A

Non-synonymous mutation density

set	ALL	BRAF_V600E	not BRAF_V600E	Fusions	not Fusions	DNA repair	not DNA repair	PI3K pathway	not PI3K pathway	Chromatin remodelers	not Chromatin remodelers
Ns	402	235	167	60	333	32	370	110	292	79	323
mean	0.406	0.418	0.389	0.369	0.416	0.541	0.392	0.503	0.366	0.571	0.363
median	0.367	0.345	0.375	0.310	0.369	0.450	0.357	0.455	0.310	0.507	0.317
stdev	0.278	0.314	0.217	0.235	0.286	0.388	0.262	0.293	0.264	0.394	0.220
MAD	0.196	0.216	0.170	0.185	0.198	0.310	0.186	0.205	0.182	0.273	0.168
IQR	0.307	0.311	0.280	0.343	0.290	0.547	0.304	0.305	0.251	0.427	0.269
MIN	0	0	0	0.033	0	0	0	0.070	0	0.035	0
MAX	2.158	2.158	1.138	1.049	2.158	1.541	2.162	2.116	2.211	2.124	1.630
P			0.878		0.301		0.046		9.33E-08		3.23E-07

Non-synonymous Mutation density age-fit residuals

set	ALL age fit residual	BRAF_V600E age fit residual	not BRAF_V600E age fit residual	Fusions age fit residual	not Fusions age fit residual	DNA repair age fit residual	not DNA repair age fit residual	PI3K pathway age fit residual	not PI3K pathway age fit residual	Chromatin remodeler age fit residual	not Chromatin remodeler age fit residual
Ns	402	235	167	60	333	32	370	110	292	79	323
mean	0.004	0.008	-0.001	0.019	0.002	0.092	-0.002	0.081	-0.024	0.121	-0.024
median	-0.024	-0.034	-0.009	-0.007	-0.030	-0.053	-0.023	0.018	-0.045	0.034	-0.043
stdev	0.240	0.261	0.206	0.212	0.244	0.333	0.229	0.285	0.215	0.322	0.202
MAD	0.169	0.178	0.156	0.153	0.170	0.266	0.163	0.199	0.156	0.224	0.152
IQR	0.260	0.266	0.246	0.218	0.261	0.422	0.251	0.308	0.236	0.309	0.240
MIN	-0.486	-0.423	-0.486	-0.337	-0.492	-0.275	-0.482	-0.368	-0.476	-0.388	-0.476
MAX	1.687	1.687	0.759	0.758	1.685	1.009	1.693	1.706	1.368	1.687	1.099
P*			0.516		0.341		0.447		3.40E-04		5.94E-05

B

Gene Fusion	# Tumours	Frequency	$BRAF^{V600E}$- vs. *RAS*-like phenotype
CCD6/RET	21	4.3%	$BRAF^{V600E}$-like (15), 6 un
NCOA4/RET	5	1.0%	$BRAF^{V600E}$-like (4), 1 un
ERC1/RET	2	0.4%	$BRAF^{V600E}$-like, all
APAK13/RET	1	0.2%	$BRAF^{V600E}$-like
FKBP15/RET	1	0.2%	*RAS*-like
SPECC1L/RET	1	0.2%	$BRAF^{V600E}$-like
TBL1XR1/RET	1	0.2%	un
TRIM27/RET	1	0.2%	un
***RET*, total**	**33**	6.8%	**$BRAF^{V600E}$-like (23), RAS-like (1), un (9)**
SND1/BRAF	3	0.6%	$BRAF^{V600E}$-like (1), un (2)
AGK/BRAF	1	0.2%	$BRAF^{V600E}$-like
AP3B1/BRAF	1	0.2%	$BRAF^{V600E}$-like
BLC2L11/BRAF	1	0.2%	un
CCNY/BRAF	1	0.2%	$BRAF^{V600E}$-like
ERC1/BRAF	1	0.2%	$BRAF^{V600E}$-like
FAM114A2/BRAF	1	0.2%	$BRAF^{V600E}$-like
MACF1/BRAF	1	0.2%	$BRAF^{V600E}$-like
MKRN1/BRAF	1	0.2%	$BRAF^{V600E}$-like
SVOPL/BRAF	1	0.2%	un
ZC3HAV1/BRAF	1	0.2%	un
***BRAF*, total**	**13**	2.7%	**$BRAF^{V600E}$-like (8), un (5)**
ETV6/NTRK3	5	1.0%	$BRAF^{V600E}$-like (3), RAS-like (1), un (1)
RBPMS/NTRK3	1	0.2%	RAS-like
***NTRK3*, total**	**6**	1.2%	**$BRAF^{V600E}$-like (3), RAS-like (2), un (1)**
RPS2P32/THADA	2	0.4%	*RAS*-like, all
IGF2BP3/THADA	2	0.4%	*RAS*-like, all
FLJ10661/THADA	1	0.2%	*RAS*-like
TG/THADA	1	0.2%	*RAS*-like
***THADA*, total**	**6**	1.2%	*RAS*-like, all
PAX8/PPARG	**4**	0.8%	***RAS*-like, all**
IRFSBP2/NTRK1	1	0.2%	$BRAF^{V600E}$-like
SQSTM1/NTRK1	1	0.2%	$BRAF^{V600E}$-like
SSBP2/NTRK1	1	0.2%	*RAS*-like
TFG/NTRK1	1	0.2%	$BRAF^{V600E}$-like
***NTRK1*, total**	**4**	0.8%	**$BRAF^{V600E}$-like (3), *RAS*-like (1)**
EML4/ALK	1	0.2%	un
GTF2IRD1/ALK	1	0.2%	$BRAF^{V600E}$-like
MALAT1/ALK	1	0.2%	$BRAF^{V600E}$-like
STRN/ALK	1	0.2%	*RAS*-like
***ALK*, total**	**4**	0.8%	**$BRAF^{V600E}$-like (2), *RAS*-like (1), un (1)**
OFD1/FGFR2	1	0.2%	*RAS*-like
VCL/FGFR2	1	0.2%	*RAS*-like
***FGFR2*, total**	**2**	0.4%	***RAS*-like, all**
TFG/MET	1	0.2%	$BRAF^{V600E}$-like
UACA/LTK	1	0.2%	$BRAF^{V600E}$-like
Total	**74**	**15.3%**	**$BRAF^{V600E}$-like (41, 55.4%)** ***RAS*-like (18, 24.3%)** **unknown (15, 20.3%)**

C

SUBNETWORK	KEGG PATHWAYS ENRICHMENTS		PROTEIN COMPLEXES (PINdb) ENRICHMENTS	
	Name	p-value	Name	p-value
ADAMTS2(3) AMBP(1) BRAF(250) CCDC88A(1) HRAS(14) ITIH1(1) KRAS(4) MAP3K1(2) NRAS(34) PIK3CA(2) PIK3CD(1) PIK3CG(1) PIK3R5(3) RAP1GAP(1) RGL1(1) RGL2(1)	Renal cell carcinoma	2 x 10^{-9}		
	ErbB signaling	6 x 10^{-8}		
	MAPK signaling	0.03		
CACHD1(2) CNTNAP4(1) IGSF1(2) KIAA0240(2) MACF1(3) NRXN1(4) NRXN2(1) PDZD2(2) RANBP10(1) SIPA1L1(1) SYT1(1) THSD7B(1) ZMIZ1(2)				
COL1A2(1) COL5A1(3) COL5A3(5) LPL(1) LRP1(5) LRPAP1(2) RELN(1) SORL1(1) THBS1(1) VLDLR(1)	ECM-receptor interaction	7x10^{-4}		
	Focal adhesion	0.02		
C4BPA(1) F10(2) F8(1) F9(1) HIST1H1C(1) MAP3K3(3) PROC(1) PROS1(2) VWF(2)	Complement and coagulation cascades	6x10^{-9}		
ACVR2A(1) ACVR2B(1) BTBD3(1) CUL9(1) DSCAML1(1) INHBA(1) MAGI2(1) MAGI3(1) PLXNB3(2)				
APOB(5) CALCR(1) CANX(1) CD3D(1) CD3E(1) CFTR(2) HSP90B1(1) MTTP(2)				
ATM(5) ATR(3) BRCA2(3) CHEK2(5) FANCD2(3) FANCF(1) FANCG(2) FANCM(1)	p53 signaling	0.02	FANCA-core; FANCA-associated	8x10^{-5}
EXPH5(1) MYO5A(1) RAB27A(2) SYTL3(2) SYTL4(2) SYTL5(1)				
FLT4(1) KDR(2) NRP1(1) SEMA3A(1) SH2D2A(1) VEGFA(1)	VEGF signaling pathway	0.03		
ABCA1(1) DLG2(1) GRIN2A(1) GRIN2B(3) PTK2B(2)				
ADAM15(2) LGALS13(1) PACSIN3(1) SNX9(1) SP4(3)				
AKAP12(1) DBN1(2) EED(2) EZH1(2) FHL1(1)				
ANK1(3) CD44(1) OBSCN(5) SPTA1(6) SPTB(1)				
APAF1(2) CASP5(1) NLRC4(2) NLRP1(2) NOD2(1)	NOD-like receptor signaling	8x10^{-6}		
CPE(2) POLR1A(1) POLR1B(2) ROBO2(2) TRIM13(1)				
FGA(1) GANAB(2) MAN2C1(1) PRKCSH(1) PRRC2A(4)				
PDS5A(1) PDS5B(1) SMC3(1) STAG1(1) STAG2(1)			SNF2h/cohesin	5x10^{-4}

D

	Gene symbol	Entrez gene ID	Subtype mutations	Total mutations	HG P-value (uncorrected)
Subtype 1 (Ras-like)	CHEK2	11200	4	5	2.31E-02
	HRAS	3265	13	13	3.70E-08
	NRAS	4893	33	33	0.00E+00
	NTRK1	4914	4	4	5.90E-03
	PAX8	7849	4	4	5.90E-03
	PPARG	5468	4	5	2.31E-02
	TG	7038	10	13	2.73E-04
Subtype 2 (Ret)	CCDC6	8030	14	14	1.33E-15
	NCOA4	8031	4	4	9.10E-05
	NTRK3	4916	5	5	8.34E-06
	RET	5979	22	22	6.66E-16
Subtype 3 (Raf-like)	BRAF	673	229	232	4.44E-16
	CACNA1E	777	4	5	3.69e-01
	CD163	9332	4	4	1.45e-01
	DNAH9	1770	6	8	3.54e-01
	EVPL	2125	4	4	1.45e-01
	GPR98	84059	4	5	3.69e-01
	ITPR2	3709	4	5	3.69e-01
	MLL	4297	5	7	4.60e-01
	MLL3	58508	4	4	1.45e-01
	OBSCN	84033	5	5	8.91e-02
	OTUD4	54726	4	5	3.69e-01
	PCDHAC2	56134	5	5	8.91e-02
	PKHD1	5314	4	4	1.45e-01
	SHANK1	50944	4	4	1.45e-01
	SPTA1	6708	6	6	5.47e-02
	TRPM4	54795	4	4	1.45e-01
	USP9X	8239	4	4	1.45e-01
	ZFHX3	463	7	7	3.35e-02

E

TUMOURS	Age	Gender	Histological type	Risk	MACIS	Purity	Mutation density, non-syn	Mutation density, non-driver	BRS	TDS	T stage	N stage	M stage	Cancer gene census gene mutations	Protein Change	Somatic Rearrangments
TCGA-BJ-A191-01A	49	FEMALE	Other specify			0.95	0.816	0.544	0.464	-0.320	T1b	N0	M0			
TCGA-BJ-A28T-01A	34	FEMALE	Classical/usual	Intermediate		0.11	0.100	0.100	-0.107	1.588	T1	N1a	M0	ATM	ATM:p.L2452P:3	
TCGA-DJ-A13R-01A	50	MALE	Follicular	Intermediate	5.5	0.56	0.701	0.501	0.448	0.782	T3	N0	M0			
TCGA-E8-A416-01A	51	FEMALE	Classical/usual	Low	4.53	0.40	0.000	0.000	0.393	1.645	T1b	N0	M0			
TCGA-EL-A3CX-01A	22	FEMALE	Classical/usual	Low	4.09	1.00	0.311	0.276	0.169	-4.084	T2	N0	M0	APC	APC:p.R213*:16	
TCGA-EL-A3H1-01A	66	FEMALE	Classical/usual	Low	5.88	0.89	1.076	0.816	0.887	1.490	T1	N0	M0	CHD4	CHD4:p.V1492G:4	translocation CYCS-WARS
TCGA-EM-A1CW-01A	39	FEMALE	Follicular	Intermediate	4.45	0.50	0.549	0.377	0.863	1.576	T3	N0	MX	NF1, KDM5A	NF1:p.E244_splice:19; KDM5A:p.K1162Q	
TCGA-EM-A2CP-01A	26	FEMALE	Follicular	Low	4.06	0.04	0.236	0.169	0.558	0.510	T2	N0	MX			Antisense fusion: NFE2L2/TG; Protein fusion: out of frame: PAX8/SLA; Protein fusion: out of frame CLCA1/RPP30; Protein fusion: in frame HERC4/CLCA1; tandem_dup TG Duplication of 12 exons: in frame; Antisense fusion NFE2L2/TG; Protein fusion: in frame PAX8/NFE2L2
TCGA-EM-A2OV-01A	64	FEMALE	Follicular	Low	5.75	0.68	0.904	0.770	0.896	1.795	T2	N0	MX	EZH1	EZH1:p.Y642F:26	
TCGA-EM-A3FL-01A	63	FEMALE	Follicular	Low	5.49	0.48	0.841	0.538	0.931	1.949	T1b	NX	MX			
TCGA-EM-A3FR-01A	55	FEMALE	Classical/usual	Intermediate	5.3	0.74	0.837	0.703	0.888	0.950	T2	N1a	MX	SPOP	SPOP:p.P94R:45	
TCGA-ET-A3DV-01A	68	FEMALE	Follicular	Intermediate	7.7	1.00	0.669	0.401	0.874	1.183	T3	N0	MX			
TCGA-FK-A3SD-01A	61	FEMALE	Classical/usual	Low		0.80	1.171	0.836	0.990	1.806	T1	N0	M0	MLL, PDE4DIP, FBXO11	MLL:p.K1574R:3; PDE4DIP:p.Q2060K; FBXO11:p.Q72*	
TCGA-FY-A2QD-01A	61	FEMALE	Classical/usual	Low	6.68	0.90	0.211	0.141	0.908	1.798	T1	N0				Protein fusion: in frame NFIX/GATAD2A

F

	Gene symbol	Gene full name	Brief function*
1	*DIO1*	deiodinase, iodothyronine, type I	activates thyroid hormone by converting the prohormone thyroxine (T4) by outer ring deiodination (ORD) to bioactive 3,3',5-triiodothyronine (T3)
2	*DIO2*	deiodinase, iodothyronine, type II	activates thyroid hormone by converting the prohormone thyroxine (T4) by outer ring deiodination (ORD) to bioactive 3,3',5-triiodothyronine (T3)
3	*DUOX1*	dual oxidase 1	involved in synthese of thyroid hormone
4	*DUOX2*	dual oxidase 2	involved in synthese of thyroid hormone
5	*FOXE1*	forkhead box E1	thyroid transcription factor which likely plays a crucial role in thyroid morphogenesis
6	*GLIS3*	GLIS family zinc finger 3	functions as both a repressor and activator of transcription and is specifically involved in the development of pancreatic beta cells, the thyroid, eye, liver and kidney
7	*NKX2−1*	NK2 homeobox 1	thyroid-specific transcription factor that binds to the thyroglobulin promoter and regulates the expression of thyroid-specific genes
8	*PAX8*	paired box 8	transcription factor involved in thyroid follicular cell development and expression of thyroid-specific genes
9	*SLC26A4*	solute carrier family 26 (anion exchanger), member 4	iodide transmembrane transporter activity
10	*SLC5A5*	solute carrier family 5 (sodium/iodide cotransporter), member 5	sodium:iodide symporter activity, responsible for the uptake of iodine in the thyroid
11	*SLC5A8*	solute carrier family 5 (sodium/monocarboxylate cotransporter), member 8	transport iodide by a passive mechanism
12	*TG*	thyroglobulin	substrate for the synthesis of thyroxine and triiodothyronine as well as the storage of the inactive forms of thyroid hormone and iodine
13	*THRA*	thyroid hormone receptor, alpha	nuclear hormone receptor for triiodothyronine
14	*THRB*	thyroid hormone receptor, beta	nuclear hormone receptor for triiodothyronine
15	*TPO*	thyroid peroxidase	iodination of tyrosine residues in thyroglobulin and phenoxy-ester formation between pairs of iodinated tyrosines to generate the thyroid hormones, thyroxine and triiodothyronine
16	*TSHR*	thyroid stimulating hormone receptor	receptor for thyrothropin and a major controller of thyroid cell metabolism

*from http://www.ncbi.nlm.nih.gov/gene/

G

mRNA clusters

	ALL	mRNA1	mRNA2	mRNA3	mRNA4	mRNA5	P value	Test used
n	482	134	67	82	93	106		
age	46.72	49.14	44.25	42.42	44.51	50.61	1.35E-03	Kruskal-Wallis test
High-Risk	24	5	1	6	3	9	1.87E-01	Chi-square test
Intermediate-Risk	251	35	36	51	50	79	1.62E-12	Chi-square test
Low-Risk	166	82	24	18	33	9	2.22E-16	Chi-square test
CTPC	311	45	51	69	75	71	<0.01	Fisher exact test
FVPC	99	78	7	1	11	2	<0.01	Fisher exact test
TCPC	34	0	3	5	1	25	<0.01	Fisher exact test
nonsil-density	0.410	0.425	0.289	0.386	0.353	0.531	1.27E-05	Kruskal-Wallis test
mut-density	0.580	0.581	0.404	0.558	0.515	0.755	5.36E-06	Kruskal-Wallis test
nonsil-density-age-fit-residual	0.014	0.018	-0.082	0.017	-0.032	0.099	2.50E-03	Kruskal-Wallis test
BRAFV600E	229	0	29	59	58	83	<0.01	Fisher exact test
RAS	52	51	1	0	0	0	<0.01	Fisher exact test
fusion	65	8	27	8	20	2	<0.01	Fisher exact test
$BRAF^{V600E}$-like	272	0	46	66	74	86	<0.01	Fisher exact test
RAS-like	119	113	4	0	2	0	<0.01	Fisher exact test
TDS	-0.003	1.237	0.406	-0.513	-0.479	-1.059	1.20E-51	Kruskal-Wallis test
BRS	-0.298	0.784	-0.518	-0.795	-0.674	-0.877	4.37E-60	Kruskal-Wallis test
mRNA cluster 1	134	134	0	0	0	0		
mRNA cluster 2	67	0	67	0	0	0		
mRNA cluster 3	82	0	0	82	0	0		
mRNA cluster 4	93	0	0	0	93	0		
mRNA cluster 5	106	0	0	0	0	106		
miRNA cluster 1	117	89	10	9	9	0	<0.01	Fisher exact test
miRNA cluster 2	61	18	12	9	13	9	4.35E-01	Fisher exact test
miRNA cluster 3	11	5	4	0	1	1	6.90E-02	Fisher exact test
miRNA cluster 4	71	21	9	12	24	5	7.84E-04	Fisher exact test
miRNA cluster 5	77	1	9	22	40	5	<0.01	Fisher exact test
miRNA cluster 6	144	0	23	30	5	86	<0.01	Fisher exact test
meth classical 1	36	0	14	0	1	21	<0.01	Fisher exact test
meth classical 2	302	18	33	82	92	77	<0.01	Fisher exact test
meth CpG island methylated	32	32	0	0	0	0	<0.01	Fisher exact test
meth follicular	112	84	20	0	0	8	<0.01	Fisher exact test
RPPA cluster 1	124	82	18	3	14	7	<0.01	Fisher exact test
RPPA cluster 2	72	3	15	13	28	13	<0.01	Fisher exact test
RPPA cluster 3	96	21	3	28	5	39	<0.01	Fisher exact test
RPPA cluster 4	65	2	9	13	25	16	<0.01	Fisher exact test

cells with most significant devation from expected value (p<0.01)