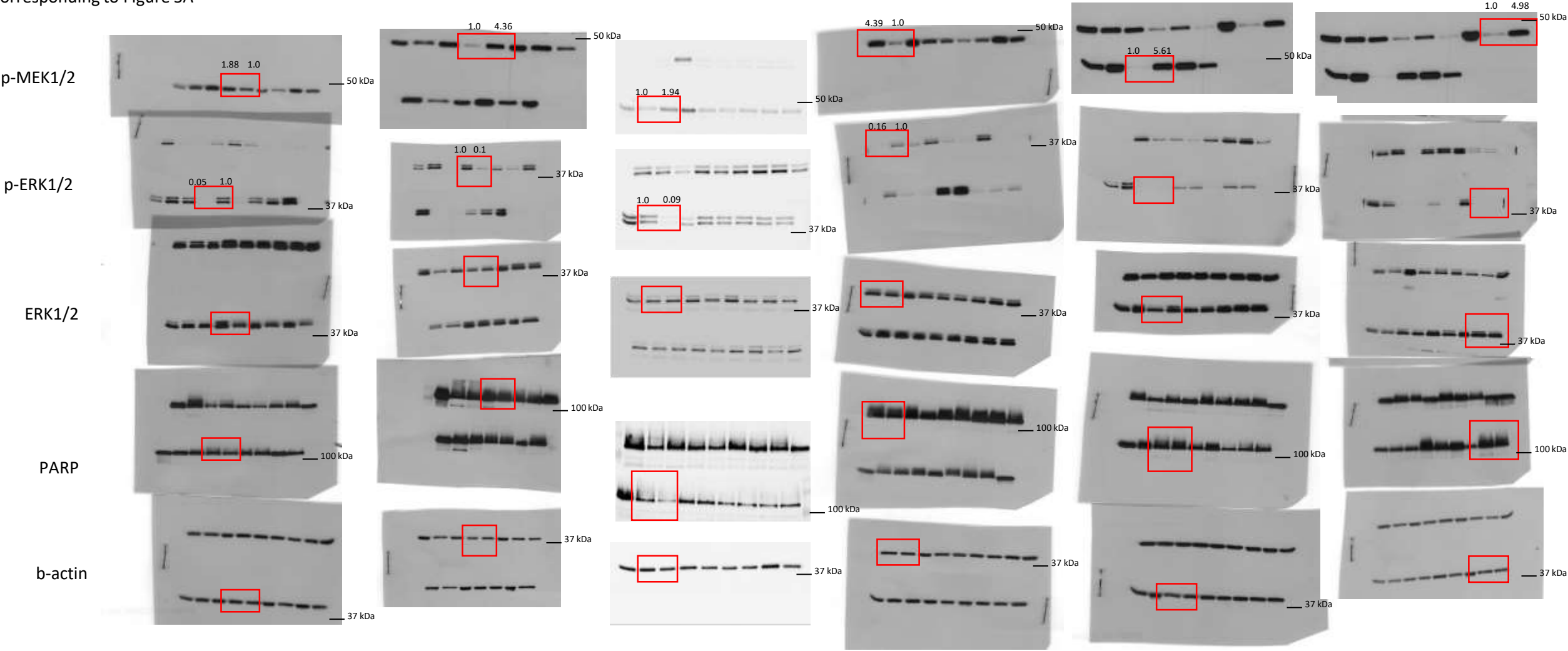
Corresponding to Figure 4B



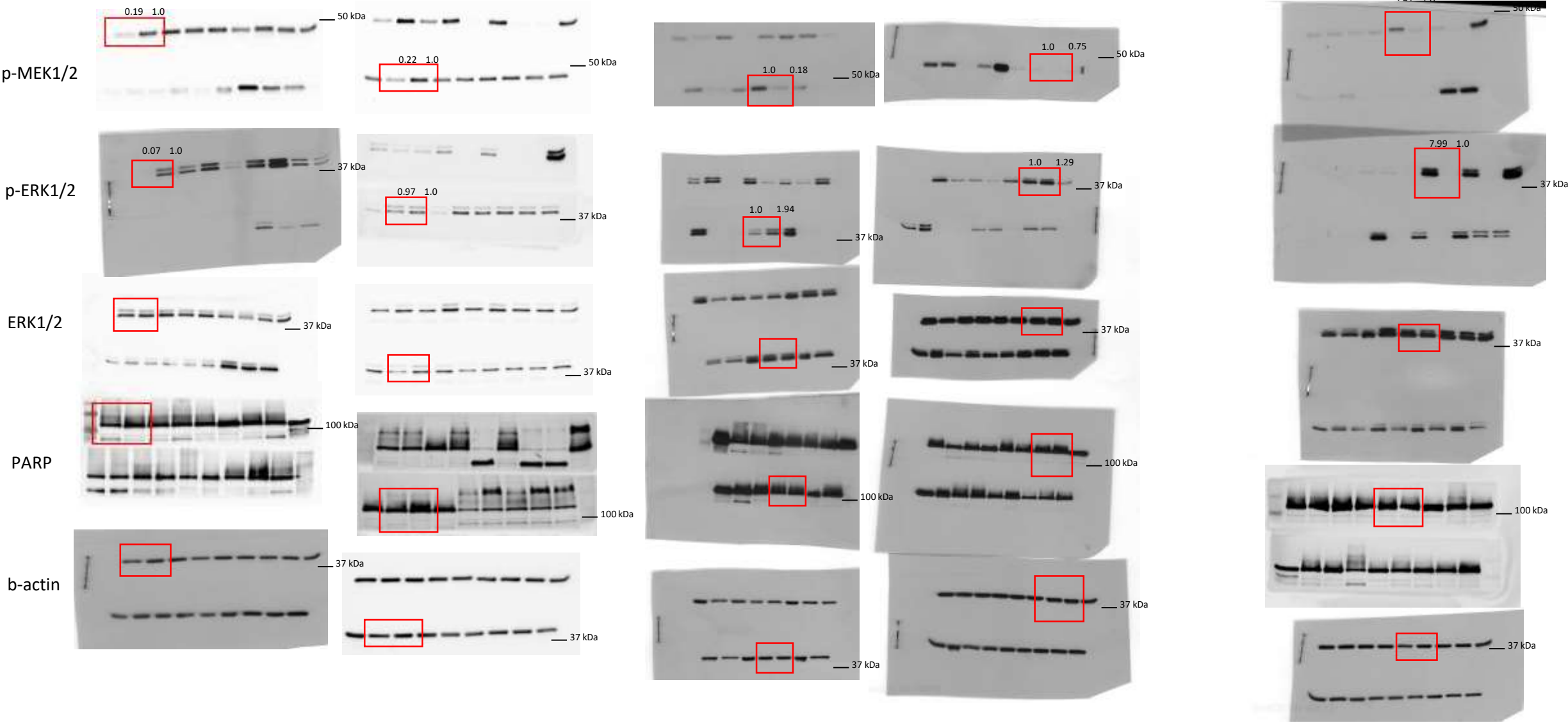
Corresponding to Figure 4D



Corresponding to Figure 5A

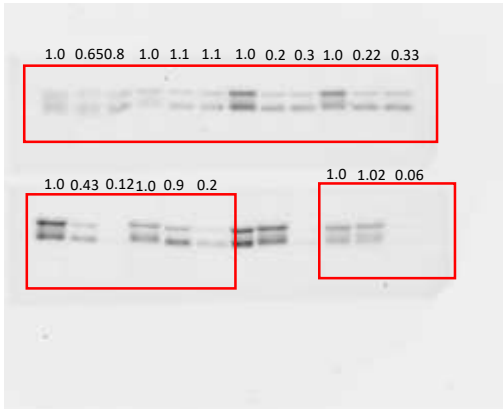


Corresponding to Figure 5A (continued)

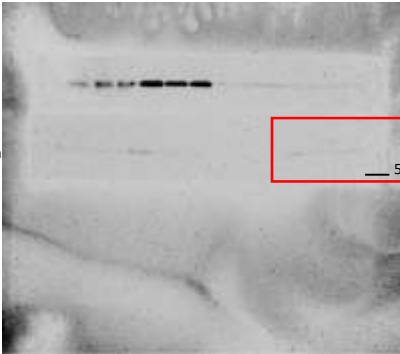
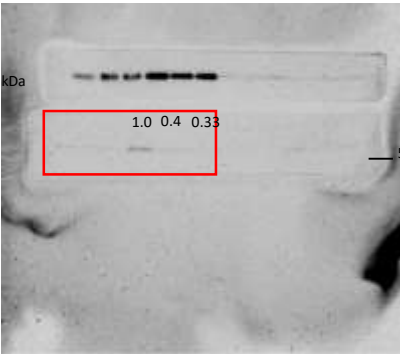
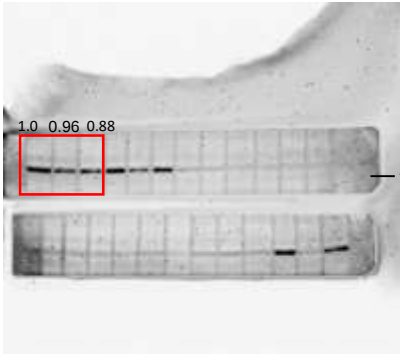


Corresponding to Figure 6B

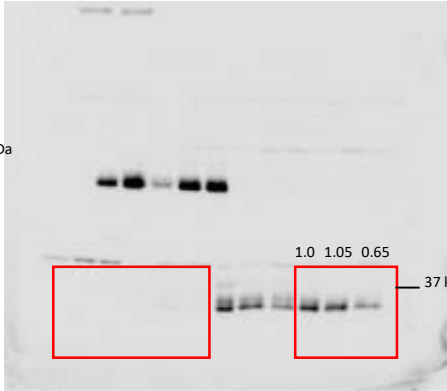
DUSP6



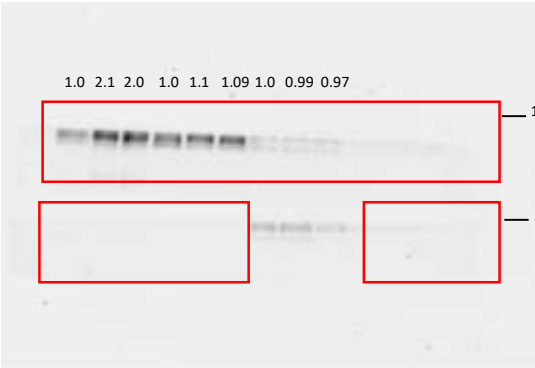
p-AKT



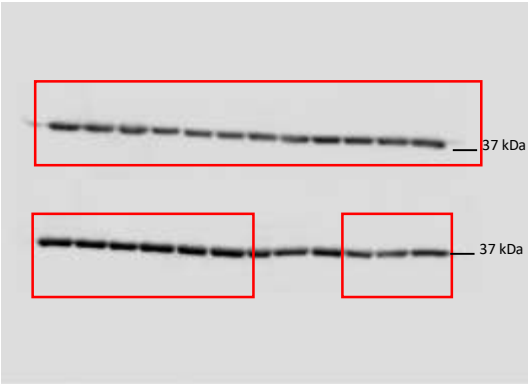
SOX2



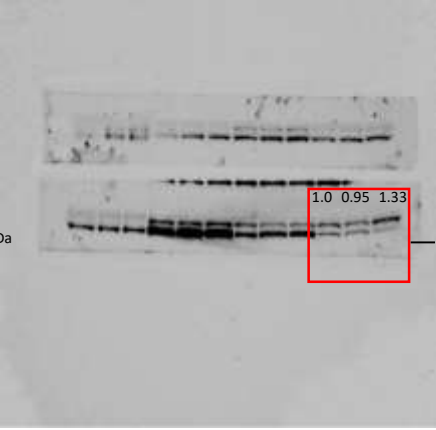
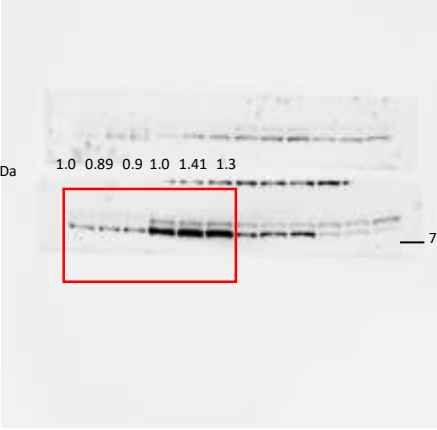
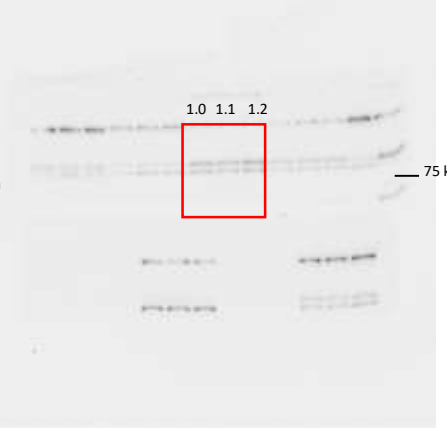
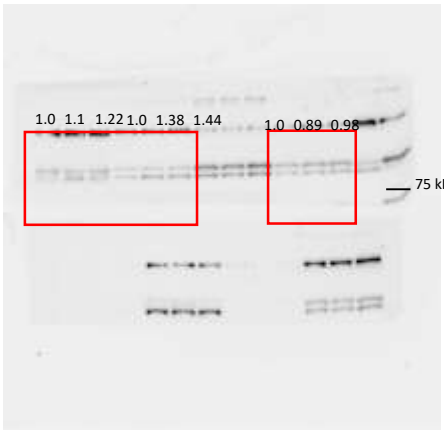
AXL



GAPDH



active
b-catenin



The original Human Phospho-Kinase Array membranes corresponding to Figures 3A and 6A.

