

SUPPLEMENTARY TABLES

Supplementary Table S1: Characteristics of primary and metastatic samples in regard to *SDHD* promoter status

		Primary Samples				Metastatic Samples					
		<i>SDHD</i> WT		<i>SDHD</i> mut		Total	<i>SDHD</i> WT		<i>SDHD</i> mut		Total
		<i>N</i>	%	<i>N</i>	%		<i>N</i>	%	<i>N</i>	%	
Sex	Female	70	42	2	1,2	72	66	42	4	2,3	70
	Male	93	56	2	1,2	95	83	52	5	3,2	88
Age at Diagnose	<=60 years	68	40	1	0,6	69	87	55	4	2,3	91
	>60 years	79	48	2	1,2	81	58	37	3	1,9	61
	Missing data	16	10	1	0,6	17	4	2,5	2	1,2	6
Mutant oncogene [#]	WT	72	44	3	1,8	75	49	32	2	1,3	51
	<i>BRAF</i> *	53	33	1	0,6	54	58	38	5	3,3	63
	<i>NRAS</i> *	31	19	0	0	31	36	24	2	1,3	38
	<i>KIT</i>	2	1,2	0	0	2	1	0,6	0	0	1
	WT	41	60	1	1,4	42	53	51	1	1	54
	<i>TERT</i> prom. mut	30	42	0	0	30	45	43	5	4,8	50
<i>BRAF</i> and <i>NRAS</i> [#]	Either mutant*	84	52	1	0,6	85	93	61	7	5	100
	Both WT	74	46	3	1,9	77	50	33	2	1,3	52
Stage at diagnosis	I	5	3	0	0	5	35	22	2	1,3	37
	II	59	35	1	0,6	60	51	32	3	1,9	54
	III	47	28	2	1,2	49	43	27	1	0,6	44
	IV	7	4	0	0	7	5	3,2	0	0	5
	Missing data	45	27	1	0,6	46	15	10	3	1,9	18
Anatomic distribution of primary	Non-acral	89	54	3	1,8	92	117	74	6	3,8	123
	Acral	18	11	0	0	18	17	11	0	0	17
	Mucosal	18	11	0	0,6	18	9	6	1	0,6	10
	Eye (conj.)	38	23	1	0	39	4	2,5	0	0	4

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		Primary Samples				Metastatic Samples					
		SDHD WT		SDHD mut		Total	SDHD WT		SDHD mut		Total
		N	%	N	%		N	%	N	%	
	Missing data	0	0	0	0	0	2	1,3	2	1,3	4
Anatomic site of skin and acral tumors	Head & neck	26	16	0	0	26	24	15	1	0,6	25
	Upper limbs	12	7	0	0	12	10	6	1	0,6	11
	Trunk	43	26	2	1,2	45	43	27	5	2,9	48
	Lower limbs	17	10	1	0,6	18	46	29	0	0	45
	Genital	7	4	0	0	7	2	1	0	0	2
	Eye (conj.)	38	22	1	0,6	39	4	3	0	0	5
	Acral	18	11	0	0	18	17	11	0	0	17
	Missing data	2	1,2	0	0	2	3	1,9	2	1,9	2
Histologic type	ALM	10	6	0	0	10	16	10	1	0,6	17
	LMM	2	1	0	0	2	2	1	0	0	2
	NM	38	23	0	0	38	34	22	2	1,2	36
	SSM	16	10	2	1,2	18	27	17	1	0,6	28
	Unclassified	97	58	2	1,2	99	70	54	5	3,6	75
Breslow thickness	0.01-1.00mm	8	5	1	0,6	9	23	13	1	0,6	24
	1.01-2.00mm	18	11	0	0	18	19	11	3	1,9	22
	2.01-4.00mm	35	21	2	1,2	37	44	26	0	0	44
	>4.00mm	50	30	0	0	50	32	19	2	1,3	34
	Missing data	52	31	1	0,6	53	31	20	3	1,9	34
Clark level (skin tumors only)	II	1	0,6	0	0	1	3	1,9	0	0	3
	III	15	9	0	0	15	17	11	3	1,7	20
	IV	26	15	1	0,6	27	42	27	1	0,6	43
	V	8	5	0	0	8	12	8	1	0,6	13
	Unknown	113	68	3	1,8	116	75	47	4	2,9	79

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		Primary Samples				Metastatic Samples					
		<i>SDHD</i> WT		<i>SDHD</i> mut		Total	<i>SDHD</i> WT		<i>SDHD</i> mut		Total
		<i>N</i>	%	<i>N</i>	%		<i>N</i>	%	<i>N</i>	%	
Ulceration	Absent	30	18	2	1,2	32	26	17	1	0,6	27
	Present	53	32	1	0,6	54	31	20	0	0	31
	Unknown	80	48	1	0,6	81	102	61	8	5,2	110
SLN	Negative	37	22	1	0,6	36	35	22	2	1,3	37
	Positive	46	28	2	1,2	48	32	20	1	0,6	33
	Not done	80	48	1	0,6	81	82	52	6	4	88

ALM = acral lentiginous melanoma; NM = nodular melanoma; SSM = superficial spreading melanoma; LMM = lentigo maligna melanoma; SLN = sentinel lymph node; WT = wild-type; prom = promoter; mut = mutant

[#]*BRAF*, *NRAS*, *KIT* were screened in *n* = 162 primary and *n* = 153 metastatic tumor samples; the *TERT* promoter was screened in *n* = 72 primary and *n* = 104 metastatic tumor samples

*1 metastatic case harbored a *BRAF* and a *NRAS* mutation

Supplementary Table S2: Associations between primary tumor location and clinico-pathologic variables of 400 melanoma samples.

	Acral		Non-acral Skin		Conjunctival		Mucosal		Occult		Missing data		Total	
	N	%	N	%	N	%	N	%	N	%	N	%	N	
Sex														
	Female	19	5	85	21	20	6	21	5	17	4	8	2	170
	Male	16	4	136	34	23	6	12	3	26	7	17	4	230
Age	<=60 years	17	4	124	31	16	4	8	2	15	4	0	0	180
	>60 years	18	5	92	23	19	5	24	6	28	7	0	0	181
	Missing data	0	0	5	0	8	2	1	0,2	0	0	25	6	39
SDHD status	Wild-type	34	9	212	53	42	11	32	8	41	10	23	6	384
	Mutant	1	0,3	9	2,3	1	0,3	1	0,3	2	0,5	2	0,5	16
SDHD mutations	Wild-type	34	9	212	53	42	11	32	8	41	10	23	6	391
	523C>T	0	0	3	0,8	1	0,3	0	0	0	0	1	0,3	5
	541C>T	0	0	3	0,8	0	0	0	0	0	0	0	0	3
	544C>T	0	0	2	0,5	0	0	0	0	1	0,3	0	0	3
	542C>A	0	0	1	0,3	0	0	1	0,3	1	0,3	0	0	3
	547C>T	0	0	0	0	0	0	0	0	0	0	1	0,3	1
	547C>A*	0	0	0	0	0	0	0	0	1	0,3	0	0	1
Mutant oncogene#	BRAF	9	2	96	26	12	3	3	0,8	20	5	2	0,5	142
	KIT	0	0	0	0	1	0,2	3	0,8	0	0	0	0	4
	NRAS	10	3	51	14	7	2	1	0,3	11	3	2	0,5	82
	TERT prom.	4	2	62	30	13	6	4	2	12	6	0	0	95

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	Acral		Non-acral Skin		Conjunctival		Mucosal		Occult		Missing data		Total
	N	%	N	%	N	%	N	%	N	%	N	%	
<i>BRAF</i> and <i>NRAS</i>	20	5	145	39	19	5	4	1	31	8	3	1	222
	15	4	72	19	23	6	29	8	10	3	5	1	154
Clinical stage at diagnosis	3	0,7	40	10	0	0	3	0,7	0	0	0	0	46
	13	3	95	24	0	0	14	3,5	0	0	0	0	122
	16	4	73	18	0	0	7	2	26	7	0	0	122
	2	0,5	6	2	0	0	5	1	16	4	0	0	29
	1	0,3	7	2	43	11	4	1	1	0,2	25	6	81
Ulceration	7	15	50	13	0	0	4	1	1	0,3	0	0	62
	15	14	65	16	1	0,3	7	2	0	0	0	0	88
	13	3	106	27	42	11	22	5	42	10	25	6	250
Sentinel lymph node	10	3	60	15	0	0	7	2	1	0,3	0	0	78
	13	3	69	17	0	0	1	0,3	1	0,3	0	0	84
	12	3	92	23	43	11	25	6	41	10	25	6	238

*546C > A *SDHD* promoter mutation was found to present in the germline;

#*BRAF*, *NRAS*, *KIT* were screened in $n = 376$, the *TERT* promoter in $n = 210$ cases; 2 cases harbored a *BRAF* and a *NRAS* mutation

Supplementary Table S3: SDHD promoter variants called in whole exome data of 92 melanomas

Patient	Sample	Chr.	Position	Reference allele	Alternative allele	Average coverage	Read coverage	Reads alternative allele	Variant frequency	Core ETS site'TTCC' changed
Pat_22	post-treatment	11	111,957,539	T	A	25.53	31	2	0.065	Abrogated, TTCC>TATCC
Pat_25	pre-treatment	11	111,957,547	C	T	21.16	27	8	0.296	Moved, TTCCC>TTTCC
Pat_25	post-treatment	11	111,957,547	C	T	22.47	30	11	0.367	Moved, TTCCC>TTTCC
Pat_52	pre-treatment	11	111,957,546	T	A	17.19	19	2	0.105	Abrogated, TTCC>TACC

The data was taken from [24]. A minimum coverage of 10 unique reads and at least 2 reads supporting a variant was required.