

**Supplementary Table S1: Genes incorporated in the FusionPlex® RadboudV1**

<b>Gene</b>	<b>NM Reference</b>	<b>Coverage (exons), 5' or 3' directionality not shown</b>
<b>ABL1</b>	NM_005157	exon 1, 2, 3, 4
<b>ABL2</b>	NM_007314	exon 2, 3, 4, 5, 6
<b>ALK</b>	NM_004304	exon 2, 4, 6, 10, 16, 17, 18, 19, 20, 21, 22, 23, 26
<b>BCOR</b>	NM_001123385	exon 6, 7, 8, 12, 14, 15
	NM_017745	exon 8
<b>BRAF</b>	NM_004333	exon 1, 2, 3, 7, 8, 9, 10, 11, 12, 13, 15, 16
<b>CAMTA1</b>	NM_015215	exon 3, 8, 9, 10
<b>CIC</b>	NM_015125	exon 18, 19, 20
<b>EGFR</b>	NM_005228	exon 1, 7, 8, 9, 16, 19, 20, 24, 25
<b>ERBB2</b>	NM_004448	exon 4, 5, 23, 24, 25, 26
<b>ERG</b>	NM_004449	exon 2, 3, 4, 5, 6, 7, 8, 9, 10, 11
<b>ETV6</b>	NM_001987	exon 1, 2, 3, 4, 5, 6, 7
<b>EWSR1</b>	NM_005243	exon 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14
<b>FGFR1</b>	NM_015850	exon 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 17
<b>FGFR2</b>	NM_000141	exon 2, 5, 7, 8, 9, 10, 16, 17
<b>FGFR3</b>	NM_000142	exon 3, 5, 8, 9, 10, 16, 17
<b>FOS</b>	NM_005252	exon 1, 2, 3, 4
<b>FOSB</b>	NM_006732	exon 1, 2, 3
	NM_001114171	exon 1, 2, 3
<b>FOXO1</b>	NM_002015	exon 1, 2, 3
<b>FUS</b>	NM_004960	exon 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14
<b>GLI1</b>	NM_005269	exon 4, 5, 6, 7
<b>HMGA2</b>	NM_003483	exon 1, 2, 3, 4, 5
<b>JAZF1</b>	NM_175061	exon 2, 3, 4
<b>MALT1</b>	NM_006785	exon 2, 3, 4, 5, 6, 7, 9, 10
<b>MAML2</b>	NM_032427	exon 2, 3
<b>MET</b>	NM_000245	exon 2, 4, 5, 6, 13, 14, 15, 16, 17, 21
<b>MKL2</b>	NM_014048	exon 11, 12, 13
<b>MYB</b>	NM_001130173	exon 7, 8, 9, 11, 12, 13, 14, 15, 16
<b>MYBL1</b>	NM_001080416	exon 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16
	NM_001144755	exon 8
<b>NCOA1</b>	NM_147223	exon 12, 13, 14, 15
<b>NCOA2</b>	NM_006540	exon 11, 12, 13, 14, 15, 16
	NM_005596	exon 5, 6, 7, 8, 9
<b>NFIB</b>	NM_001190737	exon 9, 10
<b>NR4A3</b>	NM_173200	exon 3, 4
<b>NR4A3</b>	NM_006981	exon 4
	NM_013962	exon 1
<b>NRG1</b>	NM_004495	exon 1, 2, 3, 6
	NM_013957	exon 1, 4, 8
<b>NTRK1</b>	NM_002529	exon 2, 4, 6, 8, 10, 11, 12, 13, 14, 15

<b>NTRK2</b>	NM_006180	exon 5, 7, 9, 11, 12, 13, 14, 15, 16, 17
<b>NTRK3</b>	NM_002530	exon 4, 7, 10, 12, 13, 14, 15, 16
	NM_001007156	exon 15
<b>PDGFB</b>	NM_002608	exon 2, 3
<b>PDGFRB</b>	NM_002609	exon 8, 9, 10, 11, 12, 13, 14
<b>PHF1</b>	NM_024165	exon 1, 2, 3, 4, 5, 6, 7, 8
<b>PLAG1</b>	NM_002655	exon 1, 2, 3, 4
<b>PPARG</b>	NM_015869	exon 1, 2, 3
<b>PRKD1</b>	NM_002742	exon 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17
<b>PRKD2</b>	NM_016457	exon 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17
<b>PRKD3</b>	NM_005813	exon 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17
	NM_133509	exon 11
<b>RAD51B</b>	NM_002877	exon 11
	NM_133510	exon 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11
<b>RAF1</b>	NM_002880	exon 4, 5, 6, 7, 8, 9, 10, 11, 12
<b>RET</b>	NM_020975	exon 8, 9, 10, 11, 12, 13, 14
	NM_020630	exon 2, 4, 6
<b>ROS1</b>	NM_002944	exon 2, 4, 7, 31, 32, 33, 34, 35, 36, 37
<b>SS18</b>	NM_001007559	exon 4, 5, 6, 8, 9, 10, 11
<b>STAT6</b>	NM_001178078	exon 1, 2, 3, 4, 5, 6, 7, 15, 16, 17, 18, 19, 20
<b>TFE3</b>	NM_006521	exon 2, 3, 4, 5, 6, 7, 8, 10
<b>THADA</b>	NM_022065	exon 24, 25, 26, 27, 28, 29, 30, 36, 37
<b>TMPRSS2</b>	NM_005656	exon 1, 3, 4, 5, 6
	NM_001135099	exon 1, 2
<b>USP6</b>	NM_004505	exon 1, 2, 3
<b>YWHAE</b>	NM_006761	exon 5

**Supplementary Table S2: Genes incorporated in TruSight Oncology 500 panel**

TSO500 panel										
ABL1	BRD4	CUX1	FAM175A	GATA6	IGF1	MAP3K13	NOTCH4	POLE	RPTOR	TAF1
ABL2	BRIP1	CXCR4	FAM46C	GEN1	IGF1R	MAP3K14	NPM1	PPARG	RUNX1	TBX3
ACVR1	BTG1	CYLD	FANCA	GID4	IGF2	MAP3K4	NRAS	PPM1D	RUNX1T1	TCEB1
ACVR1B	BTK	DAXX	FANCC	GLI1	IKBKE	MAPK1	NRG1	PPP2R1A	RYBP	TCF3
AKT1	C11orf30	DCUN1D1	FANCD2	GNA11	IKZF1	MAPK3	NSD1	PPP2R2A	SDHA	TCF7L2
AKT2	CALR	DDR2	FANCE	GNA13	IL10	MAX	NTRK1	PPP6C	SDHAF2	TERC
AKT3	CARD11	DDX41	FANCF	GNAQ	IL7R	MCL1	NTRK2	PRDM1	SDHB	TERT
ALK	CASP8	DHX15	FANCG	GNAS	INHA	MDC1	NTRK3	PREX2	SDHC	TET1
ALOX12B	CBFB	DICER1	FANCI	GPR124	INHBA	MDM2	NUP93	PRKAR1A	SDHD	TET2
ANKRD11	CBL	DIS3	FANCL	GPS2	INPP4A	MDM4	NUTM1	PRKCI	SETBP1	TFE3
ANKRD26	CCND1	DNAJB1	FAS	GREM1	INPP4B	MED12	PAK1	PRKDC	SETD2	TFRC
APC	CCND2	DNMT1	FAT1	GRIN2A	INSR	MEF2B	PAK3	PRSS8	SF3B1	TGFBR1
AR	CCND3	DNMT3A	FBXW7	GRM3	IRF2	MEN1	PAK7	PTCH1	SH2B3	TGFBR2
ARAF	CCNE1	DNMT3B	FGF1	GSK3B	IRF4	MET	PALB2	PTEN	SH2D1A	TMEM127
ARFRP1	CD274	DOT1L	FGF10	H3F3A	IRS1	MGA	PARK2	PTPN11	SHQ1	TMPRSS2
ARID1A	CD276	E2F3	FGF14	H3F3B	IRS2	MITF	PARP1	PTPRD	SLIT2	TNFAIP3
ARID1B	CD74	EED	FGF19	H3F3C	JAK1	MLH1	PAX3	PTPRS	SLX4	TNFRSF14
ARID2	CD79A	EGFL7	FGF2	HGF	JAK2	MLL	PAX5	PTPRT	SMAD2	TOP1
ARID5B	CD79B	EGFR	FGF23	HIST1H1C	JAK3	MLLT3	PAX7	QKI	SMAD3	TOP2A
ASXL1	CDC73	EIF1AX	FGF3	HIST1H2BD	JUN	MPL	PAX8	RAB35	SMAD4	TP53
ASXL2	CDH1	EIF4A2	FGF4	HIST1H3A	KAT6A	MRE11A	PBRM1	RAC1	SMARCA4	TP63
ATM	CDK12	EIF4E	FGF5	HIST1H3B	KDM5A	MSH2	PDCD1	RAD21	SMARCB1	TRAF2
ATR	CDK4	EML4	FGF6	HIST1H3C	KDM5C	MSH3	PDCD1LG2	RAD50	SMARCD1	TRAF7
ATRX	CDK6	EP300	FGF7	HIST1H3D	KDM6A	MSH6	PDGFRA	RAD51	SMC1A	TSC1
AURKA	CDK8	EPCAM	FGF8	HIST1H3E	KDR	MST1	PDGFRB	RAD51B	SMC3	TSC2
AURKB	CDKN1A	EPHA3	FGF9	HIST1H3F	KEAP1	MST1R	PDK1	RAD51C	SMO	TSHR
AXIN1	CDKN1B	EPHA5	FGFR1	HIST1H3G	KEL	MTOR	PDPK1	RAD51D	SNCAIP	U2AF1
AXIN2	CDKN2A	EPHA7	FGFR2	HIST1H3H	KIF5B	MUTYH	PGR	RAD52	SOCS1	VEGFA
AXL	CDKN2B	EPHB1	FGFR3	HIST1H3I	KIT	MYB	PHF6	RAD54L	SOX10	VHL
B2M	CDKN2C	ERBB2	FGFR4	HIST1H3J	KLF4	MYC	PHOX2B	RAF1	SOX17	VTCN1
BAP1	CEBPA	ERBB3	FH	HIST2H3A	KLHL6	MYCL1	PIK3C2B	RANBP2	SOX2	WISP3
BARD1	CENPA	ERBB4	FLCN	HIST2H3C	KMT2B	MYCN	PIK3C2G	RARA	SOX9	WT1
BBC3	CHD2	ERCC1	FLI1	HIST2H3D	KMT2C	MYD88	PIK3C3	RASA1	SPEN	XIAP
BCL10	CHD4	ERCC2	FLT1	HIST3H3	KMT2D	MYOD1	PIK3CA	RB1	SPOP	XPO1
BCL2	CHEK1	ERCC3	FLT3	HLA-A	KRAS	NAB2	PIK3CB	RBM10	SPTA1	XRCC2
BCL2L1	CHEK2	ERCC4	FLT4	HLA-B	LAMP1	NBN	PIK3CD	RECQL4	SRC	YAP1
BCL2L11	CIC	ERCC5	FOXA1	HLA-C	LATS1	NCOA3	PIK3CG	REL	SRSF2	YES1
BCL2L2	CREBBP	ERG	FOXL2	HNF1A	LATS2	NCOR1	PIK3R1	RET	STAG1	ZBTB2
BCL6	CRKL	ERRFI1	FOXO1	HNRNPK	LMO1	NEGR1	PIK3R2	RFWD2	STAG2	ZBTB7A
BCOR	CRLF2	ESR1	FOXP1	HOXB13	LRP1B	NF1	PIK3R3	RHEB	STAT3	ZFHX3
BCORL1	CSF1R	ETS1	FRS2	HRAS	LYN	NF2	PIM1	RHOA	STAT4	ZNF217
BCR	CSF3R	ETV1	FUBP1	HSD3B1	LZTR1	NFE2L2	PLCG2	RICTOR	STAT5A	ZNF703
BIRC3	CSNK1A1	ETV4	FYN	HSP90AA1	MAGI2	NFKBIA	PLK2	RIT1	STAT5B	ZRSR2

<i>BLM</i>	<i>CTCF</i>	<i>ETV5</i>	<i>GABRA6</i>	<i>ICOSLG</i>	<i>MALT1</i>	<i>NKX2-1</i>	<i>PMAIP1</i>	<i>RNF43</i>	<i>STK11</i>
<i>BMPR1A</i>	<i>CTLA4</i>	<i>ETV6</i>	<i>GATA1</i>	<i>ID3</i>	<i>MAP2K1</i>	<i>NKX3-1</i>	<i>PMS1</i>	<i>ROS1</i>	<i>STK40</i>
<i>BRAF</i>	<i>CTNNA1</i>	<i>EWSR1</i>	<i>GATA2</i>	<i>IDH1</i>	<i>MAP2K2</i>	<i>NOTCH1</i>	<i>PMS2</i>	<i>RPS6KA4</i>	<i>SUFU</i>
<i>BRCA1</i>	<i>CTNNB1</i>	<i>EZH2</i>	<i>GATA3</i>	<i>IDH2</i>	<i>MAP2K4</i>	<i>NOTCH2</i>	<i>PNRC1</i>	<i>RPS6KB1</i>	<i>SUZ12</i>
<i>BRCA2</i>	<i>CUL3</i>	<i>FAM123B</i>	<i>GATA4</i>	<i>IFNGR1</i>	<i>MAP3K1</i>	<i>NOTCH3</i>	<i>POLD1</i>	<i>RPS6KB2</i>	<i>SYK</i>

**Supplementary Table S3: virtual TSO500 panel that mainly contains genes in which aberrations may lead to targeted treatment**

Analyzed genes	TS/O/R <sup>1</sup>	Counted as targetable <sup>2</sup>
<i>AR</i>	O,R	No
<i>AKT1</i>	O	Mut/Amp
<i>AKT2</i>	O	Mut/Amp
<i>AKT3</i>	O	Mut/Amp
<i>ALK</i>	O,R	Fus <sup>3</sup>
<i>ATM</i>	TS	Bi-allelic inactivation
<i>BARD1</i>	TS	Bi-allelic inactivation
<i>BRAF</i>	O	Mut/Fus <sup>3</sup>
<i>BRCA1</i>	TS	Bi-allelic inactivation
<i>BRCA2</i>	TS	Bi-allelic inactivation
<i>BRIP1</i>	TS	Bi-allelic inactivation
<i>B2M</i>	R	No
<i>CCND1</i>	O	Amp
<i>CDK12</i>	TS,O	Bi-allelic inactivation
<i>CDK4</i>	O	Mut/Amp
<i>CDK6</i>	O	Amp
<i>CDKN2A</i>	TS	Bi-allelic inactivation
<i>EGFR</i>	O,R	Mut/Fus <sup>3</sup>
<i>ERBB2</i>	O	Mut/Amp
<i>ERBB4</i>	O	Mut
<i>FANCL</i>	TS	Bi-allelic inactivation
<i>FGFR1</i>	O	Mut/Amp/Fus <sup>3</sup>
<i>FGFR2</i>	O	Mut/Amp/Fus <sup>3</sup>
<i>FGFR3</i>	O	Mut/Amp/Fus <sup>3</sup>
<i>FGFR4</i>	O	Mut/Amp
<i>HRAS</i>	O	Mut
<i>JAK1</i>	R	No
<i>JAK2</i>	O,R	No
<i>KIT</i>	O,R	Mut/Amp
<i>KRAS</i>	O	Mut (only G12C)
<i>MAP2K1</i>	O	Mut
<i>MAP2K2</i>	O	Mut
<i>MAP2K4</i>	TS	Bi-allelic inactivation
<i>MAP3K1</i>	TS	Bi-allelic inactivation
<i>MET</i>	O	Mut/Amp/Fus <sup>3</sup>
<i>MLH1</i>	TS	Bi-allelic inactivation
<i>MSH2</i>	TS	Bi-allelic inactivation
<i>MSH6</i>	TS	Bi-allelic inactivation
<i>NOTCH1</i>	TS, O	Activating Mut
<i>NOTCH2</i>	O	Activating Mut
<i>NOTCH3</i>	O	Activating Mut

<i>NOTCH4</i>	TS, O	No
<i>NRAS</i>	O	Mut
<i>PALB2</i>	TS	Bi-allelic inactivation
<i>PDGFRA</i>	O	Mut/Amp
<i>PDGFRB</i>	O	Mut/Amp
<i>PIK3CA</i>	O	Mut
<i>PIK3R1</i>	TS	Bi-allelic inactivation/activating mutations
<i>PIK3R2</i>	TS	Bi-allelic inactivation
<i>POLE</i>	TS	No
<i>PPP2R2A</i>	TS	Bi-allelic inactivation
<i>PTEN</i>	TS	Bi-allelic inactivation
<i>RAD51B</i>	TS	Bi-allelic inactivation
<i>RAD51C</i>	TS	Bi-allelic inactivation
<i>RAD51D</i>	TS	Bi-allelic inactivation
<i>RAD54L</i>	TS	Bi-allelic inactivation
<i>RAF1</i>	O	No
<i>RET</i>	O	Mut/Fus <sup>3</sup>
<i>TP53</i>	TS	No
<i>TSC1</i>	TS	Bi-allelic inactivation
<i>TSC2</i>	TS	Bi-allelic inactivation
MSI	-	≥25% unstable sites; in case of 10-25% unstable sites, confirm with MMR IHC
TMB	-	≥15mut/Mb

1. TS: Tumor suppressor; O: Oncogene; R: Resistance gene  
2. Only (likely) pathogenic mutations were counted as targetable, scored following recommendations of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Bi-allelic inactivation: mut and/or loss.  
Abbreviations: Mut: mutation; Amp: amplification; Fus: fusion; MSI: microsatellite instability; MMR: mismatch repair; IHC: immunohistochemistry; TMB: tumor mutational burden.  
3. Fusions are not detectable by the TSO500 panel, but fusions in these genes were detectable by the FusionPlex® RadboudV1 panel that was used too in this study. In this panel fusions in these genes were counted as actionable: *ABL1*, *ALK*, *BRAF*, *EGFR*, *FGFR1-3*, *MAML2*, *MET*, *NRG1*, *NTRK1-3*, *RET* and *ROS1*.