Supplementary Information

Exome sequencing identifies recurrent somatic mutations in EIF1AX and SF3B1 in uveal melanoma with disomy 3

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Supplementary Figures 1, 2 and 3
Supplementary Tables 1- 5

Supplementary Figure 1. Multiple sequence alignment of *EIF1A* from diverse eukaryotes.

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Arabidopsis              MPKNKGKGGKNRKRGKNEADDEKRELIFKEDGQEYAQVLRMLGNGRCEAMCI-DGTKRLC 59
Chlamydomonas            MPKNKGKGGKNRKRGKNENEEEKRELVYKEDGQEYAQVIRMLGNGRLEAQCI-DGKKRLC 59
Saccharomyces            MGKKNTKGGKKGRRGKNDSDGPKRELIYKEEGQEYAQITKMLGNGRVEASCF-DGNKRMA 59
Schizosaccharomyces      MPKNKGKGGKNRRRGKNENENEKRELTYAEEGQMYAQVTKMLGNGRIEAACF-DGVKRLG 59
Homo sapiens             MPKNKGKGGKNRRRGKNENESEKRELVFKEDGQEYAQVIKMLGNGRLEALCF-DGVKRLC 59
Polysphondylium          MPKNKGKGGKNRRRGKNENE-QKRELQFKEDGQEYAQVIKMLGNGRLEAQCF-DGAKRLC 58
Caenorhabditis           MPKNKGKGGKNRRRGKNENDFMKRELDLKEEGQEYGQVSKMLGNGRVQVFCF-DGKQRVC 59
Cryptococcus             MPKNKGKGGKNNRRGKKEDGENKRELIFKEDGQEYAQVVKMLGNGRLEAKCQ-DGESRLA 59
Paramecium               MPKNKGRGGKNYRRGKNENL-TKRQLETKEDGQDYAQVIKLLGNGRLICVCLGDSKQRLG 59
                         * *:: :***: :***::    **:*   *:** *.*: ::*****    *  *. .*:
                                                  --------
                         ---------NTT-------------N-strand-----------OB-fold---------

Arabidopsis              HIRGKMHKKVWIAAGDIVLVGLRDYQDDKADVILKYMSDEARLLKAYGELPENTRLNEGI 119
Chlamydomonas            NIRGKMRKKVWVAQGDIVLVGLRDYQDEKADVIMKYTADEARVLKQYGELPEHIRINDTD 119
Saccharomyces            HIRGKLRKKVWMGQGDIILVSLRDFQDDQCDVVHKYNLDEARTLKNQGELPENAKINETD 119
Schizosaccharomyces      HIRGKLRKKVWINQGDIILLSLREFQDEKGDVILKYTADEARTLKNQGELPETAKINETD 119
Homo sapiens             HIRGKLRKKVWINTSDIILVGLRDYQDNKADVILKYNADEARSLKAYGELPEHAKINETD 119
Polysphondylium          HISGRLRKKEWINSGDIILLQLRDYQDDKADVVLRYTIDEARSLKTLGELPETAKINEAD 118
Caenorhabditis           HIRGKLRKKVWINVGDIILVGLRDYQDDKGDVILKYTPDEARRLKNEGLIPENAKLNEND 119
Cryptococcus             QIRGQMRKKVWIVVGDIILLSLRDFQDDRADVIHRYTPDEARNLKTYGELKDFQLVENQE 119
Paramecium               HIRGKMRRKVWIQNGDIVLVALREFQDEKCDVVYKYFPEEIKQLKNLKEIPENLEEGGGD 119
                         :* *::::* *:  .**:*: **::**:: **: :*  :* : **    : :
                                                               --helix--   ----     -
                         ----------OB-fold---------------------         --- 3_10 -----
                                                                         L     Cstrd

Arabidopsis              VGD-------------------------------LEDDDDNNDDDYVEFEDE-------- 140
Chlamydomonas            V---------------------------------IFEGEDKENQEYFDFD---------- 136
Saccharomyces            NFG--------------------------------FESDEDVNFEFGNADEDDEEGEDEE 147
Schizosaccharomyces      TFG--------------------------------AEGEDDLDFEF-------------- 133
Homo sapiens             TFG--------------------------------PGDDDEIQFDDIGDDDE-------- 139
Polysphondylium          TFD--------------------------------EMDG-EIPFEFVADND--------- 136
Caenorhabditis           EQDEGEVEFLDHVGDEGEAGEAKSDSDSSDSDSEKSDEEAGSDKEEESDDDSEEESDEDS 179
Cryptococcus             AGG---------------------------------EEDEEGGIEFEEA----------- 135
Paramecium               NIG-------------------------DNVVFVNKEESSSSDSDISDSDSD-------- 146
                                                                     :
                         -----------------------------CTT----------------------------

Arabidopsis              -DIDRV------------------------------------- 145
Chlamydomonas            -DIAEI------------------------------------- 141
Saccharomyces            LDIDDI------------------------------------- 153
Schizosaccharomyces      -DVDAI------------------------------------- 138
Homo sapiens             -DIDDI------------------------------------- 144
Polysphondylium          -DIVIISSTLHLDIHIHASLINP-------------------- 158
Caenorhabditis           DDSDNIREEDLAAGRGFKEDTRRGGNRGGKNKYGKRR------ 216
Cryptococcus             -DIDDI------------------------------------- 140
Paramecium               -DSSDSEPKQPQKQQPQKPQPQKAQAPAKDNKEKITKKDIDDI 188
                          *
                         -------------------CTT---------------------
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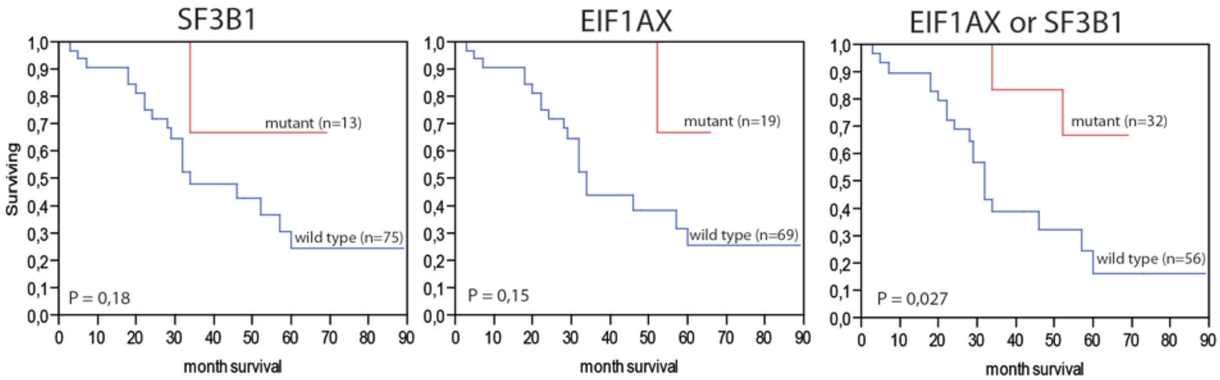
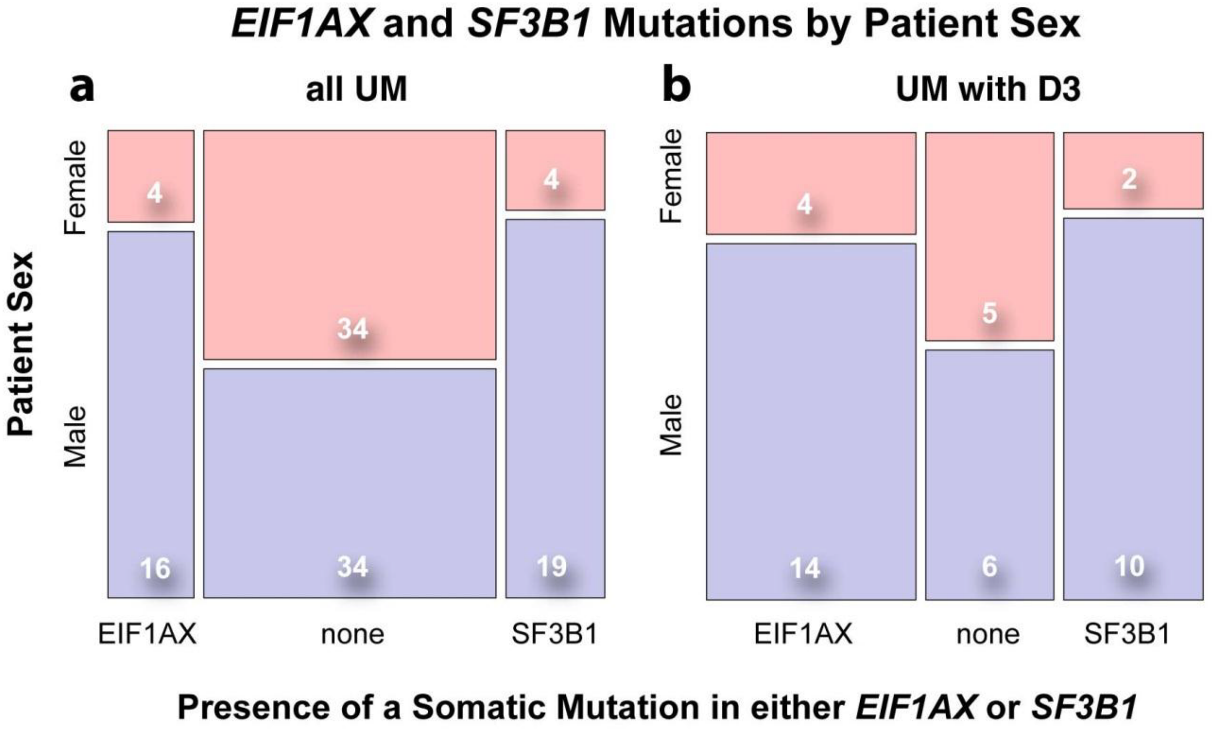
Alignments were constructed using the ClustalW2 program at http://www.ebi.ac.uk/Tools/msa/clustalw2/ using the following EIF1A sequences (accession numbers): *Saccharomyces cerevisiae* (NP_013987), *Schizosaccharomyces pombe* (NP_596359), *Homo sapiens* (NP_004672), *Polysphondylium pallidum* (EFA83042), *Arabidopsis thaliana* (AAK55703), *Caenorhabditis elegans* (NP_500650), *Chlamydomonas reinhardtii* (XP_001699781), *Cryptococcus neoformans* (XP_572552), *Paramecium tetraurelia* (XP_001451891). Sequence conservation is indicated below the last sequence, indicating invariant (*) or highly conserved (:, .) residues at the relevant positions. Beneath that are listed the structural elements identified in human EIF1A (Battiste et al, 2000), including the unstructured N-terminal tail (NTT), structured N-terminal strand (N-strand), β-barrel OB-fold, α-helix, loop, 3_{10} helix, structured C-terminal strand (Cstrd), and unstructured C-terminal tail (CTT). The first 15 residues of human *EIF1AX* are highlighted in yellow, with the positions of substitutions correlated with uveal melanoma underlined.

Supplementary Figure 2. Kaplan-Meier survival curves showing disease-specific overall survival (surviving) according to the *SF3B1* and *EIF1AX* genotype.



Kaplan-Meier analysis was used to test the statistical significance of differences between the survival curves depending on the *SF3B1* and *EIF1AX* mutation status of tumors. Analysis is based on the cohort of 88 samples comprising samples E1 to E22, M3-1 to M3-35 and D3-1 to D3-31, which were randomly chosen from the cohort of 374 tumor samples. Patients with partM3 (pM3-1 to pM3-13) and disomy 3 tumors that developed metastases (D3met-1 to D3met-10) were excluded from Kaplan Meier analysis as these samples were specifically selected for their chromosome 3 status and presence of metastatic progression, respectively. Month survival indicates the time from date of primary treatment to time of death or end of study.

Supplementary Figure 3. Association of *SF3B1* and *EIF1AX* mutations with patient sex.



Mosaic plots are used for visualization of results. (a) Numbers of tumors from male patients (blue) and female (red) patients in all uveal melanomas analyzed in this study (n=111) and (b) in the subgroup of uveal melanomas (UM) with D3 (n=51). In both cohorts, tumors with either an *EIF1AX* or a *SF3B1* mutation are more frequently from male patients (blue) compared to tumors without mutation (none). Statistical significance was reached in the cohort of all uveal melanomas (p=0.0012) Fisher's exact test.

Supplementary Table 1. Sequence variations identified by exome sequencing in 10 uveal melanomas with D3.

Gene	Nucleotide	Codon	Amino acid	Quality	Location
UM-E1 (V2)					
ABCA13	T → C	ATA → ACA	I → T	656	7:48315736
ANGPTL7	C → T	ACA → ATA	T → I	277	1:11255119
ARID2	G → A	AGA → AAA	R → K	1377	12:46287292
C11orf41	T → A	ATG → AAG	M → K	580	11:33640087
CA5BP1	C → T	ACC → ATC	T → I	866	X:15706809
CIDEB	C → G	GTT → CTT	V → L	254	14:24779900
COX7A2	T → TAA			376	6:75950109
CTAGE5	A → ATGTGTG			952	14:39784012
EIF1AX	G → C	CCC → CGC	P → R	1269	X:20159754
FGFR1	T → del 14bp			1034	8:38271136
GGN	G → GGGC			304	19:38877458
GNAQ	T → G	CAA → CCA	Q → P	1400	9:80409488
ID3	C → G	AGG → ACG	R → T	244	1:23885317
LNP1	C → ins 42 bp			10800	3:100170599
LTB4R2	C → G	AAC → AAG	N → K	254	14:24779900
MYOM2	C → T	GCC → GTC	A → V	231	8:2092886
NAGLU	C → A	CGC → AGC	R → S	423	17:40696233
PABPC1	C → CAAA			291	8:101725026
GRHPR	T → TAGGCTTGG			273	19:48613788
PRB4	T → T+ ins 60 bp			3601	12:11461553
PRDM15	C → T	GAG → AAG	E → K	1467	21:43242306
RAB5B	C → T	CGG → TGG	R → W	877	12:56385937
RIC8A	C → G	CTC → GTC	L → V	921	11:211230
SSC5D	C → CCTT			255	19:56029383
TBX21	A → G	TAC → TGC	Y → C	235	17:45822278
TSG101	TA → T			709	11:18502035
UMODL1	C → C+ ins 42 bp			1272	21:43557735
WWC3	G → A	GCC → ACC	A → T	342	X:10096160
XRCC6	G → A	GTG → ATG	V → M	1259	22:42049682
UM-E2(V1)					
ANKRD37	C → CA			281	4:186321686
ARHGDIG	T → C	TCC → CCC	S → P	91	16:331733
CD226	G → A	CGG → TGG	R → W	77	18:67530439
CLDN9	C → T	CAC → TAC	H → Y	125	16:3063111
COX7A2L	T → TA			111	2:42578274
CROCCP2	A → G	ATT → ACT	I → T	84	1:16947952
DGKI	C → T	GAA → AAA	E → K	104	7:137178550
DNAJC18	C → T	GTC → ATC	V → I	238	5:138761888
DPP6	TTACA → T			355	7:154676079
EIF1AX	T → C	AAG → GAG	K → E	126	X:20159752
EYS	A → G	TCC → CCC	S → P	84	6:65300335
FLG	C → T	AGC → AAC	S → N	76	1:152278687
GNAQ	T → A	CAA → CTA	Q → L	111	9:80409488
HIAT1	G → C			98	1:100533752
IL17RE	C → CCCCAG			637	3:9953057
KIAA1755	G → A	ACT → ATT	T → I	137	20:36868073
MTMR1	C → T	CTT → TTT	L → F	81	X:149904435
NPY5R	C → T	CCC → CTC	P → L	137	4:164265555
PIK3AP1	C → A	AGA → ATA	R → I	78	10:98353389
GRHPR	T → C	ATA → ATG	I → M	133	1:46597703
PPP1CB	C → T	ACT → ATT	T → I	178	2:28974897
PTK7	T → TAAA			70	6:43112864
SHROOM3	GAGA → G			190	4:77661673
SIGLEC1	C → T	CGT → CAT	R → H	197	20:3670193
TERT	T → C	AAT → GAT	N → D	118	5:1253283

TOM1L2	C → A	GCA → TCA	A → S	96	17:17772922
TRPM3	G → T	AAC → AAA	N → K	112	9:73151391
TRUB1	A → del 15bp			656	10:116698132
VASH1	C → A	CAC → CAA	H → Q	81	14:77229145
ZNF519	TG → T			168	18:14105271
ZNF665	C → T	CGA → CAA	R → Q	94	19:53668418
ZNF720	A → del 8bp			278	16:31769147
ZNHIT6	T → TA			103	1:86123663
UM-E3 (V2)					
ACSS2	AGTGTGT → A			487	20:33507379
DDHD1	T → TGTCGCC			786	14:53619480
DHFR	T → del 9bp			376	5:79950708
EIF1AX	T → C	AAT → GAT	N → D	2377	X:20159749
FBXO9	A → ATG			335	6:52962702
FPR1	T → C	GAG → GGG	E → G	928	19:52249682
GALK1	CCAT → C			292	17:73754552
GNA11	A → T	CAG → CTG	Q → L	961	19:3118942
HTR3D	A → ATGTCAGT			2405	3:183756836
KCND1	G → C	CCC → CGC	P → R	1224	X:48820044
KIAA1967	G → GGCAGTCC			1194	8:22477078
KRT83	G → T	TGC → TGA	C → *	1048	12:52711549
MANSC1	T → TGAA			3197	12:12483419
MICA	T → C	GTT → GCT	V → A	253	6:31380153
MSH3	TGCAGCGGCC → T			376	5:79950708
NEB	G → A	CCT → TCT	P → S	667	2:152482101
NID2	T → C	TAC → TGC	Y → C	2374	14:52472490
OBSL1	C → T	GTG → ATG	V → M	502	2:220432019
PLEKHG6	C → A	ACG → AAG	T → K	398	12:6436545
GRHPR	C → CTGG			976	8:10466024
RTKN	C → T	GAG → AAG	E → K	316	2:74666963
THSD7B	G → T	AGT → ATT	S → I	2385	2:138208478
TNXB	G → A	CGC → TGC	R → C	403	6:32025910
UM-E4(V1)					
ACSF2	G → T	GAT → TAT	D → Y	82	17:48538362
AMOTL1	G → A	GCC → ACC	A → T	79	11:94592780
C8orf17	G → A	GAA → AAA	E → K	284	8:140944536
CUL4A	G → A			118	13:113863077
FERMT1	G → T			81	20:6078161
GNA11	A → T	CAG → CTG	Q → L	127	19:3118942
MSLN	C → T	CCT → CTT	P → L	124	16:812664
OR10AG1	C → T	AGC → AAC	S → N	84	11:55735776
PAPOLB	C → T	GAT → AAT	D → N	78	7:4900817
PDXDC1	T → C	ATT → ACT	I → T	103	16:15110016
PLEKHA1	G → A	CGT → CAT	R → H	91	10:124183731
PRB4	C → ins 49 bp			547	12:11461552
RAB11FIP1	G → A	CCT → CTT	P → L	71	8:37730656
RANBP6	AT → A			73	9:6012689
RETSAT	T → C	ATC → GTC	I → V	167	2:85572948
RPS8	C → G	CTC → GTC	L → V	102	1:45242527
S1PR1	AG → A			189	1:101705688
SF3B1	C → T	GAA → AAA	E → K	84	2:198266489
SIN3A	G → A	ACG → ATG	T → M	126	15:75722562
GRHPR	G → GTT			277	1:168262525
THOC4	C → T	AGC → AAC	S → N	78	17:79849383
TMEM48	GA → G			96	1:54284760
TMSB4X	G → A	GCG → ACG	A → T	85	X:12993247
UBXN6	C → G	CGC → CCC	R → P	80	19:4457715
ZNF200	G → A	CAA → TAA	Q → *	107	16:3283671
UM-E5(V1)					
ABCE1	T → A	TAA → AAA	* → K	98	4:146044825
ADRB3	A → AGGG			91	8:37823423

AIM2	G → C	CCC → CGC	P → R	158	1:159036025
AKT1	C → CCCA			354	14:105240509
ANKLE2	A → C	GTT → GGT	V → G	87	12:133319056
ANKRD40	AAAG → A			132	17:48777819
ARHGAP8	T → TG			207	22:45182413
ARHGEF38	T → C	TCC → CCC	S → P	101	4:106552382
ATP6V1D	A → C	TTT → GTT	F → V	74	14:67819571
ATP8B4	G → A	ACG → ATG	T → M	98	15:50288951
C14orf148	C → G	TGT → TCT	C → S	84	14:77872965
C1QTNF4	C → T	GCC → ACC	A → T	161	11:47612326
C6orf27	T → C	GAG → GGG	E → G	72	6:31733787
CASK	GA → G			97	X:41383297
CCNL1	GAT → G			447	3:156870888
CGN	A → G	GAG → GGG	E → G	87	1:151502590
CIDEC	G → GCC			94	3:9911862
CTAGE12P	G → A	GCA → GTA	A → V	149	9:27610673
CTLA4	A → C	ATC → CTC	I → L	75	2:204737605
EPPK1	A → G	TTC → TCC	F → S	71	8:144946028
FAM194A	TAAC → T			210	3:150421611
FRG1	C → A	CCA → CAA	P → Q	74	4:190876293
GNA11	A → T	CAG → CTG	Q → L	160	19:3118942
GRK6	C → A	TAC → TAA	Y → *	77	5:176858882
GRPEL2P2	C → G	GTC → CTC	V → L	90	X:63917770
HDAC6	G → T	GCA → TCA	A → S	76	X:48675775
HMBOX1	T → G	TAT → TAG	Y → *	96	8:28908762
ITIH1	T → TG			125	3:52824945
KALRN	C → CT			70	3:124044864
KRT15	T → TG			178	17:39670095
KRT8P13	T → G	CTT → CGT	L → R	98	3:170213660
KRTAP19-4	G → C	TAC → TAG	Y → *	97	21:31869285
LIAS	A → C	ACC → CCC	T → P	167	4:39465205
MAN2B1	AGCT → A			363	19:12771926
MCL1	T → C	AGG → GGG	R → G	249	1:150551031
MEST	AG → A			236	7:130140501
NEFM	G → C	GGG → CGG	G → R	266	8:24775457
NHLRC3	T → TTGTGGG			1782	13:39618366
NLGN3	A → C	ACC → CCC	T → P	103	X:70387352
NRL	G → T	ACC → AAC	T → N	98	14:24551828
NTSR1	G → A	ATG → ATA	M → I	425	20:61386051
PAK1IP1	GTT → G			133	6:10695136
PAX5	TTTC → T			107	9:37034092
PEX14	C → T	CCG → CTG	P → L	112	1:10689653
PFKM	C → A	TAC → TAA	Y → *	73	12:48536648
PKP2	T → C	CAA → CGA	Q → R	86	12:32996166
PLEKHG2	G → C	GGG → CGG	G → R	92	19:39915662
POLN	C → A	GAT → TAT	D → Y	134	4:2159611
POLR1C	G → T	GAG → GAT	E → D	145	6:43497075
PPL	T → G	ACC → CCC	T → P	135	16:4935256
PSMB9	CAA → C			91	6:32824975
PUS7	C → A	GAT → TAT	D → Y	197	7:105135794
SF3B1	G → A	CGT → TGT	R → C	184	2:198267484
SH3BGRL3	TGGC → T			265	1:26606531
SLC45A4	C → T	CGG → CAG	R → Q	679	8:142231750
SLC5A3	G → A	GTT → ATT	V → I	97	21:35469715
SLC6A7	T → TG			316	5:149584111
SLC9A7P1	A → C	TGT → TGG	C → W	92	12:98849904
THOC4	CA → C			162	17:79846299
TIE1	C → T	TCT → TTT	S → F	193	1:43788419
UBE2G2	GA → G			108	21:46191155
XYLB	CTCT → C			670	3:38411758
UM-E6(V2)					

BANK1	C → A	CAA → AAA	Q → K	624	4:102965061
C3orf63	A → ATCTT			314	3:56655371
CTAGE5	GA → G			1816	14:39784901
DNM3	TGAAACAC → T			8263	1:172051048
DRG2	G → A	GAT → AAT	D → N	1525	17:18009694
EFNB1	G → A	CGG → CAG	R → Q	1542	X:68058543
EPPK1	AC → A			565	8:144940080
FAHD2B	G → T	CAC → CAA	H → Q	794	2:97751578
FAM8A6P	T → G	AAT → ACT	N → T	218	6:134925043
FOS	C → A	CCT → ACT	P → T	264	14:75747747
GIMAP2	CGTGTGTGT → C			421	7:150384193
GNAQ	T → G	CAA → CCA	Q → P	1924	9:80409488
HBE1	T → A	CAC → CTC	H → L	1014	11:5289790
LILRA4	CT → C			1537	19:54849337
LIMS2	TGGGTTGCCG → T			388	2:128432620
LRRC43	AGTAAAG → A			970	12:122687999
MTA1	C → T	CGG → TGG	R → W	277	14:105936014
MYT1L	GCTTT → G			1818	2:1844667
NEB	T → A	AAA → ATA	K → I	3050	2:152501052
GRHPR	GAATT → G			465	5:176715679
OGFOD1	C → G	CGG → GGG	R → G	1387	16:56485537
OR5T3	G → T	TGC → TTC	C → F	1945	11:56019980
PATE1	A → AC			728	11:125618727
PLA2G4C	T → TAGGCTTGG			429	19:48613788
SF3B1	C → T	CGT → CAT	R → H	1968	2:198267483
SH3D19	T → G	TTA → TTC	L → F	1132	4:152054187
SIGLEC6	CAGAGA → C			251	19:52035064
SLC19A3	ATT → A			218	2:228567111
THEM5	G → GCA			305	1:151819738
TMEM141	G → GAAGA			388	9:139694454
ZNF595	G → A	CGG → CGA	R → R	252	4:53364
ZNF99	T → T+ ins 46 bp			575	19:22939006
UM-E7(V1)					
TNFRSF8	G → T	GAG → GAT	E → D	147	1:12202435
ABCB4	A → C	TGT → TGG	C → W	73	7:87072692
ACBD5	C → T			129	10:27497174
ACOX3	G → A	CAC → TAC	H → Y	134	4:8376819
AGPAT6	G → A	CGA → CAA	R → Q	152	8:41466957
AHNAK	T → A	ATA → TTA	I → L	139	11:62292432
ALOX15P2	A → G	ATC → GTC	I → V	184	9:95678374
ANKMY1	TAAG → T			175	2:241418970
ARHGAP12	G → A	TCA → TTA	S → L	246	10:32197257
ATP5G2	G → C	GCA → GGA	A → G	102	12:54069990
BMS1P4	T → C	AAG → GAG	K → E	166	10:75479808
CARD9	G → T			144	9:139264898
CCDC141	T → G	ACT → CCT	T → P	75	2:179721067
CHKB	A → T	TAC → AAC	Y → N	88	22:51020695
CNTNAP2	C → T	ACT → ATT	T → I	213	7:146818188
CNTNAP3	T → A	TAA → TTA	* → L	96	9:39085702
CPD	G → A	GTA → ATA	V → I	174	17:28788961
CROCCP1	C → G	TCC → TGC	S → C	75	X:134571935
CTSF	T → C	GAC → GGC	D → G	94	11:66332456
CTSK	G → A	CGA → TGA	R → *	240	1:150772083
CTU2	T → G	TTT → TGT	F → C	71	16:88781759
DHX38	T → TGGG			257	16:72143354
DUPD1	G → A	CAG → TAG	Q → *	126	10:76797734
E2F1	C → T	GTA → ATA	V → I	113	20:32265070
EHMT2	G → T	TAC → TAA	Y → *	78	6:31860811
ELAC2	T → A	TTA → TTT	L → F	73	17:12920550
EMILIN3	C → T	GAG → AAG	E → K	236	20:39991371
EML1	C → T	ACT → ATT	T → I	163	14:100331923

EMR3	TG → T			162	19:14755035
EPB42	T → C	AAG → GAG	K → E	223	15:43502589
EPCAM	A → C	AAA → ACA	K → T	109	2:47606141
EPHA2	G → A	TCG → TTG	S → L	210	1:16464919
ESF1	T → C	AAA → AGA	K → R	116	20:13740377
EVL	A → G	AGC → GGC	S → G	353	14:100551148
EXOG	G → GCC			109	3:38539088
EZR	C → T	GGG → GGA	G → G	198	6:159239154
FAM38A	T → G	CAA → CAC	Q → H	71	16:88781759
GBP1	C → T	GTT → ATT	V → I	169	1:89521758
GLT25D1	C → G	GCC → GGC	A → G	74	19:17670179
GNAQ	T → G	CAA → CCA	Q → P	141	9:80409488
GPBP1	G → A	GAA → AAA	E → K	74	5:56526942
GPD1L	C → T	ACC → ATC	T → I	165	3:32181850
GPNMB	A → C			104	7:23300073
GRIA1	G → T	GTC → TTC	V → F	92	5:153077634
GRM8	C → T	CGC → CAC	R → H	219	7:126086302
H2AFY2	G → C	GGG → CGG	G → R	94	10:71835371
HCP5	T → C	TTG → TCG	L → S	420	6:31431539
HERC2P9	G → A	CGC → CAC	R → H	108	15:28900681
HEY1	C → G	GGA → GCA	G → A	317	8:80679408
HUNK	G → C	GCC → CCC	A → P	99	21:33346967
IL9RP3	G → A			121	16:83342
IQGAP3	A → G	CTC → CCC	L → P	116	1:156500012
ITGAL	A → G	CAA → CGA	Q → R	89	16:30505563
ITPR3	A → G	ATG → GTG	M → V	327	6:33639844
KCNJ1	A → G	TTT → TCT	F → S	196	11:128710101
KCNQ5	A → G	ACA → GCA	T → A	473	6:73904298
KIN	A → AC			71	10:7820992
MAPK11	G → A	CTC → TTC	L → F	112	22:50705002
MAPK7	A → G	ATG → GTG	M → V	84	17:19286718
MARCH9	T → A	GAT → GAA	D → E	166	12:58152702
MCM2	T → C	GCT → GCC	A → A	143	3:127317280
METTL14	G → A	GAA → AAA	E → K	108	4:119606619
MEX3C	T → C	TAC → TGC	Y → C	191	18:48703475
MLL5	G → A	TGT → TAT	C → Y	122	7:104750939
MLLT1	G → A	TCC → TTC	S → F	122	19:6222277
MYPN	G → A	GGA → AGA	G → R	299	10:69970244
NAPRT1	G → A	CCA → CTA	P → L	139	8:144657407
NBAS	T → G	AAA → CAA	K → Q	141	2:15694216
NDUFA4	A → G	TAC → CAC	Y → H	104	7:10973298
NR4A1	T → G	TTG → TGG	L → W	292	12:52450486
NRAP	G → A	CGT → TGT	R → C	258	10:115356934
NRSN1	A → G	AGG → GGG	R → G	138	6:24146139
NSUN7	G → C	CGA → CCA	R → P	220	4:40810367
NUDT22	G → A	GGG → AGG	G → R	76	11:63997178
NUP62	A → G	TTT → TCT	F → S	238	19:50412400
PARP4P2	C → T	TCG → TTG	S → L	137	13:19961896
PCBP2	C → A	AGC → AGA	S → R	173	12:53837549
PCDH1	G → A	CGT → TGT	R → C	129	5:141244914
PCDHA9	C → G	CAG → GAG	Q → E	74	5:140229680
PCNT	G → A	GTC → ATC	V → I	95	21:47805876
PIGO	T → TG			86	9:35095100
PIWIL3	G → A	CGT → TGT	R → C	142	22:25115756
PLAT	C → T	CGG → CAG	R → Q	135	8:42037631
PLEKHH3	C → T	GGT → AGT	G → S	168	17:40823413
POLI	C → T	CGT → TGT	R → C	173	18:51813736
POMT2	C → T	GAG → AAG	E → K	190	14:77744668
PPIL3	C → T	ATG → ATA	M → I	177	2:201746268
PRDM2	T → C	TCT → CCT	S → P	78	1:14109088
PRICKLE1	C → T	GAA → AAA	E → K	253	12:42853787

PRR13	C → A	CAT → AAT	H → N	173	12:53837549
PSMC1P9	A → G	AAT → AGT	N → S	73	12:18846957
PUS10	A → AC			78	2:61188596
PUS7L	C → A	AAG → AAT	K → N	259	12:44148905
PYGO1	G → T	CCA → CAA	P → Q	125	15:55839032
RAD52	G → A	TCT → TTT	S → F	123	12:1036290
RASSF4	G → A	CGA → CAA	R → Q	141	10:45467103
RLN1	T → C	ATG → GTG	M → V	128	9:5335550
RPAP1	G → C	ACG → AGG	T → R	396	15:41809846
RTN4IP1	G → A	CGT → TGT	R → C	209	6:107070812
SEC24C	C → T	CCT → CTT	P → L	196	10:75506754
SEC31A	A → C	CAT → CAG	H → Q	168	4:83750231
SHANK2	G → A	CCT → TCT	P → S	142	11:70319282
SIGLEC5	T → C	AAG → GAG	K → E	137	19:52115666
SLC10A2	G → A	CCG → TCG	P → S	182	13:103701690
SLC34A3	G → C	GGG → GCG	G → A	188	9:140127546
SLFN13	G → A	CTC → TTC	L → F	77	17:33769090
SPAG9	C → G	AGT → ACT	S → T	132	17:49071256
SPATA20	T → C	TCC → CCC	S → P	77	17:48626179
SSRP1	G → A	CCG → CTG	P → L	185	11:57093837
TJP2	C → A	CTT → ATT	L → I	196	9:71869368
TLN1	C → T	GCC → ACC	A → T	137	9:35706488
TMC8	C → T	GCA → GTA	A → V	263	17:76134533
TNK2	G → C			117	3:195610188
TRIM54	G → T	CAG → CAT	Q → H	277	2:27505767
TSFM	T → A	TTT → TTA	F → L	176	12:58177018
TTBK1	T → TG			77	6:43221376
TTC30B	T → C	ATC → GTC	I → V	177	2:178417020
TTN	G → A	GCA → GTA	A → V	94	2:179612821
TYK2	C → T	GAA → AAA	E → K	186	19:10488920
USP15	T → TC			262	12:62708726
VPS28	G → A	CCC → CCT	P → P	172	8:145649171
VWCE	G → C	TGC → TGG	C → W	86	11:61059000
XYLB	A → T	ACT → TCT	T → S	107	3:38411757
ZFYVE1	T → A	ATG → TTG	M → L	240	14:73442454
ZFYVE27	C → T	CGC → TGC	R → C	156	10:99508054
ZNF311	A → G	TGC → CGC	C → R	327	6:28963866
ZNF337	TGAG → T			266	20:25656747
ZNF471	A → G	AAA → GAA	K → E	83	19:57022937
ZNF714	G → A	GGT → AGT	G → S	112	19:21299771
ZSCAN12	T → C	GAA → GGA	E → G	130	6:28358610
ZSCAN5C	G → A	GCC → ACC	A → T	106	19:56718497
UM-E8 (V2)					
ABCD4	T → TCCAGAAC			797	14:74756296
ACTG2	G → GCACA			660	2:74128695
C9orf9	A → G	AGA → GGA	R → G	234	9:135765524
CHPF	T → TGG			201	2:220404354
DDX39B	AGAC → A			693	6:31498381
DDX54	C → T	GCT → ACT	A → T	219	12:113614922
DGCR8	G → ins 13 bp			3648	22:20096314
FAM177A1	TC → T			248	14:35515953
GNA11	A → T	CAG → CTG	Q → L	240	19:3118942
GRIN2B	CGTA → C			375	12:13716259
HECW2	C → G	GAC → CAC	D → H	229	2:197084802
IRF2BPL	AGCG → A			218	14:77493647
KIAA0100	CCT → C			244	17:26945865
MRPL4	GA → G			240	19:10369521
PPP2R3A	G → A	ATG → ATA	M → I	228	3:135864037
PRB4	T → ins 62 bp			631	12:11461553
TBX19	AGTGTGT → A			343	1:168262522
ZNF331	G → GTGA			274	19:54081561

UM-E9(V2)					
ACAT1	TTAAAAA → T			547	11:108018284
ACTA2	G → GT			350	10:90706753
AKR7L	A → ATTTG			308	1:19592799
BAI3	C → G	CAG → GAG	Q → E	1683	6:69943291
BBOX1	A → AC			250	11:27149300
C12orf43	AAAAG → A			2163	12:121444022
CDH8	C → T	GGC → GAC	G → D	1449	16:61761002
CDSN	G → C	CCC → GCC	P → A	248	6:31083197
CP	T → TCACAC			983	3:148897498
CPA1	A → AAC			243	7:130024308
CTNND2	G → A	TCA → TTA	S → L	3225	5:10988339
CYB5D2	A → C	GAG → GCG	E → A	217	17:4046946
DACH2	T → TTGA			284	X:86083797
DPP6	C → CATG			342	7:154675606
DUSP14	TCTC → T			292	17:35873048
DYRK1A	T → TTAAG			1060	21:38792452
FBXW7	T → G	AAA → ACA	K → T	3218	4:153251894
GNA11	A → T	CAG → CTG	Q → L	1323	19:3118942
GRB10	CTCTCTT → C			229	7:50663293
GRHPR	A → T	CAG → CTG	Q → L	241	9:37429608
HOXD3	G → A	GGG → AGG	G → R	573	2:177033774
KDM3B	GAAAA → G			227	5:137762570
LRRC46	G → C	GGA → CGA	G → R	647	17:45913048
MITF	TC → T			339	3:70014309
NCAM1	T → TTTG			1463	11:113073066
PAX4	C → CACAT			535	7:127250640
PCDHGA6	AGTG → A			818	5:140755576
PEX14	A → C	GAC → GCC	D → A	225	1:10596547
PRG4	A → ACTC			367	1:186276262
RBM43	A → G	ATA → ACA	I → T	2450	2:152107316
RFTN2	AAAC → A			299	2:198540351
RNF2	T → G	TTT → TGT	F → C	907	1:185069348
SIGLEC6	CAGAGA → C			345	19:52035064
SLC35B1	GCGCA → G			958	17:47780708
SLC35G5	A → del 9bp			221	8:11188433
SMURF2	AAGG → A			471	17:62541850
SPANXN1	C → CCT			302	X:144337370
TAC4	C → CAG			616	17:47925048
TBX19	G → GTT			2197	1:168262525
TBX4	A → AGTGT			1829	17:59560974
TCHH	T → T + ins 40bp			6356	1:152084175
TTC31	C → CTCTGA			375	2:74710771
TUBB4Q	TG → T			286	4:190904030
VAV2	A → ATGAGGGC			1659	9:136637177
VCX3A	C → A	AGC → ATC	S → I	358	X:6452024
ZFYVE21	G → ins 13bp			2958	14:104193285
ZNF544	CCTT → C			1183	19:58773994
UM-E10 (V1)					
ACOT13	G → A	TGG → TGA	W → *	123	6:24704176
ANKRD23	T → TC			233	2:97499144
CAMK4	C → CACAT			177	5:110822240
CNNM3	T → TC			233	2:97499144
DGAT1	G → T	TCC → TAC	S → Y	133	8:145539960
FAM47E	C → T	CCC → CCT	P → P	116	4:77135334
HPCAL4	C → G	GCC → CCC	A → P	84	1:40157202
KIT	A → T	AAT → TAT	N → Y	182	4:55604664
LRCH4	A → ACG			132	7:100172241
MYEF2	A → T	CTA → CAA	L → Q	74	15:48441252
NOC2L	G → C	CAC → CAG	H → Q	85	1:893910
NOL11	G → T			75	17:65732012

OLFML2B	C → T	CGA → CAA	R → Q	70	1:161953880
PAICSP2	C → T	CCA → TCA	P → S	163	9:94374087
PCDH8P1	A → G	CAC → CGC	H → R	80	13:53776427
PRKCZ	C → G	CGC → GGC	R → G	89	1:2005009
PSMD6	C → A	GTT → TTT	V → F	72	3:63996654
PXDNL	G → C	CCT → CGT	P → R	134	8:52321728
RBM12B	A → T	TTT → TAT	F → Y	80	8:94751244
GRHPR	A → ACG			132	7:100172241
SESN1	G → A	CTT → TTT	L → F	74	6:109319979
TUFT1	C → A	CTT → ATT	L → I	80	1:151538596

Supplementary Table 2. Sequence variations identified by exome sequencing in 12 uveal melanomas with M3

Gene	Nucleotide	Codon	Amino acid	Quality	Location
UM-E11(V1)					
ABCA13	TG → T			130	7:48684204
ANAPC4	AG → A			192	4:25418699
BAP1	TTCTC → T			2415	3:52437209
C14orf148	C → del 8bp			707	14:77872971
C1orf118	T → C	GAA → GGA	E → G	73	1:78353632
CDK10	CAAGA → C			306	16:89753093
CDKN2AIPNL	AG → A			1965	1:226680961
CPE	G → A	CGG → CAG	R → Q	1642	4:166388901
DPP8	A → T	TTG → ATG	L → M	124	15:65809032
EML5	A → T	GAT → GAA	D → E	631	14:89091436
ERLIN2	A → G	ATA → GTA	I → V	76	8:37616155
ESF1	T → C	GAC → GGC	D → G	808	20:13698022
FAM63B	A → T	TGA → TGT	* → C	71	15:59147514
FBXW7	AC → A			120	4:153268226
FUNDC2	C → T	ACG → ATG	T → M	123	X:154275504
GAS2L2	G → C	CTG → GTG	L → V	1960	17:34073102
GNAQ	T → G	CAA → CCA	Q → P	1574	9:80409488
GPR85	A → G	TGA → CGA	* → R	86	7:112720515
GRPEL2	A → G	AAA → AGA	K → R	952	5:148730682
HPS3	T → TCTCTCA			367	3:148890105
KIF20B	T → TAGAA			370	10:91492872
MIOS	G → C	GAT → CAT	D → H	1605	7:7625269
MPST	C → A	CTT → ATT	L → I	74	22:37423740
NLRC4	C → T	CGT → CAT	R → H	80	2:32490776
NPEPPS	G → GTA			175	17:45663680
OSBPL9	G → A	GGC → AGC	G → S	112	1:52250178
PAPSS1	G → ins 15bp			1456	4:108641363
PKP1	G → A	GGG → GAG	G → E	70	1:201299842
PLEC	C → T	TGG → TAG	W → *	135	8:145011849
PLK2	C → CA			317	5:57755013
PMPCB	G → A	ATG → ATA	M → I	165	7:102949698
PRMT2	C → CAA			76	21:48063387
PVT1	A → G	GAG → GGG	E → G	77	8:128867011
RFX3	A → C	TTT → GTT	F → V	87	9:3219817
RND3	A → ins 11bp			829	2:151343988
RNF216	GA → G			192	7:5752975
SENP8	G → T	GAG → TAG	E → *	638	15:72432172
SH3PXD2B	G → A	CCA → TCA	P → S	74	5:171765153
SLC38A10	G → GT			138	17:79225074
SYT17	T → TTAA			142	16:19278429
TICAM1	G → A	CCG → CTG	P → L	453	19:4817623
TLK1	AAAG → A			140	2:171850198
TPTE2	T → TA			78	13:20041493
UBN2	G → A	AGC → AAC	S → N	146	7:138992407
USP46	G → A	CCT → CTT	P → L	150	4:53525471
VOPP1	AG → A			129	7:55589428
UM-E12(V2)					
ABCA3	C → T	GGG → AGG	G → R	331	16:2347378
ARHGEF4	G → A	CGG → CAG	R → Q	612	2:131801909
BAP1	C → CA			318	3:52439796

C17orf107	G → GC			334	17:4805179
C18orf55	G → ins 8bp			857	18:71825720
CYP26B1	G → A	TCC → TTC	S → F	244	2:72362310
DSCAML1	T → C	TAC → TGC	Y → C	590	11:117387247
ECD	G → A	ACG → ATG	T → M	647	10:74894519
ESRP2	C → G	AGA → ACA	R → T	973	16:68266368
EXOC1	G → C	TTG → TTC	L → F	388	4:56756492
GNA11	A → T	CAG → CTG	Q → L	234	19:3118942
INTS12	A → G	CTA → CCA	L → P	307	4:106604077
IPPK	C → G			929	9:95411734
ITGA2	C → G			1037	5:52344185
KANK1	A → C	AAC → ACC	N → T	534	9:738472
KRTAP9-1	T → T + ins 33 bp			1979	17:39346595
LPO	GAGACAC → G			464	17:56321449
OBSCN	A → T	ATG → TTG	M → L	733	1:228432008
PARP4	G → C	CAA → GAA	Q → E	534	13:25043224
RBM11	T → G	GTG → GGG	V → G	1918	21:15599223
SEMA3C	T → C			377	7:80546138
SMG6	C → CGG			234	17:1964759
SNX27	A → C			975	1:151633272
SYTL4	A → G	ATG → ACG	M → T	674	X:99931104
TBX22	C → T	ACG → ATG	T → M	480	X:79278020
UM-E13(V2)					
ADSS	T → C			949	1:244601077
BAP1	C → T	GAG → AAG	E → K	2303	3:52443601
BRWD1	T → C	AAA → GAA	K → E	1466	21:40571463
CEP350	C → T	ACC → ATC	T → I	671	1:179989530
CTSA	C → CCTG			394	20:44520237
CYSLTR2	T → A	CTG → CAG	L → Q	2601	13:49281339
EEF1E1	T → A	CAT → CTT	H → L	1751	6:8090429
EIF4G2	C → CGCCTAA			4498	11:10823576
EPB41L3	T → A	AAA → TAA	K → *	1614	18:5398073
HOXD8	C → A	CCC → CAC	P → H	266	2:176995462
IGKV1-16	C → CAA			284	2:89399858
ITLN2	C → A	GGG → GTG	G → V	1712	1:160917750
KIFC1	C → CTGTG			836	6:33377482
KRTAP10-13	C → CA			453	21:46122300
LANCL1	G → GAAAA			505	2:211320041
MCC	G → ins 14bp			11479	5:112406785
MED4	T → TA			418	13:48664556
MYO1E	C → T			1384	15:59465940
NCOR2	C → ins 9bp			4722	12:124824721
NUCKS1	T → TA			207	1:205686166
OR4C7P	A → G	AGA → GGA	R → G	1076	11:51483640
PITRM1	T → ins 19bp			4170	10:3208567
PLXND1	T → G	GAA → GAC	E → D	1131	3:129281619
PRB4	T → ins 60 bp			5075	12:11461553
SH3GLB1	C → T	CGG → TGG	R → W	302	1:87170526
SRD5A2	G → GAA			253	2:31751175
TRBV6-5	GT → G			201	7:142180634
UM-E14(V1)					
ABCA5	G → A			86	17:67257406
ACOT13	A → T	CAC → CTC	H → L	102	6:24667285
ANXA2	A → G	TAG → CAG	* → Q	75	15:60674767
ATOX1	C → T	GGA → AGA	G → R	85	5:151122448

CARS	G → C	TCT → TGT	S → C	74	11:3028290
CRTAM	G → T			130	11:122738808
EPB41L3	GA → G			183	18:5398116
IL34	C → T	CGC → TGC	R → C	87	16:70694371
MAK16	C → A	GAC → GAA	D → E	194	8:33354800
OR5P2	G → ins 12bp			244	11:7818383
PRKRIRP7	T → A	AAG → ATG	K → M	127	8:79672511
SBSN	C → T	GAG → AAG	E → K	200	19:36018742
SCNM1	G → GA			189	1:151138531
SELENBP1	C → T	GGC → GAC	G → D	86	1:151339509
STXBP4	C → T	ACA → ATA	T → I	74	17:53240738
SYNJ1	G → A	CGG → TGG	R → W	96	21:34067417
TMEM67	C → T			106	8:94816980
UMODL1	C → T	CGG → TGG	R → W	79	21:43535988
VPS13D	C → G	TCC → TGC	S → C	75	1:12343300
WDR78	G → A	CCT → CTT	P → L	88	1:67370709
ZNF34	T → G	AAG → ACG	K → T	78	8:145999168
ZNF599	C → A	CGC → CTC	R → L	77	19:35263882
UM-E15(V1)					
ACSM3	G → A	ATG → ATA	M → I	127	16:20797597
ADAP1	GGA → G			231	7:944952
ANKRD5	AT → A			111	20:10036321
ARHGAP5	G → T	GAA → TAA	E → *	79	14:32561316
ATG12	CA → C			84	5:115167564
AUTS2	A → AC			278	7:69900773
C6orf25	CA → C			99	6:31692675
C7orf30	CA → C			99	7:23347410
C8orf82	T → del 15bp			756	8:145753458
CHIC2	G → C	ATC → ATG	I → M	130	4:54876307
CLCC1	C → CT			156	1:109477463
CTU2	C → ins 60 bp			195	16:88779323
DDX39B	AGAC → A			560	6:31498381
DDX41	C → G	CAG → CAC	Q → H	254	5:176938855
DENND1A	T → TG			76	9:126146187
EEF1D	T → C	GAG → GGG	E → G	103	8:144671548
ELF2	ACACT → A			308	4:140005455
EML3	G → A			106	11:62370723
FAM108A1	A → G	TTG → TCG	L → S	98	19:1881408
FAM53A	G → A	CGG → TGG	R → W	146	4:1642932
FAM73B	A → C	AGA → AGC	R → S	90	9:131823557
GNA11	A → T	CAG → CTG	Q → L	86	19:3118942
GNB1L	A → AC			91	22:19794180
HACL1	G → A	CTT → TTT	L → F	76	3:15613276
HIST1H2BF	CAGCTCTA → C			629	6:26200155
HMCN1	AC → A			204	1:186007176
HNF1A	C → CTCAT			233	12:121434630
INPP5D	G → T	CGA → CTA	R → L	71	2:233925074
KCNA5	T → C	TCC → CCC	S → P	89	12:5154553
KCNH4	G → A	CAG → TAG	Q → *	267	17:40330141
KLHDC8A	T → TC			75	1:205308910
KRT7	A → ATGTG			351	12:52631510
LAP3	GA → G			264	4:17583580
LHX2	A → AC			94	9:126783420
LRRC45	C → G	GCG → GGG	A → G	71	17:79987039
MAN2B1	G → C	GCC → GGC	A → G	71	19:12774558

MLC1	T → G	TAC → TCC	Y → S	95	22:50506878
MTA2	G → A	CTC → TTC	L → F	164	11:62369027
NBPF10	G → A	GAC → AAC	D → N	100	1:145304580
NEDD4	A → G	CTC → CCC	L → P	83	15:56285825
PAK1IP1	GTT → G			106	6:10695136
PDE1B	T → TGAGAGA			853	12:54967640
POLE	GAA → G			78	12:133237753
PRAF2	A → C	GTG → GGG	V → G	105	X:48930262
PSMB9	CAA → C			79	6:32824975
PTK2B	G → A	GGC → GAC	G → D	324	8:27315818
RANBP3L	C → A	GGT → TGT	G → C	226	5:36262057
RBPMS	C → del 13bp			648	8:30242556
RETN	ATGATGATG → A			428	19:7735323
RYR1	T → G	TTC → GTC	F → V	152	19:39061280
SDAD1P2	G → A	CGA → CAA	R → Q	97	20:10368429
SDCCAG8	G → T			117	1:243471186
SESN2	T → TG			111	1:28598877
SFXN3	T → G			100	10:102795430
SPDEF	G → C	CCC → GCC	P → A	93	6:34508890
SPECC1L	A → G			105	22:24761603
SZT2	C → G	GCT → GGT	A → G	182	1:43898016
TBX19	G → GTT			366	1:168262525
TTC5	A → G	TCC → CCC	S → P	84	14:20757725
WDR70	C → T	CCC → CTC	P → L	91	5:37723123
UM-E16(V1)					
CALCOCO1	C → A	GAC → TAC	D → Y	144	12:54105937
CCDC9	G → A			115	19:47768204
GNA11	A → T	CAG → CTG	Q → L	110	19:3118942
HAGH	A → C	CTT → CGT	L → R	83	16:1859172
HSD17B14	C → T	GGC → AGC	G → S	102	19:49318329
INTS8	G → T	TTG → TTT	L → F	328	8:95872032
KCNH3	T → TGG			74	12:49937653
LCN8	G → ins 33 bp			451	9:139650167
PLG	T → C	ATA → ACA	I → T	72	6:161127300
PREX2	G → GCC			119	8:69104723
UBR5	A → G	CTT → CCT	L → P	80	8:103372087
UM-E17(V1)					
AKAP10	AT → A			76	17:19850685
C1orf111	G → A	CCA → TCA	P → S	71	1:162343719
C20orf202	CAG → C			179	20:1187534
C6orf118	C → T	TGG → TGA	W → *	124	6:165715571
COG5	T → TCA			356	7:106898895
CYP7B1	C → T	TGG → TAG	W → *	79	8:65509011
DICER1	C → CACAA			577	14:95566108
EFCAB2	A → G	AAA → AGA	K → R	85	1:245133372
EFCAB6	G → A	CCT → TCT	P → S	146	22:44028071
LONRF2	A → C	CTT → CGT	L → R	75	2:100891098
MACF1	G → T	GTA → TTA	V → L	78	1:39929509
MICAL3	C → CA			210	22:18359222
NHLRC3	T → TTGTGGG			1011	13:39618366
NUAK1	T → A			132	12:106500175
PAGE1	C → A	GAG → GAT	E → D	111	X:49458727
PPBPL2	C → G	GCT → CCT	A → P	78	4:74920219
PRPF6	G → T	TGG → TTG	W → L	84	20:62648179
PRSS1	T → C	CCT → CCC	P → P	72	7:142459820

SLC38A6	A → AG			102	14:61497329
SLC44A2	G → T	GGC → TGC	G → C	136	19:10736283
SLITRK2	C → A	CAC → CAA	H → Q	71	X:144902589
SLITRK3	T → A	AGG → TGG	R → W	118	3:164906500
UM-E18(V1)					
ACOT8	C → CATCT			350	20:44485952
AL137162.1	TGA → T			278	20:55176869
BIK	G → A	CGG → CAG	R → Q	143	22:43525331
BLK	G → T	GGT → TGT	G → C	96	8:11367016
BLOC1S2	TA → T			114	10:102035182
BMP2K	C → G	CAC → CAG	H → Q	165	4:79792166
CA13	A → AG			130	8:86171692
CEP164	G → C	GGG → GCG	G → A	146	11:117283020
CRK	GAA → G			80	17:1326754
CROCCP3	G → A	AGC → AGT	S → S	126	1:16802405
CUL4B	GAA → G			97	X:119676896
EMP1	CA → C			150	12:13364426
FAM46A	CTT → C			126	6:82459345
GALNT9	C → T	CGT → CAT	R → H	84	12:132689997
GNA11	A → T	CAG → CTG	Q → L	259	19:3118942
GNG11	A → AG			168	7:93551420
GTF2F1	C → T	GCG → ACG	A → T	156	19:6389582
HOTTIP	AGC → A			171	7:27245994
INTS4	T → TAA			121	11:77672189
MAGEA11	C → T	ACT → ATT	T → I	74	X:148798000
NDOR1	C → T	CAC → TAC	H → Y	79	9:140109565
NEMF	CG → C			174	14:50319523
NUPL2	CT → C			124	7:23239063
PARP10	G → C	TTC → TTG	F → L	200	8:145060617
PCYOX1	AT → A			191	2:70488522
PDE4DIP	C → T	AGC → AAC	S → N	79	1:144855771
PQLC1	G → A	CGG → TGG	R → W	206	18:77662788
PRG4	AAGG → A			168	1:186276055
PSG5	T → C	ACG → GCG	T → A	104	19:43689255
PXMP2	A → AG			318	12:133277869
RAD51AP1	A → AC			162	12:4648047
SEMA3D	GA → G			95	7:84671609
SNX9	G → A	GTT → ATT	V → I	84	6:158294203
STK32B	G → A	TGG → TGA	W → *	80	4:5448723
SUCLG1	AT → A			71	2:84650856
TMEM48	GAA → G			75	1:54252939
TPP2	C → T	GCT → GTT	A → V	127	13:103330827
TRPC4AP	G → GT			148	20:33657219
UBTF	T → C	AAT → GAT	N → D	265	17:42290282
UM-E19(V2)					
ABCA13	G → A	CGG → CAG	R → Q	2269	7:48634343
ANXA1	G → GGTGTGTGT			1082	9:75783796
ARHGAP15	C → T			206	2:144193167
ATP5SL	TG → T			337	19:41949872
BAP1	GC → G			1352	3:52440848
C16orf7	G → A	GCG → GTG	A → V	241	16:89775697
C9orf100	C → del 18bp			928	9:35674190
CACNA1E	AC → A			1858	1:181549749
CDAN1	C → T			401	15:43017682
COG4	G → A			1094	16:70548422

CSMD1	A → AAAC			262	8:2794977
CYP21A2	A → C	CCA → CCC	P → P	247	6:32006119
DAZAP2	C → CTGTGTG			1094	12:51640388
DNAJC28	A → C	CTT → CGT	L → R	4542	21:34860628
FHDC1	C → T	CGG → TGG	R → W	240	4:153897087
FOXI2	G → T	AGG → AGT	R → S	601	10:129536902
GNAQ	T → A	CAA → CTA	Q → L	2315	9:80409488
ITGA5	G → C	CCC → GCC	P → A	217	12:54789902
KRT4	G → A	CCT → TCT	P → S	1407	12:53200839
MLL	A → C	AAG → ACG	K → T	1138	11:118375489
MYL3	G → A	CCC → CTC	P → L	1220	3:46904813
MYO15A	A → AGTGTGT			1627	17:18034131
NBN	C → CA			228	8:90947085
NCKAP5L	C → T	GTG → ATG	V → M	208	12:50186044
PCLO	T → TTAA			3826	7:82581488
PLA2G4C	T → ins 13bp			500	19:48613788
PNLDC1	AC → A			1246	6:160241544
PTPRC	T → C			1479	1:198672503
RBMX	A → AT			226	X:135961585
RECQL	C → CAAA			1349	12:21623284
REPS2	A → G	AGT → GGT	S → G	1888	X:17092257
SCYL3	G → A	ACG → ATG	T → M	2542	1:169824996
SGOL2	A → G	AAT → AGT	N → S	497	2:201437159
SNX13	C → T			2103	7:17838631
SNX7	G → C	GAG → GAC	E → D	5610	1:99225627
TAC4	TACAC → T			325	17:47925032
TRIM60P15	AAT → A			632	8:47703897
TTC28	G → A	CGT → TGT	R → C	1047	22:28504290
WDPCP	A → ACGCCGC			626	2:63815498
ZDHHC11B	C → ins 32 bp			1057	5:712012
ZNF250	A → C	TTA → GTA	L → V	223	8:146105917
UM-E20(V1)					
ABCA6	CTAAA → C			273	17:67125893
ACOT1	T → G	GTG → GGG	V → G	80	14:74004406
ALX3	A → ins 10bp			337	1:110603286
BBC3	A → C			72	19:47729819
BNC2	G → GAATGCACA			383	9:16418871
CAMK2B	G → C	CTA → GTA	L → V	72	7:44269469
CELA3A	G → A	GGT → GAT	G → D	125	1:22331989
CENPP	G → GGTGCCCC			409	9:95373521
GNAQ	T → A	CAA → CTA	Q → L	213	9:80409488
GNB2L1	CAAA → C			167	5:180668426
HK2P1	C → T	GCT → ACT	A → T	114	X:79827418
HUWE1	T → G	ACC → CCC	T → P	88	X:53596718
KRT2	A → AAAGCC			215	12:53045639
NPPB	T → G	GAA → GCA	E → A	84	1:11918927
PSMA6P2	GA → G			139	X:12844471
RNF19A	TAAAAA → T			79	8:101280911
SHH	A → C	TTC → GTC	F → V	87	7:155604729
SMG6	C → CGG			163	17:1964759
TBC1D24	G → T	GGC → GTC	G → V	82	16:2546274
TCEAL3	C → CA			93	X:102864220
TF	C → T	CGT → TGT	R → C	76	3:133466081
TONSL	C → T	GAG → AAG	E → K	73	8:145658320
UM-E21(V2)					

ARGFXP1	G → GCAGCAC			2719	5:122011916
C15orf62	G → A	CGG → CAG	R → Q	501	15:41062767
CDH20	T → G	TTT → GTT	F → V	1246	18:59157764
CHPT1	G → A	GTG → ATG	V → M	271	12:102091862
CYP2C19	G → A			1424	10:96484093
CYP4F12	C → CT			286	19:15784302
DLD	A → AGC			731	7:107531492
EPS8L2	G → GGGGACA			378	11:721725
FAM160A1	C → CTT			345	4:152583907
FAM75C2	G → del 17bp			702	9:90748562
FLVCR1	G → GA			1304	1:213068548
GNAQ	T → G	CAA → CCA	Q → P	1998	9:80409488
GNB2	TACG → T			844	7:100276186
GZMH	C → A	GAC → TAC	D → Y	1144	14:25075922
IGFN1	A → A + ins 70bp			1935	1:201178924
IGHV4-31	G → C	CCA → CGA	P → R	592	14:106805480
KCNN3	T → TTGC			226	1:154842330
LCE1B	T → C	TGC → CGC	C → R	429	1:152784992
MST1	C → G	TAG → TAC	* → Y	349	3:49721461
RBM15B	C → CT			208	3:51433688
SMPD1	T → del 12 bp			818	11:6411935
TCHH	T → del 17bp			2104	1:152084175
TNRC18C	G → A	GCT → ACT	A → T	215	7:57063667
TSHR	T → ins 14bp			15026	14:81574845
USP15	G → T	GGA → GTA	G → V	1778	12:62688058
ZNF169	T → TTTGTG			351	9:97054889
ZNF267	C → T	CAT → TAT	H → Y	653	16:31926129
UM-E22(V1)					
AACS	G → A			226	12:125609242
ACCN4	C → T	CCC → CTC	P → L	128	2:220402953
ANKRD10	TCTC → T			369	13:111532241
ARAP1	C → A	TGC → TTC	C → F	302	11:72423723
ARL5B	C → G	TCT → TGT	S → C	77	10:18964179
ARL8B	T → G	TTT → TGT	F → C	89	3:5212420
ASPH	C → T	GGT → GAT	G → D	349	8:62627060
BMP1	G → A	GGG → GAG	G → E	117	8:22051583
CD276	G → T	AGC → ATC	S → I	194	15:73995419
CHSY3	G → A	GGG → AGG	G → R	103	5:129521104
CITED2	CTGG → C			440	6:139694962
CNTNAP1	T → C	GTG → GCG	V → A	298	17:40841002
CSMD2	G → A			137	1:33985558
CSNK2B	G → C	TGT → TCT	C → S	140	6:31636695
DEGS1	A → AGCC			325	1:224370958
DGKI	G → A	CGT → TGT	R → C	142	7:137076016
DICER1	G → C	CTA → GTA	L → V	130	14:95569742
ELAC2	G → C	CGG → GGG	R → G	191	17:12920903
FAM120A	C → T	CCC → CTC	P → L	277	9:96318764
FAM178B	AG → A			138	2:97541815
FGFRL1	C → T			140	4:1016270
FNIP1	G → T	ACT → AAT	T → N	72	5:130762725
FOXK2	A → G			76	17:80544085
GDF15	G → A	ATG → ATA	M → I	81	19:18499664
GNAQ	T → G	CAA → CCA	Q → P	71	9:80409488
GRK5	A → C			168	10:121211954
HIST1H2BE	G → A	GGG → GAG	G → E	280	6:26184337

HMCN1	T → C	GTT → GCT	V → A	143	1:185963992
IL22RA1	C → T	GTG → ATG	V → M	81	1:24463780
ING3	T → A	TCA → ACA	S → T	102	7:120610800
INSM2	G → T	GGG → GTG	G → V	156	14:36005002
ITGAD	G → A	GTG → ATG	V → M	272	16:31424258
KLK3	GT → G			123	19:51362902
KLK7	C → T	GGC → AGC	G → S	114	19:51485671
LRGUK	G → T	ATG → ATT	M → I	73	7:133884031
MAPK10	G → GTGT			173	4:87024270
MAPKAP1	GC → G			110	9:128201009
MST1	T → C	AGC → GGC	S → G	74	3:49726195
MST1P9	A → G	TCA → CCA	S → P	91	1:17085189
MYBBP1A	G → C	TCG → TGG	S → W	74	17:4453362
MYH8	C → A			92	17:10315922
NAA10	A → G	TTT → TCT	F → S	132	X:153195297
NBPF10	G → C	GTT → CTT	V → L	126	1:145303936
OCA2	G → C			224	15:28270051
OR2T12	CAGA → C			516	1:248458351
PCDH9	C → T	GCA → ACA	A → T	130	13:67799890
PDE6B	C → CA			357	4:651290
PI4KA	G → A	CTC → TTC	L → F	101	22:21064203
PTPRG	C → A	ACT → AAT	T → N	179	3:62254804
RASA1	G → T	GGT → GTT	G → V	105	5:86564735
RN7SL1	C → A	CGC → AGC	R → S	75	14:50053297
RNF212	T → C	ATG → GTG	M → V	84	4:1090375
RTKN	C → T	TGG → TAG	W → *	135	2:74653130
SART3	G → A	CCT → TCT	P → S	120	12:108926144
SCAF4	T → G	AGT → CGT	S → R	157	21:33043671
SDC4	C → T	GGA → AGA	G → R	161	20:43964431
SEMA4D	G → C	ACC → AGC	T → S	142	9:91978814
SLCO4A1	C → T	CGT → TGT	R → C	72	20:61292475
SNX5	G → A	CCC → TCC	P → S	107	20:17948836
SPANXD	C → G	GGG → CGG	G → R	83	X:140785597
SPINLW1	A → G	TCT → CCT	S → P	138	20:44170617
SREBF1	G → A	CCG → CTG	P → L	176	17:17717013
STX10	C → T	CTG → CTA	L → L	124	19:13260990
TRAF2	G → A	GAC → AAC	D → N	157	9:139820195
UBE3B	C → T	CCG → CTG	P → L	180	12:109958895
USH2A	C → G	GGT → GCT	G → A	130	1:215821882
WDR47	T → C	AAA → AGA	K → R	130	1:109553799

Supplementary Table 3. Clinical, histopathological and genetic features of 111 uveal melanoma patients and respective tumor samples.

	Patient			**Tumor**												
ID	age	met. death	sex	Chr. 3	LBD [mm]	height [mm]	ciliary body inv.	celltype	EOG	mutant genes GNAQ/11	others	position	Type	predicted AA change	EIF1AX cDNA seq.	EIF1AY expression
E1	79		m	D3	14	87	no	spindle	no	GNAQ	EIF1AX	X:20159754	C→G	p.P2R	no	na
E2	46		m	D3	11.6	8.9	no	spindle	no	GNAQ	EIF1AX	X:20159752	A→G	p.K3E	no	na
E3	39		m	D3	12.9	6.6	no	spindle	no	GNA11	EIF1AX	X:20159749	A→G	p.N4D	no	na
E4	54		m	D3	12.2	na	yes	spindle	no	GNA11	SF3B1	2:198266489	G→A	p.E783K	no	na
E5	48		f	D3	19	14	yes	spindle	yes	GNA11	SF3B1	2:198267484	C→T	p.R625C	no	na
E6	69		f	D3	11.2	5.8	no	spindle	na	GNAQ	SF3B1	2:198267483	G→A	p.R625H	yes	no
E7	71		m	D3	13	6.9	no	spindle	no	GNAQ					no	na
E8	88		m	D3	11	na	no	spindle	yes	GNA11					no	na
E9	48		f	D3	16	10.8	no	spindle	na	GNA11					no	na
E10	69		m	D3	11.9	5.8	no	na	no	none					no	na
E11	20	yes	f	M3	15.5	11.3	yes	spindle	no	GNAQ	BAP1	3:52437209	4bp del	frame shift	no	na
E12	71		f	M3	13.6	10.4	no	mixed	no	GNA11	BAP1	3:52439796	C→CA	frame shift	no	na
E13	77		m	M3	11	na	yes	spindle	no	none	BAP1	3:52443601	G→A	p.E31K	no	na
											EPB41L3	18:5398073	A→T	p.K807*		
E14	77		m	M3	15	14	yes	spindle	no	none	EPB41L3	18:5398116	GA→G	frame shift	no	na
E15	74		m	M3	12.1	11.6	yes	na	na	GNA11					no	na
E16	65		f	M3	22.8	10.2	yes	spindle	no	GNA11					no	na
E17	84	yes	m	M3	nd	12.9	yes	spindle	no	none					no	na
E18	70		f	M3	16	10	yes	na	no	GNA11					no	na
E19	63	yes	f	M3	15.8	13.4	no	spindle	no	GNAQ	BAP1	3:52440848	GC→G	frame shift	no	na
E20	24		f	M3	19.2	11.1	yes	mixed	no	GNAQ					no	na
E21	71		m	M3	11	na	no	spindle	no	GNAQ					no	na
E22	50	yes	f	M3	na	13	yes	spindle	no	GNAQ					no	na
D3-1	69		m	D3	8.8	8.4	no	mixed	no	GNA11	EIF1AX	X:20159752	A→G	p.K3E	no	na
D3-2	49		m	D3	17.5	9.3	no	spindle	no	GNA11	EIF1AX	X:20156713	G→A	p.G15D	no	na
D3-3	63		m	D3	na	na	na	na	na	nd	EIF1AX	X:20156740	G→A	p.G6D	yes	na
D3-4	64		m	D3	10.4	10.6	no	spindle	no	GNAQ	EIF1AX	X:20156738	14bp del	p.K7_G8del	yes	yes
D3-5	55		m	D3	18.1	na	yes	spindle	no	nd	EIF1AX	X:20156719	G→C	p.R13P	yes	yes

D3-6	64		m	D3	13.4	12.1	yes	mixed	no	GNAQ	EIF1AX	X:20159754	C→A	p.P2H	yes	no
D3-7	67		m	D3	13.9	14.3	yes	spindle	no	GNAQ	EIF1AX	X:20159743	G→C	p.G6R	yes	no
D3-8	38		m	D3	9.4	na	yes	spindle	no	GNAQ	EIF1AX	X:20159743	G→C	p.G6R	yes	no
D3-9	74		f	D3	na	13.4	yes	spindle	no	GNAQ	EIF1AX	X:20159748	A→G	p.N4S	yes	na
D3-10	55		f	D3	na	8.5	no	na	na	GNAQ	EIF1AX	X:20159748	A→G	p.N4S	no	na
D3-11	64		f	D3	na	4.4	no	na	no	GNA11	EIF1AX	X:20159747	T→G	p.N4T	yes	no
D3-12	68		m	D3	13.1	13.3	yes	spindle	no	GNAQ	EIF1AX	X:20156719	G→A	p.R13H	yes	yes
D3-13	88		f	D3	9.9	11.5	no	spindle	no	GNAQ	EIF1AX	X:20159743	G→C	p.G6R	no	na
D3-14	68		m	D3	8.4	1.5	no	na	no	GNAQ	EIF1AX	X:20156731	GAGG→G	p.G9del	yes	yes
D3-15	57		m	D3	13.9	12	no	spindle	no	GNAQ	EIF1AX	X:20156742	A→G	p.K7_G8del	yes	yes
D3-16	48		m	D3	12.4	8.6	na	spindle	no	GNA11	SF3B1	2:198267484	C→T	p.R625C	no	na
D3-17	72		m	D3	13.5	11.7	yes	spindle	no	GNAQ	SF3B1	2:198267483	G→A	p.R625H	yes	no
D3-18	62		m	D3	14.5	11.3	yes	spindle	no	GNA11	SF3B1	2:198267483	G→A	p.R625H	yes	yes
D3-19	68		m	D3	13.7	4.5	no	na	no	GNA11	SF3B1	2:198267484	C→T	p.R625C	yes	yes
D3-20	75		m	D3	17.4	11.4	yes	mixed	no	GNAQ	SF3B1	2:198267483	G→A	p.R625H	yes	yes
D3-21	65		m	D3	12.1	8.5	yes	spindle	no	GNAQ	SF3B1	2:198267483	G→A	p.R625H	yes	yes
D3-22	45		m	D3	21.3	16.2	yes	spindle	no	none	SF3B1	2:198267483	G→A	p.R625H	yes	yes
D3-23	62		m	D3	na	na	na	na	na	GNAQ	SF3B1	2:198267484	C→T	p.R625C	no	na
D3-24	57		m	D3	na	7.9	no	spindle	no	GNAQ	SF3B1	2:198267751	CGTG→C	p.V576del	no	na
D3-25	44		f	D3	17.6	8.8	no	spindle	no	nd					yes	na
D3-26	66		f	D3	23.3	11.4	yes	spindle	no	none					yes	na
D3-27	59		f	D3	13.5	13.3	yes	spindle	no	GNAQ					no	na
D3-28	26		m	D3	17.7	12.2	yes	spindle	no	GNAQ					no	na
D3-29	72		m	D3	20.7	7.4	no	mixed	no	none					no	no
D3-30	60		f	D3	12.2	9.9	yes	spindle	no	nd					no	na
D3-31	68		m	D3	8.3	1.9	no	na	no	nd					no	na
M3-1	54	yes	m	M3	13.7	13.1	no	na	no	GNA11	EIF1AX BAP1	X:20159748 exon 9 deletion	A→C	p.N4T	no	na
M3-2	61		m	M3	10.4	10.6	yes	spindle	no	GNA11					no	na
M3-3	37	yes	m	M3	13.3	11.9	yes	na	na	GNA11					no	na
M3-4	74		m	M3	13.5	5.1	no	na	no	GNAQ					no	na
M3-5	60	yes	f	M3	na	13.4	yes	spindle	no	GNAQ					no	na
M3-6	85		m	M3	na	10.5	no	spindle	no	GNA11					no	na

M3-7	61	yes	f	M3	22	12.1	yes	mixed	no	GNA11					no	na
M3-8	41		f	M3	na	7.5	yes	na	no	GNA11					no	na
M3-9	81	yes	f	M3	21	6.9	no	spindle	no	GNA11					no	na
M3-10	74		m	M3	2.1	11.6	yes	na	no	GNA11					no	na
M3-11	75		f	M3	na	12.2	yes	spindle	no	GNA11					no	na
M3-12	69	yes	m	M3	16.9	11.9	yes	spindle	no	nd					no	na
M3-13	56	yes	m	M3	11.6	12.3	yes	spindle	no	none	SF3B1	2:198267484	C→T	p.R625C	no	na
											BAP1	3:52438566	C→T	p.R385*		
M3-14	63	yes	f	M3	na	12.9	yes	spindle	no	none					no	na
M3-15	63		f	M3	14	9.9	yes	spindle	no	none					no	na
M3-16	68	yes	m	M3	12.7	6.9	yes	mixed	no	GNA11					no	na
M3-17	48		f	M3	na	13.8	yes	spindle	no	GNA11					no	na
M3-18	60	yes	f	M3	na	na	na	na	na	GNAQ					no	na
M3-19	39		m	M3	16.6	5.7	yes	mixed	no	GNAQ					no	na
M3-20	56		m	M3	12.6	na	yes	mixed	no	GNAQ					no	na
M3-21	67		f	M3	13.4	12	yes	na	no	GNA11					no	na
M3-22	63	yes	m	M3	1.4	11.3	yes	mixed	no	GNAQ					no	na
M3-23	63	yes	f	M3	15.8	13.8	no	spindle	no	GNAQ					no	na
M3-24	63	yes	m	M3	11.7	12.6	yes	spindle	no	none					no	na
M3-25	91		f	M3	11.8	11	no	spindle	no	GNAQ					no	na
M3-26	62	yes	f	M3	21.6	12.6	no	spindle	no	GNA11					no	na
M3-27	69		f	M3	15.3	13.2	yes	spindle	no	GNAQ					no	na
M3-28	50	yes	f	M3	18	13.6	yes	na	na	GNA11					no	na
M3-29	70		f	M3	16	10	yes	na	no	GNA11					no	na
M3-30	56		m	M3	11.7	8.4	yes	na	na	GNA11					no	na
M3-31	52		f	M3	14.4	12	no	spindle	na	GNAQ					no	na
M3-32	70		m	M3	21	10.7	yes	mixed	no	GNAQ					no	na
M3-33	70	yes	m	M3	13.4	10.1	yes	na	no	GNA11					no	na
M3-34	73		m	M3	na	16	no	epithelioid	no	GNA11					no	na
M3-35	48		m	M3	14.7	5.2	no	spindle	no	GNA11					no	na
pM3-1	41		m	partM3q	16.1	8.1	no	na	no	GNAQ	SF3B1	2:198267483	G→A	p.R625H	no	yes
pM3-2	76		m	partM3q	15.6	8.4	no	spindle	no	GNAQ	SF3B1	2:198267484	C→T	p.R625C	no	no
pM3-3	55	yes	m	partM3q	na	8.4	no	spindle	no	GNAQ	SF3B1	2:198267484	C→T	p.R625C	no	yes

pM3-4	51		m	partM3q	20	14.4	no	spindle	no	none	SF3B1	2:198267483	G→A	p.R625H	no	yes
pM3-5	57		m	partM3q	9.5	8.7	no	na	no	GNA11	SF3B1	2:198267483	G→A	p.R625H	no	no
pM3-6	65		m	partM3q	22.9	11.5	no	mixed	no	GNA11	SF3B1	2:198267483	G→A	p.R625H	no	yes
pM3-7	57		f	partM3p	12.6	10.9	yes	spindle	na	GNA11	SF3B1	2:198267483	G→A	p.R625H	no	na
pM3-8	52		m	partM3p,q	22	11	no	spindle	no	GNAQ	EIF1AX	X:20156742	A→C	p.K7_G8del	no	na
pM3-9	57		f	partM3p,q	18.4	7.4	no	spindle	no	GNAQ					no	na
pM3-10	70		m	partM3p,q	14.7	13.8	no	mixed	no	GNAQ					no	no
pM3-11	47		m	partM3q	20.6	11.9	no	spindle	no	GNA11					no	yes
pM3-12	51		f	partM3p,q	18.7	12.8	yes	spindle	na	GNA11					no	na
pM3-13	73		m	partM3p	16.8	9.5	no	spindle	na	nd					no	yes
D3met-1	78	yes	f	D3	na	11.3	no	epithelioid	no	GNAQ	SF3B1	2:198267741	GAAC→G	p.EP579A	no	na
D3met-2	39	yes	m	D3	20.9	9.2	yes	epithelioid	no	GNA11	SF3B1	2:198267490	T→C	p.Y623H	no	na
D3met-3	47	yes	m	D3	18.1	4.9	no	mixed	no	none	SF3B1	2:198267491	G→C	p.E622D	no	na
D3met-4	61	yes	m	D3	na	10.8	yes	na	no	nd					no	na
D3met-5	47	yes	f	D3	11.3	9.3	no	spindle	no	GNAQ					no	na
D3met-6	70	yes	m	D3	18.2	12.4	yes	spindle	no	GNA11					no	na
D3met-7	71	yes	f	D3	na	11.6	no	na	no	none					no	na
D3met-8	67	yes	m	D3	14.6	3	no	mixed	yes	none					no	na
D3met-9	62	yes	f	D3	17.4	12.6	yes	spindle	yes	nd					no	na
D3met-10	71	yes	m	D3	18	14.8	yes	spindle	no	GNAQ	BAP1	3:52438450	44bp del		no	na

Tumor samples E-1 to E-22 were analyzed by Exome Sequencing. Targeted re-sequencing was performed on samples M3-1 to M3-35 and D3-1 to D3-31 which were randomly chosen from the cohort of 374 tumor samples and on selected samples with partial monosomy 3 (pM3-1 to pM3-13) and disomy 3 that developed metastases (D3met-1 to D3met-10). Chr.3, chromosome 3 status as determined by microsatellite analysis (MSA); age, age at diagnosis; met.death, death of patient due to metastases; LBD, largest basal tumor diameter; height, tumor height; EOG, extra ocular growth; position, mutations are referred to by giving the first affected nucleotide of the mutation according to the hg19/GRCh37 assembly; type, nucleotide change refers to the coding strand; *EIF1AX* cDNA seq, indicates samples in which entire *EIF1AX* coding sequencing was performed on cDNA; na, data not available; nd, not determined due to shortage of DNA; none, neither *GNAQ* nor *GNA11* mutations were detected. *EPB41L3* was sequenced in all tumor samples excluding the following: D3-3, D3-5, D3-19, D3-25, D3-31, D3met-3, D3met-4, D3met-6, D3met-9, pM3-13. *BAP1* was sequenced in all D3, partM3, D3met tumors and those M3 tumors with a mutation in either *SF3B1* or *EIF1AX*, excluding samples D3met-4, D3met-9, D3-19, D3-25, D3-31, pM3-3, pM3-

6. In all these samples, sequencing was not performed due to shortage of DNA. A gene is listed in table 3 if a mutation was identified. In all cases mutations in *GNAQ* or *GNA11* affect amino acid (AA) Q209. We sequenced exon 4 (R183) in all samples without a mutation of Q209 but could not detected any mutation. An exon 9 deletion of *BAP1* was identified in tumor sample M3-1 by multiplex ligation-dependent probe amplification (MLPA) using the SALSA MLPA KIT P027-C1 (MRC-Holland).

Supplementary Table 4. Association of *SF3B1* and *EIF1AX* genotype with clinical and histopathological features of uveal melanoma.

	SF3B1			EIF1AX			SF3B1 or EIF1AX		
Variable	wt	mut	p	wt	mut	p	wt	mut	p
age at diagnosis									
median [years]	62	58	0.1	61	61	0.79	62	59	0.25
largest basal diameter									
median [mm]	14.6	15.5	0.75	15.1	13.1	**0.007**	15	14.4	0.06
tumor height									
median [mm]	10.5	9.9	0.5	10.5	9.9	0.45	10.6	9.8	0.25
ciliary body involvement									
yes	45 (51%)	11 (48%)	0.75	50 (55%)	6 (30%)	0.1	39 (57%)	17 (40%)	0.1
no	42(49%)	12 (52%)		40 (45%)	14 (70%)		28 (41%)	26 (60%)	
cell type									
epithelioid	1 (1%)	2 (10%)	0.24	3 (4%)	0 (0%)	0.44	1 (2%)	2 (6%)	0.5
mixed	13 (20%)	3 (16%)		14 (20%)	2 (13%)		11 (22%)	5 (15%)	
spindle	53 (79%)	14 (74%)		54 (76%)	13 (87%)		40 (76%)	27 (79%)	
EOG									
yes	3 (4%)	1 (5%)	1	4 (5%)	0 (0%)	1	3 (5%)	1 (3%)	1
no	74 (96%)	19 (95)		75 (95%)	18 (100%)		56 (95%)	37 (97%)	
GNAQ status									
GNAQ mut	35 (45%)	10 (48%)	1	32 (40%)	13 (72%)	**0.02**	22 (37%)	23 (59%)	**0.04**
GNAQ wt	43 (55%)	11 (52%)		49 (60%)	5 (28%)		38 (63%)	16 (41%)	
GNA11 status									
GNA11 mut	32 (41%)	8 (38%)	1	35 (43%)	5 (28%)	0.3	27 (45%)	13 (33%)	0.3
GNA11 wt	46 (59%)	13 (62%)		46 (47%)	13 (72%)		33 (55%)	26 (67%)	
sex									
female	38 (43%)	4 (17%)	**0.029**	38 (42%)	4 (20%)	0.080	34 (50%)	8 (19%)	**0.0012**
male	50 (57%)	19 (83%)		53 (58%)	16 (80%)		34 (50%)	35 (81%)	
chromosome 3 status									
M3	46 (52%)	1 (4%)	**>0.0001**	46 (51%)	1 (5%)	**>0.0001**	45 (66%)	2 (5%)	**>0.0001**
partM3	6 (7%)	7 (31%)		12 (13%)	1 (5%)		5 (7%)	8 (18%)	
D3	36 (41%)	15 (65%)		33 (36%)	18 (90%)		18 (27%)	33 (77%)	

Associations between clinical tumor characteristics and *SF3B1* and *EIF1AX* genotype were assessed by Fisher's exact two tailed t-test for categorical variables. Numerical variables such as age at diagnosis, tumor height, and largest basal diameter were analyzed by Chi-square approximation. The standard deviations in these datasets were similar between the groups being compared. wt, no mutation detected, P = p-value. For other abbreviations, see legend to Supplementary Table 3. The association between *GNAQ* and *EIF1AX* mutation status barely reaches significance. Taking multiple testing into account this difference should not be regarded as significant.

Supplementary Table 5. Primers used for amplification and sequencing of the coding regions of *SF3B1, EPB41L3, EIF1AX* on genomic DNA and the entire *EIF1AX* or *EIF1AY* coding regions on cDNA. All primer sequences are given from 5’ to 3’ direction.

Gene	**Exon**	**amplicon size [bp]**	**fw Primer**	**rev Primer**
EPB41L3	2	338	GAGCATCCTAGTTTTCTTGCAG	ACCAAGGTTAAAGCCGATCC
EPB41L3	3	450	AAATGGCAAACAGTATTTAGGC	TGATCCCCTGTTACAGACTAGG
EPB41L3	4	275	TGGTTTTATCTCTGATATTTGGG	GTGGAGAAAGTGATCCACCC
EPB41L3E	5	209	CGCACTGCATTTAGGGAGAG	TGGGCTACCAATTCAGACAAC
EPB41L3	6	246	TTAAGGCAGTTCTGGCCATC	GCTACCAGATGTAAGCACGC
EPB41L3	7	385	GGAGAAATTATTTGCCCACG	GAAGAGGTGGGTTGTGTGC
EPB41L3	8	336	TGGTGCCTCCATAGGACTTC	GCTTAAAAGACAAGCAGAGATTTG
EPB41L3	9	376	TTTTGCATAAGTAAACCAGCC	CACTGTGTCCCACAATGCTC
EPB41L3	10	416	TTTATACCTGCAGCATTTTAAAGAC	GGTGACAATGAACTTGAAGGG
EPB41L3	11	386	CATGCAAAACACATGACCTC	GCTTTTCAACATACAATATCCAGG
EPB41L3	12	423	CAAGGCAAACCTGGTATTTTG	TCCTGGTTTACAGCCTCAGC
EPB41L3	13-1	506	GGCAACAGTGGCATGCAG	AAAGGTTGGGGAAAGAGAGG
EPB41L3	13-2	419	AGCTACAGACAGCAAACTGGC	GCCAGCTAACACTGTTTCGG
EPB41L3	14	216	GTCTGACCTGTGCCAGAGC	CTTAAACACAGAGCCACCCC
EPB41L3	15	220	TACACGTGCCCACATTTAGC	TGAACGCTGTAGACAAACAATG
EPB41L3	16	492	TGTTTGTGGTAGTGCCATGAG	CTGTTGGAGCACTGAGCATC
EPB41L3	17	289	AAGCTGTGAATGTTTATGTGCC	CTGGATGCAACCACACACTC
EPB41L3	18	538	CTGGCTTTAGACATCCTGGC	TGCTGATCTAAATTTCCAGGC
EPB41L3	19	293	AACCACCAAGAGAGGAAAAGG	TGCAGTTCTATGTAAACACACTAGG
EPB41L3	20	259	TGCCTTAAATAACGTAGCCAAC	CCAACCTGTGAGGAGTTCTG
EPB41L3	21-22	632	ATGATGTCAGCATCTTCGGC	ATGAGAGGGAAGTGCCCC
SF3B1	12	439	AACTCATGCTGTCTATGTAAAATGTG	ACATGTATGGTGTGTACTTGTGC
SF3B1	13-14	679	TCCCTTGATTAACAAAAGTCCTG	TGAGTCCAGTCTGGGCAAC
SF3B1	15-16	616	TGAACATATTCTGCAGTTTGGC	TCAAACAGTATTCGTGTAACATACAG
EIF1AX	1	320	GAAAAGCGACGCAAAGAGTC	CTGGGTGACCTGCAATCTAC
EIF1AX	2	406	GGGTAGGGAGGTGATAATGTG	CTGTAATCGTGCCACCACAC
EIF1AX	3	326	CCCAACTGGTGCAACTTTATTC	TTACCAAGGTAAGTCTTTTGGG
EIF1AX	4	245	ACCGCTCCTGGCCTAAAATC	ATGCCTGAAACAAAACTGGC
EIF1AX	5	263	AGTAAAACGGTGAGATTTGATTG	CATAGTTCCTTCACCTAACCAGC
EIF1AX	6	315	CTCCCATCTTGACTTAGCAGTG	GGATGTTAGGGGAAAGTTGG
EIF1AX	7	163	TGGATTTGTTTCTCACATAGCC	GGACAATCTTCAGAAAAGATGGA
GNAQ/11			see reference 7 and 8	
BAP1			see reference 10	
cDNA sequencing				
EIF1AY/XcDNA	1-3	136	TGCCCAAGAATAAAGGTAAAGG	GTCCATTTCCCAACTTTTGAT
EIF1AYcDNA	all coding	695	GTGCGCGTCAGCAGTTTATTAG	CAGTTTGCTTTCAGAAACTACACAC
EIF1AXcDNA	all coding	608	CCTCCAGCACCTACTTGGTC	TCTGCTTTAACAAATTGCATTCAT