Supplementary table 1: Position of SVs and their heteroplasmy percentage in *Ifnar*$^{-/-}$ mice.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Insertions	249-249	3	*mt-Rnr1*	37.76
	293-293	1	*mt-Rn1*	1.09
	476-476	31	*mt-Rn1*	33.33
	871-871	1	*mt-Rn1*	2.18
	891-891	1	*mt-Rn1*	2.13
	894-894	1	*mt-Rn1*	23.89
	2688-2688	22	*mt-Tl*	0.05
	2698-2698	1	*mt-Tl*	0.04
	2756-2756	1	*mt-Nd1*	8.06
	2759-2759	4	*mt-Nd1*	1.22
	2926-2926	2	*mt-Nd1*	6.86
	2928-2928	1	*mt-Nd1*	36.59
	3619-3619	1	*mt-Nd1*	5.62
	3655-3655	1	*mt-Nd1*	3.55
	3721-3721	3	*mt-Ti*	13.79
	4857-4857	3	*mt-Nd2*	1.65
	4859-4859	1	*mt-Nd2*	2.73
	5713-5713	1	*mt-Cox1*	23.08
	6006-6006	1	*mt-Cox1*	27.27
	8557-8557	1	*mt-Atp6*	1.20
	8684-8684	2	*mt-Atp6*	1.73
	8801-8801	1	*mt-Atp6*	5.76
	8861-8861	1	*mt-Atp6*	3.70
	8938-8938	1	*mt-Atp6*	2.65
	8939-8939	1	*mt-Atp6*	2.78
	9034-9034	1	*mt-Atp6*	16.28
	9158-9158	2	*mt-Atp6*	30.00
	9204-9204	21	*mt-Atp6*	2.00
	12376-12376	1	*mt-Nd5*	2.89
	13436-13436	1	*mt-Nd5*	1.90
	13698-13698	1	*mt-Nd6*	1.40
	13702-13702	1	*mt-Nd6*	1.48
	13770-13770	26	*mt-Nd6*	4.35
	13808-13808	5	*mt-Nd6*	8.00
	13820-13820	1	*mt-Nd6*	13.64
	16181-16181	1	*D-loop*	17.86

	16288-16288	8	*D-loop*	14.29
	16290-16290	3	*D-loop*	40.00
Deletions	259-260	1	*mt-Rnr1*	1.18
	341-342	1	*mt-Rnr1*	0.40
	372-373	1	*mt-Rnr1*	1.09
	631-632	1	*mt-Rnr1*	0.10
	645-646	1	*mt-Rnr1*	0.08
	704-705	1	*mt-Rnr1*	0.17
	746-747	1	*mt-Rnr1*	0.14
	799-804	5	*mt-Rnr1*	0.25
	2500-2502	2	*mt-Rnr2*	0.16
	2518-2519	1	*mt-Rnr2*	0.17
	2665-2666	1	*mt-Rnr2*	0.08
	2683-2684	1	*mt-Tl*	0.06
	2698-2699	1	*mt-Tl*	0.04
	2728-2729	1	*mt-Tl*	0.05
	2808-2809	1	*mt-Nd1*	0.08
	2831-2832	1	*mt-Nd1*	0.10
	2927-2928	1	*mt-Nd1*	2.20
	3468-3469	1	*mt-Nd1*	1.06
	3579-3580	1	*mt-Nd1*	0.16
	3599-3600	1	*mt-Nd1*	0.13
	3812-3813	1	*mt-Tq*	22.22
	4525-4602	77	*mt-Nd2*	0.62
	4851-4914	63	*mt-Nd2*	3.09
	4876-4934	58	*mt-Nd2*	2.00
	4903-4904	1	*mt-Nd2*	3.45
	8254-8661	407	*mt-Atp6…mt-Cox3*	1.72
	8555-8674	119	*mt-Atp6…mt-Cox3*	1.04
	8685-8686	1	*mt-Cox3*	0.61
	11380-11381	1	*mt-Nd4*	4.51
	12501-12503	2	*mt-Nd5*	0.30
	12624-12816	192	*mt-Nd5*	3.75
	12631-12823	192	*mt-Nd5*	1.63
	12957-12958	1	*mt-Nd5*	10.81
	13427-13657	230	*mt-Nd5*	1.84
	13430-13681	251	*mt-Nd5… mt-Nd6*	1.88
	13675-13732	57	*mt-Nd6*	0.34
	13677-13774	97	*mt-Nd6*	0.37

	13700-13706	6	*mt-Nd6*	0.52
	13701-13702	1	*mt-Nd6*	1.89
	13773-13774	1	*mt-Nd6*	1.83
	15152-15153	1	*mt-Cytb*	20.00
Inversions	158-255	97	*mt-Rnr1*	1.92
	294-711	417	*mt-Rnr1*	1.51
	296-541	245	*mt-Rnr1*	1.15
	308-467	159	*mt-Rnr1*	6.86
	348-528	180	*mt-Rnr1*	0.97
	377-460	83	*mt-Rnr1*	0.61
	567-2199	1632	*mt-Rnr1*	1.63
	667-732	65	*mt-Rnr1*	0.18
	672-845	173	*mt-Rnr1*	2.40
	889-969	80	*mt-Rnr1*	3.12
	2550-2639	89	*mt-Rnr2*	0.23
	2681-2757	76	*mt-Tl1 ... mt-Nd1*	0.07
	2747-2840	93	*mt-Tl1 ... mt-Nd1*	0.20
	2759-2921	162	*mt-Nd1*	12.15
	3530-3620	90	*mt-Nd1*	0.37
	4900-5077	177	*mt-Nd2 ... mt-Ta*	14.28
	5716-6003	287	*mt-Co1*	38.46
	8785-8868	83	*mt-Co3*	10.57
	8866-8934	68	*mt-Co3*	1.28
	8931-9030	99	*mt-Co3*	2.63
	8932-9029	97	*mt-Co3*	3.85
	9027-9159	132	*mt-Co3*	8.33
	12763-12954	191	*mt-Nd5*	100.00
	13718-13805	87	*mt-Nd5*	0.88
Tandem duplications	249-881	632	*mt-Rnr1*	2.22
	253-885	632	*mt-Rnr1*	67.67
	373-464	91	*mt-Rnr1*	0.28
	598-668	70	*mt-Rnr1*	0.06
	607-685	78	*mt-Rnr1*	0.11
	2581-2646	65	*mt-Rnr2*	0.14
	2655-2737	82	*mt-Rnr2*	0.08
	2726-2787	61	*mt-Rnr2*	0.05
	2766-2805	39	*mt-Nd1*	0.21
	2806-2858	52	*mt-Nd1*	0.09
	2858-2936	78	*mt-Nd1*	0.14

	3652-3710	58	*mt-Nd1*	0.43
	4401-4481	80	*mt-Nd2*	2.67
	4598-4640	42	*mt-Nd2*	0.61
	8406-8487	81	*mt-Atp6*	0.61
	8419-8500	81	*mt-Atp6*	0.58
	8973-9039	66	*mt-Co3*	0.98
	12378-12849	471	*mt-Nd5*	25.33
	13591-13689	98	*mt-Nd6*	0.36
	13608-13689	81	*mt-Nd6*	0.36
	13666-13723	57	*mt-Nd6*	1.03
	13668-13725	57	*mt-Nd6*	0.34
	13673-13730	57	*mt-Nd6*	0.37
	13702-13817	115	*mt-Nd6*	4.00

Supplementary table 2: Position of SNVs, their consequences, and heteroplasmy percentage in *Ifnar*$^{-/-}$ mice.

Substitution	**Consequence**	**Gene**	**HET%**
m.112A>G	non-coding	*mt-Tf*	12.8
m.115C>T	non-coding	*mt-Tf*	87.63
m.363T>G	non-coding	*mt-Tf*	34.72
m.481A>C	non-coding	*mt-Tf*	49.71
m.551T>G	non-coding	*mt-Tf*	28.97
m.628C>G	non-coding	*mt-Tf*	34.45
m.756G>C	non-coding	*mt-Tf*	54.05
m.898C>T	non-coding	*mt-Tf*	10.8
m.899G>A	non-coding	*mt-Tf*	44.65
m.1419A>T	non-coding	*mt-Tv*	75.3
m.1537G>C	non-coding	*mt-Tv*	45.89
m.1714A>G	non-coding	*mt-Tv*	71.87
m.1723A>C	non-coding	*mt-Tv*	85.81
m.1745A>T	non-coding	*mt-Tv*	55.32
m.1751A>G	non-coding	*mt-Tv*	67.31
m.1772C>T	non-coding	*mt-Tv*	20.27
m.1883A>G	non-coding	*mt-Tv*	21.03
m.1986C>G	non-coding	*mt-Tv*	51.24
m.2012T>C	non-coding	*mt-Tv*	74.24
m.2094C>T	non-coding	*mt-Tv*	26.8
m.2260C>G	Interegenic	_	61.54
m.2423A>C	Interegenic	_	75.17
m.2437G>C	Interegenic	_	33.81
m.2530C>G	Interegenic	_	18.22
m.2573G>T	Interegenic	_	19.85
m.2650G>A	Interegenic	_	47.88
m.2687A>C	Interegenic	_	41.29
m.2700T>C	Interegenic	_	42.6
m.2885T>A	missense variant	*mt-Nd1*	44.36
m.2898G>C	missense variant	*mt-Nd1*	17.34
m.2950C>G	missense variant	*mt-Nd1*	35.12
m.2951T>G	missense variant	*mt-Nd1*	35
m.2973C>T	missense variant	*mt-Nd1*	56.16
m.3116C>G	missense variant	*mt-Nd1*	61.51
m.3321G>C	missense variant	*mt-Nd1*	50.93
m.3341C>T	missense variant	*mt-Nd1*	14.74
m.3343T>C	missense variant	*mt-Nd1*	16.39
m.3354G>T	missense variant	*mt-Nd1*	47.11

m.3378G>C	missense variant	*mt-Nd1*	52.48
m.3431G>T	missense variant	*mt-Nd1*	56.6
m.3705T>C	missense variant	*mt-Nd1*	22
m.3764T>C	missense variant	*mt-Ti*	30.04
m.4078A>T	missense variant	*mt-Nd2*	88.21
m.4110C>G	missense variant	*mt-Nd2*	96.84
m.4239C>G	missense variant	*mt-Nd2*	25.25
m.4626C>G	missense variant	*mt-Nd2*	65.73
m.5116A>G	missense variant	*mt-Tn*	74.18
m.5145A>C	missense variant	*mt-Tn*	51.64
m.5211T>C	missense variant	*mt-Tc*	79.04
m.5232T>A	missense variant	*mt-Tc*	60.31
m.5403G>C	missense variant	*mt-Cox1*	77.63
m.5460G>T	missense variant	*mt-Cox1*	50.82
m.5702A>G	missense variant	*mt-Cox1*	36.8
m.5862T>G	missense variant	*mt-Cox1*	62.26
m.5935C>A	missense variant	*mt-Cox1*	24.59
m.6133G>A	missense variant	*mt-Cox1*	40.54
m.6272T>G	missense variant	*mt-Cox1*	75.02
m.6612C>G	missense variant	*mt-Cox1*	50.79
m.6625T>G	missense variant	*mt-Cox1*	96.74
m.6884A>T	missense variant	*mt-Ts1*	40.87
m.7045C>G	missense variant	*mt-Cox2*	18.34
m.7129C>G	missense variant	*mt-Cox2*	24.45
m.7130T>G	missense variant	*mt-Cox2*	49.59
m.7188A>C	missense variant	*mt-Cox2*	87.59
m.7415C>G	missense variant	*mt-Cox2*	37.64
m.7435A>C	missense variant	*mt-Cox2*	37.91
m.7477A>T	missense variant	*mt-Cox2*	41.38
m.7598T>C	missense variant	*mt-Cox2*	66.87
m.8000T>G	missense variant	*mt-Atp6*	32.29
m.8106C>A	missense variant	*mt-Atp6*	53.21
m.8124A>C	missense variant	*mt-Atp6*	47.13
m.8127A>G	missense variant	*mt-Atp6*	35.05
m.8130A>C	missense variant	*mt-Atp6*	87.59
m.8168C>T	missense variant	*mt-Atp6*	43.2
m.8200T>C	missense variant	*mt-Atp6*	63.19
m.8201T>A	missense variant	*mt-Atp6*	75.44
m.8254G>T	missense variant	*mt-Atp6*	57.49
m.8457T>G	missense variant	*mt-Atp6*	61.76
m.8742G>C	missense variant	*mt-Co3*	76.03

m.8766A>G	missense variant	*mt-Co3*	50.79
m.8810A>G	missense variant	*mt-Co3*	38.64
m.8890C>A	missense variant	*mt-Co3*	33.63
m.8958C>G	missense variant	*mt-Co3*	17.65
m.8966A>C	missense variant	*mt-Co3*	25.98
m.9024T>C	missense variant	*mt-Co3*	46.76
m.9042T>A	missense variant	*mt-Co3*	28.57
m.9137A>C	missense variant	*mt-Co3*	49.57
m.9190C>G	missense variant	*mt-Co3*	78.57
m.9556C>G	missense variant	*mt-Nd3*	24.47
m.9683A>G	missense variant	*mt-Nd3*	49.44
m.9835T>C	missense variant	*mt-Tr*	35.58
m.9886T>C	missense variant	*mt-Nd4l*	34.66
m.10288G>T	missense variant	*mt-Nd4*	77.09
m.10825A>C	missense variant	*mt-Nd4*	94.42
m.11110T>A	missense variant	*mt-Nd4*	78.59
m.11273T>G	missense variant	*mt-Nd4*	55.82
m.11373A>C	missense variant	*mt-Nd4*	23.21
m.11376T>G	missense variant	*mt-Nd4*	15.84
m.11408C>A	missense variant	*mt-Nd4*	47.03
m.11440A>G	missense variant	*mt-Nd4*	22.85
m.11445T>A	missense variant	*mt-Nd4*	44.09
m.11448C>T	missense variant	*mt-Nd4*	68.6
m.11539G>A	missense variant	*mt-Nd4*	14.29
m.11541G>A	missense variant	*mt-Nd4*	63.68
m.11586A>C	missense variant	*mt-Th*	19.71
m.12007C>A	missense variant	*mt-Nd5*	43.85
m.12054T>G	missense variant	*mt-Nd5*	24.22
m.12058T>C	missense variant	*mt-Nd5*	10
m.12176G>C	missense variant	*mt-Nd5*	93.45
m.12264A>G	missense variant	*mt-Nd5*	55.22
m.12323A>T	missense variant	*mt-Nd5*	39.43
m.12348A>G	missense variant	*mt-Nd5*	77.89
m.12426C>G	missense variant	*mt-Nd5*	35.42
m.12574T>G	missense variant	*mt-Nd5*	36
m.12685T>C	missense variant	*mt-Nd5*	63.96
m.12735T>G	missense variant	*mt-Nd5*	52.28
m.12872C>G	missense variant	*mt-Nd5*	59.22
m.13341A>T	missense variant	*mt-Nd5*	76.16
m.13550T>A	missense variant	*mt-Nd5*	46.6
m.13828T>G	missense variant	*mt-Nd6*	91.61

m.13993T>C	missense variant	*mt-Nd6*	81.07
m.14151C>T	missense variant	*mt-Cytb*	21.85
m.14353A>T	missense variant	*mt-Cytb*	31.39
m.14379T>G	missense variant	*mt-Cytb*	93.72
m.14464T>A	missense variant	*mt-Cytb*	47.22
m.14768A>C	missense variant	*mt-Cytb*	32.17
m.14823A>T	missense variant	*mt-Cytb*	36.81
m.14922C>A	missense variant	*mt-Cytb*	44.74
m.14955T>G	missense variant	*mt-Cytb*	94.42
m.14990C>G	missense variant	*mt-Cytb*	45.3
m.15309G>C	missense variant	*mt-Tt*	14.02
m.15377C>A	missense variant	*mt-Tp*	49.18
m.15383C>A	missense variant	*mt-Tp*	42.54
m.15441C>G	non coding	D-loop	37.67
m.15602C>G	non coding	D-loop	75.12
m.15613G>C	non coding	D-loop	59.89
m.15615C>T	non coding	D-loop	11.52
m.15618A>G	non coding	D-loop	16.6
m.15622C>A	non coding	D-loop	17.99
m.15833C>G	non coding	D-loop	28.77
m.15950A>C	non coding	D-loop	73.36
m.15975T>C	non coding	D-loop	46.53
m.16007G>A	non coding	D-loop	34.2

Supplementary table 3: 6 *Ifnar*$^{-/-}$ cells are representing some common variations.

Single DA neuron's name	No. Shared variations	SNP
Ifnar-12 & Ifnar-13 & Ifnar-21	1	m.12054T>G
Ifnar-12 & Ifnar-13 & Ifnar-23	1	m.2650G>A
Ifnar-11 & Ifnar-12	2	m.13828T>G m.8254G>T
Ifnar-11 & Ifnar-21	1	m.8127A>G
Ifnar-12 & Ifnar-13	1	m.899G>A
Ifnar-13 & Ifnar-23	2	m.15602C>G m.898C>T
Ifnar-21 & Ifnar-33	2	m.2423A>C m.5145A>C

Supplementary table 4: Position of SVs and their heteroplasmy percentage in bulk MCF7 cell line.

Type of SVs	Breakpoints	Size (nt)	Gene	HET%
Deletions	2509-2515	5	*MT-RNR2*	1.4
	10687-10688	1	*MT-ND4L*	1.32
	6746-6771	24	*MT-CO1*	2.1
	7477-7483	5	*MT-CO2*	1.3
Inversions	1108-1199	94	*MT-ND4*	1.9
	7019-7116	98	*MT-CO1*	1
Insertions	5742-5742	1	intergenic	2.47
	5897-5898	1	*MT-TY*	1.2
	5894-5894	1	intergenic	11.11

Supplementary table 5: Position of SVs and their heteroplasmy percentage in single MCF7 cells.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Deletions	9439-9440	1	*MT-CO3*	8
	11692-11693	1	*MT-ND4*	23.81
	16230-16231	1	D-loop	7.65
Inversions	7994-8167	174	*MT-CO2*	16.39
	7996-8156	161	*MT-CO2*	3
	7783-7783	2	*MT-CO2*	10.71
	7790-7790	6	*MT-CO2*	4.44
	7799-7799	1	*MT-CO2*	21.43
	7995-7995	1	*MT-CO2*	2.79
	7996-7996	4	*MT-CO2*	2.62
	8067-8067	13	*MT-CO2*	3.16
	8118-8118	3	*MT-CO2*	3.45
	8172-8172	1	*MT-CO2*	6.67
	9161-9161	3	*MT-ATP6*	7.69
	9311-9311	1	*MT-CO3*	7.69
	11705-11705	2	*MT-ND4*	5
	12662-12662	1	*MT-ND5*	4.65
	14438-14438	1	*MT-ND6*	8.33
	16135-16135	1	*MT-ND6*	17.46
	16142-16142	4	D-loop	59.64
	16221-16221	1	D-loop	76.75
	16217-16217	2	D-loop	2.56
Tandem duplications	7819-7984	166	*MT-CO2*	9.09

Supplementary table 6: Position of SNVs, their consequences, and heteroplasmy percentage in bulk MCF7 cell line.

Substitution	**Consequence**	**Impact**	**Gene**	**Amino acid substitution**	**Codons**	**HET%**	**Existing variants**	**Phenotype data**
m.3977T>G	missense variant	MODERATE	*MT-ND1*	p.F224C	tTc/tGc	11.43		
m.5390A>C	missense variant	MODERATE	*MT-ND2*	p.M307I	atA/atC	12.84		
m.9387G>C	missense variant	MODERATE	*MT-CO3*	p.V61L	Gta/Cta	16.47		
m.9447T>G	missense variant	MODERATE	*MT-CO3*	p.Y81D	Tac/Gac	11.54		
m.12771G>T	missense variant	MODERATE	*MT-ND5*	p.E145D	gaG/gaT	12.12	COSM1155528	Endometrium tumor
m.14294T>G	missense variant	MODERATE	*MT-ND6*	p.Y127S	tAt/tCt	10.89	COSM1138256& COSM1138257	Kidney tumor
m.14417A>G	missense variant	MODERATE	*MT-ND6*	p.V86A	gTt/gCt	10.99	rs878905427	
m.15097T>G	missense variant	MODERATE	*MT-CYB*	p.I117M	atT/atG	17.36		
m.12596T>G	Stop-gained	HIGH	*MT-ND5*	p.M87X	aTa/aGa	16.67		
m.14283C>T	Stop-gained	HIGH	*MT-ND6*	p.G131X	Ggg/Agg	12.61		

COSMIC: The Catalogue Of Somatic Mutations In Cancer
Condel: Consensus deleterious score for an amino acid substitution based on SIFT and PolyPhen2
X: stop codon

Supplementary table 7: Position of SNVs, their consequences, and heteroplasmy percentage in single MCF7 cells.

Substitution	Consequence	Gene	Impact	Amino acid change	HET%	Codons	Existing variants	Phenotype data
m.3422T>A	Missense variant	*MT-ND1*	MODERATE	p.V39D	18.18	gTt/gAt		
m.3764C>T	Missense variant	*MT-ND1*	MODERATE	p.T153M	15.15	aCa/aTa		
m.3797C>G	Missense variant	*MT-ND1*	MODERATE	p.T164S	18.92	aCc/aGc		
m.3929T>C	Missense variant	*MT-ND1*	MODERATE	p.V208A	11.11	gTc/gCc		
m.4070A>C	Missense variant	*MT-ND1*	MODERATE	p.Y255S	15.52	tAc/tCc		
m.4073C>A	Missense variant	*MT-ND1*	MODERATE	p.T256K	40.62	aCa/aAa		
m.4075A>G	Missense variant	*MT-ND1*	MODERATE	p.T257A	20.51	Aca/Gca		
m.4133C>A	Missense variant	*MT-ND1*	MODERATE	p.A276E	31.43	gCa/gAa		
m.4206A>C	Missense variant	*MT-ND1*	MODERATE	p.L300F	51.92	ttA/ttC		
m.4226T>C	Missense variant	*MT-ND1*	MODERATE	p.M307T	35.9	aTa/aCa		
m.4246A>C	Missense variant	*MT-ND1*	MODERATE	p.I314L	13.33	Att/Ctt		
m.4494A>T	Missense variant	*MT-ND2*	MODERATE	p.I9F	14.49	Atc/Ttc		
m.4572A>G	Missense variant	*MT-ND2*	MODERATE	p.M35V	19.57	Ata/Gta		
m.4592T>G	Missense variant	*MT-ND2*	MODERATE	p.I41M	26.92	atT/atG		
m.4692C>G	Missense variant	*MT-ND2*	MODERATE	p.L75V	24.07	Ctc/Gtc		
m.4708T>C	Missense variant	*MT-ND2*	MODERATE	p.L80P	11.9	cTc/cCc		
m.4831G>A	Missense variant	*MT-ND2*	MODERATE	p.G121D	66.67	gGc/gAc		
m.4869C>T	Stop-gained	*MT-ND2*	HIGH	p.Q134X	22.22	Caa/Taa		
m.4888C>A	Stop-gained	*MT-ND2*	HIGH	p.S140X	10.81	tCa/tAa		
m.5230T>G	Missense variant	*MT-ND2*	MODERATE	p.L254R	34.38	cTg/cGg		
m.6009C>G	Missense variant	*MT-CO1*	MODERATE	p.L36V	50	Ctt/Gtt		
m.6203A>C	Missense variant	*MT-CO1*	MODERATE	p.M100I	12.12	atA/atC		
m.6403C>A	Missense variant	*MT-CO1*	MODERATE	p.T167K	10.81	aCa/aAa		
m.6438T>G	Missense variant	*MT-CO1*	MODERATE	p.Y179D	41.33	Tac/Gac		
m.6698A>T	Missense variant	*MT-CO1*	MODERATE	p.K265N	17.95	aaA/aaT		
m.6782T>G	Missense variant	*MT-CO1*	MODERATE	p.F293L	10.2	ttT/ttG		
m.6795G>T	Missense variant	*MT-CO1*	MODERATE	p.D298Y	54.84	Gac/Tac		
m.6967G>A	Missense variant	*MT-CO1*	MODERATE	p.G355D	12.82	gGc/gAc		
m.6976T>G	Missense variant	*MT-CO1*	MODERATE	p.L358W	12.9	tTa/tGa	COSM1331631& COSM1331632	Ovary tumour
m.7051T>G	Stop-gained	*MT-CO1*	HIGH	p.M383X	33.33	aTa/aGa		
m.7291C>G	Stop-gained	*MT-CO1*	HIGH	p.T463X	11.43	aCa/aGa		
m.7756C>A	Missense variant	*MT-CO2*	MODERATE	p.D57E	22.22	gaC/gaA		
m.7950T>G	Stop-gained	*MT-CO2*	HIGH	p.M122X	13.56	aTa/aGa		
m.7968T>G	Missense variant	*MT-CO2*	MODERATE	p.L128R	12.5	cTa/cGa		
m.8178A>T	Missense variant	*MT-CO2*	MODERATE	p.E198V	10.81	gAa/gTa		
m.8567T>C	Missense variant	*MT-ATP8*	MODERATE	p.S68P	21.88	Tcc/Ccc		
m.9070T>A	Missense variant	*MT-ATP6*	MODERATE	p.S182T	21.67	Tca/Aca		

m.9194A>G	Missense variant	*MT-ATP6*	MODERATE	p.H223R	13.16	cAc/cGc		
m.9235T>C	Missense variant	*MT-CO3*	MODERATE	p.M10T	45.45	aTa/aCa		
m.9303A>G	Missense variant	*MT-CO3*	MODERATE	p.M33V	10.42	Atg/Gtg		
m.9396G>T	Stop-gained	*MT-CO3*	HIGH	p.E64X	15.91	Gaa/Taa		
m.9399A>C	Missense variant t	*MT-CO3*	MODERATE	p.S65R	52.17	Agc/Cgc		
m.9562C>G	Stop-gained	*MT-CO3*	HIGH	p.T119X	11.11	aCa/aGa		
m.9717C>A	Missense variant	*MT-CO3*	MODERATE	p.L171I	32.56	Ctc/Atc		
m.9885T>A	Missense variant	*MT-CO3*	MODERATE	p.F227I	11.11	Ttt/Att		
m.9960C>G	Missense variant	*MT-CO3*	MODERATE	p.L252V	10.59	Ctg/Gtg		
m.10192C>T	Missense variant	*MT-ND3*	MODERATE	p.S45F	11.76	tCc/tTc		
m.10820C>T	Missense variant	*MT-ND4*	MODERATE	p.H21Y	36.59	Cac/Tac		
m.10923C>T	Missense variant	*MT-ND4*	MODERATE	p.T55I	12.12	aCc/aTc		
m.11217C>A	Missense variant	*MT-ND4*	MODERATE	p.T153N	15	aCc/aAc		
m.11286T>C	Missense variant	*MT-ND4*	MODERATE	p.I176T	55.1	aTt/aCt		
m.11546G>A	Missense variant	*MT-ND4*	MODERATE	p.V263M	44.64	Gta/Ata		
m.11598C>G	Stop-gained	*MT-ND4*	HIGH	p.T280X	64.29	aCa/aGa		
m.11700T>A	Missense variant	*MT-ND4*	MODERATE	p.I314N	20.37	aTt/aAt		
m.11787T>A	Missense variant	*MT-ND4*	MODERATE	p.I343N	19.15	aTc/aAc		
m.11792T>C	Missense variant	*MT-ND4*	MODERATE	p.S345P	11.29	Tct/Cct		
m.11795C>G	Missense variant	*MT-ND4*	MODERATE	p.Q346E	11.32	Caa/Gaa		
m.12027T>A	Missense variant	*MT-ND4*	MODERATE	p.I423N	58.33	aTt/aAt		
m.12452T>A	Missense variant	*MT-ND5*	MODERATE	p.I39N	32.35	aTt/aAt		
m.12517G>T	Missense variant	*MT-ND5*	MODERATE	p.V61F	44.23	Gtt/Ttt		
m.12653G>C	Missense variant	*MT-ND5*	MODERATE	p.W106S	62.69	tGa/tCa		
m.12659T>G	Stop-gained	*MT-ND5*	HIGH	p.M108X	12.77	aTa/aGa		
m.12694T>C	Missense variant	*MT-ND5*	MODERATE	p.Y120H	27.94	Tat/Cat		
m.12764G>C	Missense variant	*MT-ND5*	MODERATE	p.G143A	21.43	gGc/gCc		
m.12925G>A	Missense variant	*MT-ND5*	MODERATE	p.D197N	15	Gac/Aac		
m.13026C>G	Missense variant	*MT-ND5*	MODERATE	p.H230Q	69.33	caC/caG		
m.13438C>A	Missense variant	*MT-ND5*	MODERATE	p.L368I	45.71	Ctc/Atc		
m.13462G>C	Missense variant	*MT-ND5*	MODERATE	p.G376R	12.9	Ggc/Cgc		
m.13813G>A	Missense variant	*MT-ND5*	MODERATE	p.V493I	12.9	Gtc/Atc		
m.14098T>G	Missense variant	*MT-ND5*	MODERATE	p.F588V	22.22	Ttc/Gtc		
m.14109C>G	Missense variant	*MT-ND5*	MODERATE	p.F591L	23.19	ttC/ttG		
m.14187C>A	Missense variant	*MT-ND6*	MODERATE	p.G163C	19.44	Ggt/Tgt		
m.14291T>G	Missense variant	*MT-ND6*	MODERATE	p.E128A	41.77	gAa/gCa	COSM1155551& COSM1155552	Endometrium tumor
m.14656A>C	Missense variant	*MT-ND6*	MODERATE	p.F6L	15.62	ttT/ttG		
m.14658A>C	Missense variant	*MT-ND6*	MODERATE	p.F6V	27.82	Ttt/Gtt		
m.14886C>T	Missense variant	*MT-CYB*	MODERATE	p.T47M	32.5	aCa/aTa		
m.15011A>G	Missense variant	*MT-CYB*	MODERATE	p.M89V	26.83	Ata/Gta		

m.15054A>C	Missense variant	*MT-CYB*	MODERATE	p.Y103S	18.75	tAt/tCt		
m.15117T>C	Missense variant	*MT-CYB*	MODERATE	p.M124T	40.32	aTa/aCa		
m.15213T>A	Missense variant	*MT-CYB*	MODERATE	p.I156N	15	aTt/aAt		
m.15263C>A	Missense variant	*MT-CYB*	MODERATE	p.P173T	10.64	Ccc/Acc		
m.15301G>C	Missense variant	*MT-CYB*	MODERATE	p.L185F	20.29	ttG/ttC	rs193302991	**Familial cancer of breast (OMIM: 114480)**
m.15483C>G	Missense variant	*MT-CYB*	MODERATE	p.S246W	70.69	tCa/tGa		
m.15510A>C	Missense variant	*MT-CYB*	MODERATE	p.N255T	10.81	aAt/aCt		
m.15818T>C	Missense variant	*MT-CYB*	MODERATE	p.Y358H	11.32	Tac/Cac		

Supplementary table 8: Position of SVs and their heteroplasmy percentage in bulk SW620 cell line.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Deletions	720-721	1	*MT-RNR1*	4.35
	6377-6378	1	*MT-CO1*	3.03
	8805-8806	1	*MT-ATP6*	2.82
	10687-10688	2	*MT-ND4L*	3.51
	15628-15629	1	*MT-CYB*	3.28
	16089-16090	1	D-loop	3.92
Insertions	1385-1385	2	*MT-RNR1*	2.22
	3696-3696	1	*MT-ND1*	4.35
	5302-5302	1	*MT-ND2*	5.13
	16560-16560	21	D-loop	13.04

Supplementary table 9: Position of SVs and their heteroplasmy percentage in single SW620 cells.

Type of SVs	Breakpoints	Size (nt)	Gene	HET%
Deletions	5304-5316	12	*MT-ND2*	0.66
	5311-5317	6	*MT-ND2*	4.44
	13907-13908	1	*MT-ND5*	6.06
	10339-10340	1	*MT-ND3*	1.80
Insertions	6368-6368	1	*MT-CO1*	3.09
	5305-5305	15	*MT-ND2*	0.62
	5308-5308	24	*MT-ND2*	1.07
	6491-6491	15	*MT-CO1*	10.00
	6583-6583	85	*MT-CO1*	14.29
Tandem duplications	5294-5333	39	*MT-ND2*	3.28
	5295-14065	8770	*MT-ND2 … MT-ND5*	2.21
	5296-12473	7177	*MT-ND2 … MT-ND5*	0.89
	14051-14066	15	*MT-ND5*	5.13

Supplementary table 10: Position of SNVs, their consequences, and heteroplasmy percentage in bulk SW620 cell line.

Substitution	**Consequence**	**Gene**	**Impact**	**Amino acid change**	**HET%**	**Codons**	**Existing variants**	**Phenopte data**
m.7332G>C	Missense variant	*MT-CO1*	MODERATE	p.A477P	15.38	Gct/Cct		
m.10104C>A	Missense variant	*MT-ND3*	MODERATE	p.L16M	20	Cta/Ata		
m.13759G>A	Missense variant	*MT-ND5*	MODERATE	p.A475T	10	Gca/Aca	rs386420024	

Supplementary table 11: Position of SNVs, their consequences, and heteroplasmy percentage in single SW620 cells.

Substitution	Consequence	Gene	Impact	Amino acid change	HET%	Codons	Existing variants	Phenopte data
m.3397A>C	Missense variant	*MT-ND1*	MODERATE	p.M31L	11.76	Ata/Cta		
m.3400C>T	Stop-gained	*MT-ND1*	HIGH	p.Q32X	12.5	Caa/Taa		
m.3430C>A	Missense variant	*MT-ND1*	MODERATE	p.P42T	10.53	Ccc/Acc		
m.3581C>G	Missense variant	*MT-ND1*	MODERATE	p.P92R	15	cCc/cGc		
m.3841T>A	Stop-gained	*MT-ND1*	HIGH	p.W179X	32.43	Tga/Aga		
m.3900C>G	Missense variant	*MT-ND1*	MODERATE	p.F198L	13.79	ttC/ttG		
m.3923A>T	Missense variant	*MT-ND1*	MODERATE	p.E206V	38.1	gAa/gTa		
m.4213T>A	Stop-gained	*MT-ND1*	HIGH	p.W303X	14.06	Tga/Aga		
m.4508C>A	Missense variant	*MT-ND2*	MODERATE	p.I13M	14.29	atC/atA		
m.4629G>T	Stop-gained	*MT-ND2*	HIGH	p.E54X	25	Gaa/Taa		
m.4707C>T	Missense variant	*MT-ND2*	MODERATE	p.L80F	20.83	Ctc/Ttc		
m.4781A>T	Missense variant	*MT-ND2*	MODERATE	p.M104I	68.57	atA/atT		
m.4813T>C	Missense variant	*MT-ND2*	MODERATE	p.V115A	52.38	gTc/gCc		
m.4815C>A	Missense variant	*MT-ND2*	MODERATE	p.P116T	14	Cca/Aca		
m.4909C>T	Missense variant	*MT-ND2*	MODERATE	p.P147L	25.86	cCc/cTc		
m.5247T>C	Missense variant	*MT-ND2*	MODERATE	p.F260L	50.6	Ttt/Ctt		
m.5254C>G	Missense variant	*MT-ND2*	MODERATE	p.P262R	11.43	cCc/cGc		
m.6085A>C	Missense variant	*MT-CO1*	MODERATE	p.H61P	93.99	cAt/cCt		
m.6334A>G	Missense variant	*MT-CO1*	MODERATE	p.D144G	21.21	gAc/gGc		
m.6440C>G	Stop-gained	*MT-CO1*	HIGH	p.Y179X	28.57	taC/taG		
m.6501C>T	Missense variant	*MT-CO1*	MODERATE	p.P200S	15.13	Cca/Tca		
m.6630G>T	Missense variant	*MT-CO1*	MODERATE	p.V243F	35.9	Gtt/Ttt		
m.6771C>G	Missense variant	*MT-CO1*	MODERATE	p.H290D	21.18	Cac/Gac		
m.6772A>C	Missense variant	*MT-CO1*	MODERATE	p.H290P	11.11	cAc/cCc		
m.6798G>A	Missense variant	*MT-CO1*	MODERATE	p.V299M	37.59	Gta/Ata		
m.6909G>T	Missense variant	*MT-CO1*	MODERATE	p.A336S	30.95	Gct/Tct		
m.6921T>A	Stop-gained	*MT-CO1*	HIGH	p.W340X	51.16	Tga/Aga		
m.7057C>G	Missense variant	*MT-CO1*	MODERATE	p.A385G	10.53	gCt/gGt		
m.7165T>C	Missense variant	*MT-CO1*	MODERATE	p.V421A	12.5	gTa/gCa		
m.7246C>G	Missense variant	*MT-CO1*	MODERATE	p.T448S	13.33	aCc/aGc		
m.7276C>T	Missense variant	*MT-CO1*	MODERATE	p.S458L	73.13	tCa/tTa		
m.7443A>C	Stop-lost	*MT-CO1*	HIGH	p.X514R	16.13	Aga/Cga		
m.7700C>G	Missense variant	*MT-CO2*	MODERATE	p.L39V	19.15	Ctg/Gtg		
m.8082C>G	Missense variant	*MT-CO2*	MODERATE	p.P166R	15.62	cCc/cGc		
m.8391G>T	Missense variant	*MT-ATP8*	MODERATE	p.W9L	15.46	tGg/tTg		
m.8627C>A	Missense variant	*MT-ATP6*	MODERATE	p.S34Y	27.27	tCc/tAc		

m.8710A>C	Missense variant	*MT-ATP6*	MODERATE	p.N62H	85.71	Aac/Cac		
m.8918A>G	Missense variant	*MT-ATP6*	MODERATE	p.Q131R	23.53	cAa/cGa		
m.8927C>A	Missense variant	*MT-ATP6*	MODERATE	p.P134H	13.82	cCt/cAt		
m.9167T>G	Missense variant	*MT-ATP6*	MODERATE	p.F214C	51.16	tTc/tGc		
m.9169A>G	Missense variant	*MT-ATP6*	MODERATE	p.T215A	16.67	Aca/Gca		
m.9169A>T	Missense variant	*MT-ATP6*	MODERATE	p.T215S	15.62	Aca/Tca		
m.9188A>C	Missense variant	*MT-ATP6*	MODERATE	p.Y221S	14.29	tAc/tCc		
m.9398A>C	Missense variant	*MT-CO3*	MODERATE	p.E64D	76.06	gaA/gaC		
m.9859G>C	Missense variant	*MT-CO3*	MODERATE	p.C218S	61.76	tGc/tCc	COSM1138444 & COSM1138445	Kidney tumour
m.9942G>T	Missense variant	*MT-CO3*	MODERATE	p.D246Y	57.25	Gat/Tat		
m.9954C>A	Missense variant	*MT-CO3*	MODERATE	p.L250M	10.26	Cta/Ata		
m.9965T>G	Stop-gained	*MT-CO3*	HIGH	p.Y253X	17.53	taT/taG		
m.10098G>T	Missense variant	*MT-ND3*	MODERATE	p.A14S	16.67	Gcc/Tcc		
m.10213C>G	Missense variant	*MT-ND3*	MODERATE	p.S52C	21.05	tCc/tGc		
m.10242T>G	Missense variant	*MT-ND3*	MODERATE	p.F62V	28.89	Ttc/Gtc		
m.10255A>T	Missense variant	*MT-ND3*	MODERATE	p.D66V	21.95	gAt/gTt		
m.10543A>C	Missense variant	*MT-ND4L*	MODERATE	p.H25P	21.88	cAc/cCc		
m.10656A>G	Missense variant	*MT-ND4L*	MODERATE	p.M63V	45.45	Ata/Gta	rs28645634	
m.10665T>C	Missense variant	*MT-ND4L*	MODERATE	p.F66L	27.12	Ttt/Ctt		
m.10722T>C	Missense variant	*MT-ND4L*	MODERATE	p.Y85H	72.22	Tat/Cat		
m.10731G>C	Missense variant	*MT-ND4L*	MODERATE	p.D88H	13.95	Gac/Cac		
m.10997A>G	Missense variant	*MT-ND4*	MODERATE	p.S80G	32.35	Agc/Ggc		
m.11000C>A	Missense variant	*MT-ND4*	MODERATE	p.Q81K	83.91	Caa/Aaa		
m.11051A>G	Missense variant	*MT-ND4*	MODERATE	p.M98V	21.88	Ata/Gta		
m.11053A>C	Missense variant	*MT-ND4*	MODERATE	p.M98I	34	atA/atC		
m.11063C>G	Missense variant	*MT-ND4*	MODERATE	p.L102V	10.81	Cta/Gta		
m.11090A>C	Missense variant	*MT-ND4*	MODERATE	p.T111P	88.89	Aca/Cca		
m.11101A>C	Missense variant	*MT-ND4*	MODERATE	p.E114D	63.83	gaA/gaC		
m.11181A>T	Missense variant	*MT-ND4*	MODERATE	p.E141V	28.57	gAa/gTa		
m.11187T>G	Missense variant	*MT-ND4*	MODERATE	p.L143R	58.82	cTg/cGg		
m.11325C>T	Missense variant	*MT-ND4*	MODERATE	p.S189F	19.72	tCc/tTc		
m.11354T>C	Missense variant	*MT-ND4*	MODERATE	p.Y199H	10.08	Tac/Cac		
m.11501C>A	Missense variant	*MT-ND4*	MODERATE	p.L248I	46.88	Ctc/Atc		
m.11502T>A	Missense variant	*MT-ND4*	MODERATE	p.L248H	17.28	cTc/cAc		
m.11726T>C	Missense variant	*MT-ND4*	MODERATE	p.S323P	14.06	Tcc/Ccc		
m.11894C>G	Missense variant	*MT-ND4*	MODERATE	p.L379V	13.89	Ctc/Gtc		
m.11895T>C	Missense variant	*MT-ND4*	MODERATE	p.L379P	38.71	cTc/cCc		
m.12030A>C	Missense variant	*MT-ND4*	MODERATE	p.N424T	28.04	aAc/aCc		
m.12048T>A	Missense variant	*MT-ND4*	MODERATE	p.F430Y	30.95	tTc/tAc		

m.12075T>C	Missense variant	*MT-ND4*	MODERATE	p.M439T	16.22	aTa/aCa		
m.12087C>A	Missense variant	*MT-ND4*	MODERATE	p.P443H	21.6	cCc/cAc		
m.12631T>A	Missense variant	*MT-ND5*	MODERATE	p.S99T	47.92	Tcc/Acc		
m.12655T>C	Missense variant	*MT-ND5*	MODERATE	p.Y107H	10	Tat/Cat		
m.12669C>A	Missense variant	*MT-ND5*	MODERATE	p.D111E	78.85	gaC/gaA		
m.12703A>T	Missense variant	*MT-ND5*	MODERATE	p.I123F	17.14	Atc/Ttc		
m.12928C>A	Missense variant	*MT-ND5*	MODERATE	p.P198T	20	Cca/Aca		
m.13153A>C	Missense variant	*MT-ND5*	MODERATE	p.I273L	46.81	Atc/Ctc		
m.13462G>T	Missense variant	*MT-ND5*	MODERATE	p.G376C	31.91	Ggc/Tgc		
m.13621C>G	Missense variant	*MT-ND5*	MODERATE	p.L429V	72.22	Ctc/Gtc		
m.13678C>A	Missense variant	*MT-ND5*	MODERATE	p.P448T	34.58	Ccc/Acc		
m.13994T>C	Missense variant	*MT-ND5*	MODERATE	p.L553P	36.17	cTa/cCa	COSM6716769	**Large intestine tumor**
m.14107T>A	Missense variant	*MT-ND5*	MODERATE	p.F591I	17.14	Ttc/Atc		
m.14107T>C	Missense variant	*MT-ND5*	MODERATE	p.F591L	40	Ttc/Ctc		
m.14110T>G	Missense variant	*MT-ND5*	MODERATE	p.F592V	22.64	Ttc/Gtc	COSM6716773	**Large intestine tumor**
m.14181A>G	Missense variant	*MT-ND6*	MODERATE	p.Y165H	25.71	Tat/Cat		
m.14360C>T	Stop-gained	*MT-ND6*	HIGH	p.W105X	70.59	tGg/tAg		
m.14553C>T	Missense variant	*MT-ND6*	MODERATE	p.V41I	50	Gtt/Att		
m.14561A>T	Missense variant	*MT-ND6*	MODERATE	p.V38D	15	gTc/gAc		
m.14648C>T	Missense variant	*MT-ND6*	MODERATE	p.S9N	19.51	aGt/aAt		
m.14758A>T	Missense variant	*MT-CYB*	MODERATE	p.M4I	11.43	atA/atT		
m.14886C>T	Missense variant	*MT-CYB*	MODERATE	p.T47M	25.71	aCa/aTa		
m.14961A>T	Missense variant	*MT-CYB*	MODERATE	p.D72V	30.3	gAc/gTc		
m.15018T>C	Missense variant	*MT-CYB*	MODERATE	p.F91S	27.12	tTt/tCt		
m.15257G>T	Missense variant	*MT-CYB*	MODERATE	p.D171Y	97.56	Gac/Tac	COSM1138306 & COSM1138307	Kidney tumour
m.15312T>A	Missense variant	*MT-CYB*	MODERATE	p.I189N	53.33	aTt/aAt		
m.15482T>A	Missense variant	*MT-CYB*	MODERATE	p.S246T	15.62	Tca/Aca		
m.15503C>A	Missense variant	*MT-CYB*	MODERATE	p.P253T	20	Cca/Aca		
m.15692A>T	Missense variant	*MT-CYB*	MODERATE	p.M316L	16	Ata/Tta		

Supplementary table 12: Position of SVs and their heteroplasmy percentage in single myeloid cells obtained from healthy donors.

Type of SVs	Breakpoints	Size (nt)	Gene	HET%
Deletions	105-106	1	D-loop	2.35
	16-17	1	D-loop	2.63
	115-116	1	D-loop	18.97
	119-120	1	D-loop	12.24
	2703-2704	1	MT-*RNR2*	27.94
	16230-16232	2	D-loop	4.60
	16275-16276	1	D-loop	1.75
	16454-16455	1	D-loop	2.93
	2457-2458	1	*MT-RNR2*	2.70
	4894-5317	423	*MT-ND2*	20.00
Inversions	65-273	208	D-loop	19.23
	2499-2591	92	*MT-RNR2*	1.79
	2499-2693	194	*MT-RNR2*	30.82
	2642-2731	89	*MT-RNR2*	4.84
	16291-16471	184	D-loop	1.65
Insertions	5-5	4	D-loop	9.38
	98-98	8	D-loop	3.77
	107-107	12	D-loop	32.56
	110-110	4	D-loop	11.94
	277-277	1	D-loop	6.82
	288-288	5	D-loop	18.18
	339-339	1	D-loop	9.52
	341-341	2	D-loop	12.50
	2330-2330	2	MT-*RNR2*	28.12
	2502-2502	8	MT-*RNR2*	2.40
	16223-16223	6	D-loop	15.38
	16229-16229	4	D-loop	39.73
	16269-16269	3	D-loop	3.20
	16278-16278	4	D-loop	12.29
	16289-16289	1	D-loop	1.11
	16374-16374	1	D-loop	1.06
	16461-16461	14	D-loop	5.79
	16528-16528	9	D-loop	2.15
	16560-16560	21	D-loop	10.96
	16561-16561	24	D-loop	1.14
	16562-16562	18	D-loop	1.13
	16563-16563	7	D-loop	1.88

	16564-16564	15	D-loop	6..33
	16565-16565	9	D-loop	7.19

Supplementary table 13: Position of SNVs, their consequences, and heteroplasmy percentage in single myeloid cells obtained from healthy donors.

Substitution	Consequence	Gene	Impact	Amino acid change	HET%	Codons	Existing variants	Phenotype data
m.3356T>C	Missense variant	*MT-ND1*	MODERATE	p.M17T	58.24	aTg/aCg		
m.3697G>C	Missense variant	*MT-ND1*	MODERATE	p.G131R	32.89	Ggc/Cgc	COSM6119903 & COSM6119904	Lung tumor
m.3958G>C	Missense variant	*MT-ND1*	MODERATE	p.G218R	32.69	Ggc/Cgc		
m.4069T>G	Missense variant	*MT-ND1*	MODERATE	p.Y255D	47.62	Tac/Gac		
m.4160T>A	Missense variant	*MT-ND1*	MODERATE	p.L285H	42.86	cTc/cAc		
m.4516G>A	Missense variant	*MT-ND2*	MODERATE	p.G16D	24.63	gGc/gAc		
m.4543A>C	Missense variant	*MT-ND2*	MODERATE	p.H25P	46.05	cAc/cCc		
m.4662A>G	Missense variant	*MT-ND2*	MODERATE	p.T65A	79.29	Acc/Gcc		
m.4909C>T	Missense variant	*MT-ND2*	MODERATE	p.P147L	30.83	cCc/cTc		
m.4935A>T	Missense variant	*MT-ND2*	MODERATE	p.T156S	81.14	Act/Tct		
m.5206C>T	Missense variant	*MT-ND2*	MODERATE	p.S246F	50	tCc/tTc		
m.5304C>A	Missense variant	*MT-ND2*	MODERATE	p.P279T	67.94	Ccc/Acc		
m.5305C>T	Missense variant	*MT-ND2*	MODERATE	p.P279L	75.58	cCc/cTc		
m.5911C>T	Missense variant	*MT-CO1*	MODERATE	p.A3V	16.16	gCc/gTc	rs879227822	
m.5943G>T	Missense variant	*MT-CO1*	MODERATE	p.D14Y	81	Gac/Tac		
m.6088C>T	Missense variant	*MT-CO1*	MODERATE	p.A62V	46.48	gCa/gTa		
m.6147C>A	Missense variant	*MT-CO1*	MODERATE	p.L82M	40.5	Cta/Ata		
m.6223C>T	Missense variant	*MT-CO1*	MODERATE	p.P107L	71.97	cCc/cTc		
m.6519A>G	Missense variant	*MT-CO1*	MODERATE	p.I206V	55.43	Atc/Gtc		
m.6544A>G	Missense variant	*MT-CO1*	MODERATE	p.N214S	67.88	aAc/aGc		
m.6939T>G	Missense variant	*MT-CO1*	MODERATE	p.F346V	92.9	Ttt/Gtt		
m.7213C>G	Missense variant	*MT-CO1*	MODERATE	p.P437R	11.7	cCc/cGc		
m.8559C>T	Missense variant	*MT-ATP8*	MODERATE	p.P65L	73.58	cCc/cTc		
m.8852G>C	Missense variant	*MT-ATP6*	MODERATE	p.W109S	24.26	tGa/tCa		
m.8927C>A	Missense variant	*MT-ATP6*	MODERATE	p.P134H	57.14	cCt/cAt		
m.9022G>C	Missense variant	*MT-ATP6*	MODERATE	p.A166P	4.1	Gca/Cca		
m.9352C>G	Missense variant	*MT-CO3*	MODERATE	p.T49S	50.86	aCc/aGc		
m.9402A>G	Missense variant	*MT-CO3*	MODERATE	p.T66A	43.66	Aca/Gca		
m.9567A>G	Missense variant	*MT-CO3*	MODERATE	p.I121V	51.28	Atc/Gtc		
m.9964A>C	Missense variant	*MT-CO3*	MODERATE	p.Y253S	51.38	tAt/tCt		
m.10201G>T	Missense variant	*MT-ND3*	MODERATE	p.R48L	6.12	cGc/cTc		
m.10206C>G	Missense variant	*MT-ND3*	MODERATE	p.P50A	46.49	Cct/Gct		
m.10835A>G	Missense variant	*MT-ND4*	MODERATE	p.N26D	44.55	Aac/Gac		
m.11173C>G	Missense variant	*MT-ND4*	MODERATE	p.N138K	36.14	aaC/aaG		
m.11189A>T	Missense variant	*MT-ND4*	MODERATE	p.N144Y	81.86	Aac/Tac		

m.11297A>T	Missense variant	*MT-ND4*	MODERATE	p.T180S	64.04	Act/Tct		
m.11303A>T	Missense variant	*MT-ND4*	MODERATE	p.T182S	20.87	Act/Tct		
m.11715A>G	Missense variant	*MT-ND4*	MODERATE	p.H319R	40.37	cAc/cGc		
m.11909A>C	Missense variant	*MT-ND4*	MODERATE	p.T384P	37.04	Acc/Ccc	COSM1155515 & COSM1155516	Endometrium tumor
m.11910C>G	Missense variant	*MT-ND4*	MODERATE	p.T384S	35.66	aCc/aGc		
m.12470T>C	Missense variant	*MT-ND5*	MODERATE	p.I45T	73.77	aTt/aCt		
m.12506T>A	Missense variant	*MT-ND5*	MODERATE	p.L57Q	57.14	cTa/cAa		
m.12628T>G	Missense variant	*MT-ND5*	MODERATE	p.W98G	37.63	Tgg/Ggg		
m.12933A>T	Missense variant	*MT-ND5*	MODERATE	p.Q199H	48.64	caA/caT		
m.12935A>G	Missense variant	*MT-ND5*	MODERATE	p.Q200R	10	cAa/cGa		
m.13073T>C	Missense variant	*MT-ND5*	MODERATE	p.L246P	46.38	cTa/cCa	COSM6716796	Large intestine tumor
m.13285A>C	Missense variant	*MT-ND5*	MODERATE	p.I317L	24.32	Atc/Ctc		
m.13357A>G	Missense variant	*MT-ND5*	MODERATE	p.M341V	43.55	Atg/Gtg		
m.13392T>G	Missense variant	*MT-ND5*	MODERATE	p.N352K	59.22	aaT/aaG		
m.13541C>A	Missense variant	*MT-ND5*	HIGH	p.S402X	10.03	tCa/tAa		
m.13811C>A	Missense variant	*MT-ND5*	MODERATE	p.A492D	84.69	gCt/gAt		
m.13889G>A	Missense variant	*MT-ND5*	MODERATE	p.C518Y	60	tGc/tAc		
m.14062A>T	Missense variant	*MT-ND5*	MODERATE	p.I576F	60.87	Atc/Ttc		
m.14107T>G	Missense variant	*MT-ND5*	MODERATE	p.F591V	18.04	Ttc/Gtc		
m.14178T>C	Missense variant	*MT-ND6*	MODERATE	p.I166V	54.05	Att/Gtt	rs28357671	
m.14351T>A	Missense variant	*MT-ND6*	MODERATE	p.E108V	34.85	gAg/gTg	COSM1155555 & COSM1155556	Endometrium tumor
m.14357A>T	Missense variant	*MT-ND6*	MODERATE	p.V106E	78.67	gTg/gAg		
m.14796C>G	Missense variant	*MT-CYB*	MODERATE	p.S17W	50	tCa/tGa		
m.14801A>G	Missense variant	*MT-CYB*	MODERATE	p.I19V	45.12	Atc/Gtc		
m.15039T>G	Missense variant	*MT-CYB*	MODERATE	p.I98S	43.04	aTc/aGc		
m.15209T>C	Missense variant	*MT-CYB*	MODERATE	p.Y155H	61.7	Tac/Cac		
m.15210A>C	Missense variant	*MT-CYB*	MODERATE	p.Y155S	2.67	tAc/tCc		
m.15219C>A	Missense variant	*MT-CYB*	MODERATE	p.T158K	36.36	aCa/aAa		
m.15231A>G	Missense variant	*MT-CYB*	MODERATE	p.Q162R	44.78	cAa/cGa		
m.15257G>C	Missense variant	*MT-CYB*	MODERATE	p.D171H	45.57	Gac/Cac	COSM1138306 & COSM1138307	Kidney tumor
m.15438G>T	Missense variant	*MT-CYB*	MODERATE	p.G231V	38.05	gGc/gTc		

Supplementary table 14: Position of SVs and their heteroplasmy percentage in bulk myeloid cells from 3 AML patients.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Deletion	68-73	4	D-LOOP	1.75
	7027-7035	7	*MT-CO1*	0.37
	8802-8809	6	*MT-ATP6*	0.22
Inversion	2735-2796	62	*MT-RNR2*	0.23
	7166-7230	63	*MT-CO1*	0.69
	10521-10566	58	*MT-ND4L*	0.32
	9224-9303	78	*MT-CO3*	0.78
Tandem duplication	6328-7163	834	*MT-CO1*	0.71
	13794-13858	63	*MT-ND5*	0.85

Supplementary table 15: Position of SVs and their heteroplasmy percentage in single myeloid cells from 3 AML patients.

Type of SVs	**Breakpoints**	**Size (nt)**	Gene	**HET%**
Deletions	297–349	52	D-LOOP	3.45
	2457–2458	1	*MT-RNR2*	3.45
	2703–2704	1	*MT-RNR2*	12.50
	10650–10651	1	*MT-ND4L*	10.61
	12083–12386	303	*MT-ND4 … MT-ND5*	25.00
	12296–12297	1	*MT-ND5*	5.41
	13041–13042	1	*MT-ND5*	4.17
	16207–16209	2	D-LOOP	15.38
	16211–16212	1	D-LOOP	8.70
Inversions	120–229	109	D-LOOP	1.85
	170–251	81	D-LOOP	17.74
	559–653	94	D-LOOP	15.38
	628–725	97	MT-RNR1	33.33
	2410–2600	190	D-LOOP	10.42
	2496–2697	201	D-LOOP	30.21
	2641–2826	185	D-LOOP	26.83
	10658–10722	64	*MT-ND4L*	11.11
	11307–11456	149	*MT-ND4*	30.00
	12062–12126	64	*MT-ND4*	12.50
	12297–12507	210	*MT-TL2*	40.00
	13179–13466	287	*MT-ND5*	48.00
Insertions	4–4	18	D-LOOP	14.29
	65–65	1	D-LOOP	10.00
	114–114	6	D-LOOP	2.16
	176–176	4	D-LOOP	8.41
	179–179	4	D-LOOP	1.98
	181–181	1	D-LOOP	3.37
	306–306	11	D-LOOP	1.15
	326–326	1	D-LOOP	11.32
	328–328	1	D-LOOP	10.17
	334–334	6	D-LOOP	9.09
	548–548	3	D-LOOP	8.00
	660–660	10	MT-*RNR1*	15.00
	711–711	3	*MT-RNR1*	3.28
	719–719	1	*MT-RNR1*	10.34
	1005–1005	1	*MT-RNR1*	4.65
	1007–1007	3	*MT-RNR1*	7.89

	1013–1013	1	MT-RNR1	7.69
	2337–2337	4	MT-RNR2	25.93
	2422–2422	2	*MT-RNR2*	2.15
	2457–2457	1	*MT-RNR2*	13.64
	2502–2502	3	*MT-RNR2*	3.19
	2591–2591	1	*MT-RNR2*	2.25
	2641–2641	1	*MT-RNR2*	5.17
	2690–2690	1	*MT-RNR2*	5.26
	3507–3507	27	MT-*ND1*	14.29
	4518–4518	127	*MT-ND2*	50.00
	4735–4735	1	*MT-ND2*	17.39
	10506–10506	1	*MT-ND4L*	10.53
	10720–10720	2	*MT-ND4L*	10.42
	11264–11264	1	*MT-ND4*	3.28
	11976–11976	3	*MT-ND4*	6.06
	13054–13054	4	*MT-ND5*	1.72
	13179–13179	1	*MT-ND5*	4.65
	13469–13469	1	*MT-ND5*	50.00
	13473–13473	5	*MT-ND5*	24.00
	13477–13477	3	*MT-ND5*	6.90
	13540–13540	1	*MT-ND5*	10.26
	16392–16392	2	D-LOOP	6.06
Tandem duplications	13043–13410	367	*MT-ND5*	17.65
	13058–13129	71	*MT-ND5*	11.76

Supplementary table 16: Position of SNVs, their consequences, and heteroplasmy percentage in bulk myeloid cells from 3 AML patients.

Substitution	Consequence	Gene	Impact	Amino acid substitution	Codons	HET%	Existing variants	Phenotype data
m.3322C>A	Missense variant	*MT-ND1*	MODERATE	p.L6I	Ctc/Atc	12.78		
m.3359C>A	Missense variant	*MT-ND1*	MODERATE	p.A18E	gCa/gAa	15.56		
m.3406C>G	Missense variant	*MT-ND1*	MODERATE	p.R34G	Cgc/Ggc	41.67		
m.3459C>G	Missense variant	*MT-ND1*	MODERATE	p.D51E	gaC/gaG	30.77		
m.3474C>G	Missense variant	*MT-ND1*	MODERATE	p.F56L	ttC/ttG	13.69		
m.3549C>G	Missense variant	*MT-ND1*	MODERATE	p.I81M	atC/atG	11.76		
m.3566C>A	Missense variant	*MT-ND1*	MODERATE	p.T87N	aCc/aAc	15.38		
m.3593T>G	Missense variant	*MT-ND1*	MODERATE	p.V96G	gTc/gGc	18		
m.3602A>G	Missense variant	*MT-ND1*	MODERATE	p.N99S	aAc/aGc	12.32		
m.3626C>A	Missense variant	*MT-ND1*	MODERATE	p.A107D	gCc/gAc	15		
m.3700G>T	Missense variant	*MT-ND1*	MODERATE	p.A132S	Gca/Tca	10.61		
m.3706C>G	Missense variant	*MT-ND1*	MODERATE	p.R134G	Cga/Gga	13.04		
m.3785T>G	Missense variant	*MT-ND1*	MODERATE	p.F160C	tTt/tGt	13.08		
m.3875T>G	Missense variant	*MT-ND1*	MODERATE	p.L190R	cTa/cGa	12.77		
m.3900C>G	Missense variant	*MT-ND1*	MODERATE	p.F198L	ttC/ttG	30		
m.3910G>T	Stop-gained	*MT-ND1*	HIGH	p.E202X	Gaa/Taa	12.3		
m.3945C>G	Missense variant	*MT-ND1*	MODERATE	p.I213M	atC/atG	44.15		
m.4024A>G	Missense variant	*MT-ND1*	MODERATE	p.T240A	Aca/Gca	13.43		
m.4039A>C	Missense variant	*MT-ND1*	MODERATE	p.T245P	Aca/Cca	12.9		
m.4064A>C	Missense variant	*MT-ND1*	MODERATE	p.E253A	gAa/gCa	13.64		
m.4090A>C	Missense variant	*MT-ND1*	MODERATE	p.K262Q	Aag/Cag	13.47		
m.4234A>C	Missense variant	*MT-ND1*	MODERATE	p.T310P	Aca/Cca	13.64		
m.4237A>T	Missense variant	*MT-ND1*	MODERATE	p.I311F	Atc/Ttc	15.62		
m.4540C>T	Missense variant	*MT-ND2*	MODERATE	p.S24L	tCg/tTg	10.53		
m.4548T>G	Missense variant	*MT-ND2*	MODERATE	p.F27V	Ttt/Gtt	10.34		
m.4638A>T	Missense variant	*MT-ND2*	MODERATE	p.I57F	Atc/Ttc	10		
m.4646T>A	Stop-gained	*MT-ND2*	HIGH	p.Y59X	taT/taA	10.36		
m.4654C>G	Stop-gained	*MT-ND2*	HIGH	p.T62X	aCg/aGg	20		
m.4762T>A	Missense variant	*MT-ND2*	MODERATE	p.I98N	aTc/aAc	28.57		
m.4822T>G	Missense variant	*MT-ND2*	MODERATE	p.V118G	gTt/gGt	11.11	rs28571027	
m.4879C>A	Missense variant	*MT-ND2*	MODERATE	p.A137D	gCc/gAc	11.81		
m.4966G>C	Missense variant	*MT-ND2*	MODERATE	p.S166T	aGt/aCt	10.33		
m.5056A>C	Missense variant	*MT-ND2*	MODERATE	p.Y196S	tAc/tCc	11.76		
m.5073A>C	Missense variant	*MT-ND2*	MODERATE	p.I202L	Att/Ctt	12.5		
m.5198A>C	Missense variant	*MT-ND2*	MODERATE	p.L243F	ttA/ttC	11.76		
m.5206C>T	Missense variant	*MT-ND2*	MODERATE	p.S246F	tCc/tTc	23.2		
m.5212T>G	Missense variant	*MT-ND2*	MODERATE	p.L248R	cTc/cGc	14.75		

m.5221T>C	Missense variant	*MT-ND2*	MODERATE	p.L251P	cTa/cCa	11.25		
m.5270C>G	Missense variant	*MT-ND2*	MODERATE	p.I267M	atC/atG	16.67		
m.5300C>G	Missense variant	*MT-ND2*	MODERATE	p.I277M	atC/atG	16.85		
m.5390A>C	Missense variant	*MT-ND2*	MODERATE	p.M307I	atA/atC	12.05		
m.5420T>G	Missense variant	*MT-ND2*	MODERATE	p.F317L	ttT/ttG	12.5		
m.5909C>G	Missense variant	*MT-CO1*	MODERATE	p.F2L	ttC/ttG	12.59		
m.6024C>A	Missense variant	*MT-CO1*	MODERATE	p.L41M	Ctg/Atg	58.47		
m.6040A>C	Missense variant	*MT-CO1*	MODERATE	p.N46T	aAc/aCc	10		
m.6054G>A	Missense variant	*MT-CO1*	MODERATE	p.D51N	Gac/Aac	15.38		
m.6097T>G	Stop-gained	*MT-CO1*	HIGH	p.M65X	aTa/aGa	10.53		
m.6115T>G	Stop-gained	*MT-CO1*	HIGH	p.M71X	aTa/aGa	12.5		
m.6189C>A	Missense variant	*MT-CO1*	MODERATE	p.R96S	Cgc/Agc	18		
m.6243G>T	Missense variant	*MT-CO1*	MODERATE	p.A114S	Gca/Tca	10.64		
m.6273A>C	Missense variant	*MT-CO1*	MODERATE	p.T124P	Aca/Cca	10.53		
m.6456G>C	Missense variant	*MT-CO1*	MODERATE	p.V185L	Gtc/Ctc	12.5		
m.6474A>C	Missense variant	*MT-CO1*	MODERATE	p.T191P	Aca/Cca	28.57		
m.6535C>A	Missense variant	*MT-CO1*	MODERATE	p.T211K	aCa/aAa	11.43		
m.6568C>A	Missense variant	*MT-CO1*	MODERATE	p.P222H	cCc/cAc	11.76		
m.6656C>G	Missense variant	*MT-CO1*	MODERATE	p.F251L	ttC/ttG	11.7		
m.6672A>T	Missense variant	*MT-CO1*	MODERATE	p.I257F	Att/Ttt	11.36		
m.6693A>G	Missense variant	*MT-CO1*	MODERATE	p.K264E	Aaa/Gaa	10.5		
m.6737A>C	Missense variant	*MT-CO1*	MODERATE	p.M278I	atA/atC	12		
m.6768G>T	Missense variant	*MT-CO1*	MODERATE	p.A289S	Gca/Tca	12.08		
m.6783A>T	Missense variant	*MT-CO1*	MODERATE	p.T294S	Aca/Tca	12.07		
m.6797C>G	Missense variant	*MT-CO1*	MODERATE	p.D298E	gaC/gaG	13.33		
m.6828A>G	Missense variant	*MT-CO1*	MODERATE	p.T309A	Acc/Gcc	11.11		
m.6887C>G	Missense variant	*MT-CO1*	MODERATE	p.H328Q	caC/caG	19.23		
m.6976T>A	Stop-gained	*MT-CO1*	HIGH	p.L358X	tTa/tAa	12.12	COSM1331631 & COSM1331632	Ovary tumor
m.7314A>C	Missense variant	*MT-CO1*	MODERATE	p.M471L	Atg/Ctg	11.54		
m.7325A>C	Missense variant	*MT-CO1*	MODERATE	p.E474D	gaA/gaC	16.26		
m.7331C>G	Missense variant	*MT-CO1*	MODERATE	p.F476L	ttC/ttG	10.98		
m.7385A>T	Missense variant	*MT-CO1*	MODERATE	p.W494C	tgA/tgT	12.12		
m.7657T>A	Missense variant	*MT-CO2*	MODERATE	p.H24Q	caT/caA	14.49		
m.7667C>A	Missense variant	*MT-CO2*	MODERATE	p.L28I	Ctc/Atc	34.62		
m.7695T>A	Missense variant	*MT-CO2*	MODERATE	p.L37Q	cTa/cAa	12.5		
m.7784A>C	Missense variant	*MT-CO2*	MODERATE	p.I67L	Atc/Ctc	18.25		
m.7814G>T	Missense variant	*MT-CO2*	MODERATE	p.A77S	Gcc/Tcc	10.58	COSM1155680	Endometrium tumor
m.7823T>A	Missense variant	*MT-CO2*	MODERATE	p.S80T	Tcc/Acc	12.5		
m.7842T>C	Missense variant	*MT-CO2*	MODERATE	p.M86T	aTa/aCa	13.71		

m.7877A>T	Stop-gained	*MT-CO2*	HIGH	p.K98X	Aaa/Taa	15.79		
m.7909C>G	Stop-gained	*MT-CO2*	HIGH	p.Y108X	taC/taG	11.21		
m.7936C>G	Missense variant	*MT-CO2*	MODERATE	p.I117M	atC/atG	14.06		
m.7939C>G	Missense variant	*MT-CO2*	MODERATE	p.F118L	ttC/ttG	13.51		
m.7985C>G	Missense variant	*MT-CO2*	MODERATE	p.R134G	Cga/Gga	14.02		
m.8022T>G	Missense variant	*MT-CO2*	MODERATE	p.I146S	aTt/aGt	28.4		
m.8066C>A	Missense variant	*MT-CO2*	MODERATE	p.H161N	Cac/Aac	18.94		
m.8151C>A	Missense variant	*MT-CO2*	MODERATE	p.P189Q	cCg/cAg	20		
m.8247T>C	Missense variant	*MT-CO2*	MODERATE	p.M221T	aTa/aCa	14.1		
m.8259T>A	Missense variant	*MT-CO2*	MODERATE	p.F225Y	tTt/tAt	11.18		
m.8400T>G	Stop-gained	*MT-ATP8*	HIGH	p.M12X	aTa/aGa	10.53		
m.8439A>T	Missense variant	*MT-ATP8*	MODERATE	p.Q25L	cAa/cTa	36.75		
m.8526A>G	Stop-gained	*MT-ATP8*	HIGH	p.K54X	aAa/aGa	15.08		
m.8570T>C	Missense variant	*MT-ATP6*	MODERATE	p.L15P	cTa/cCa	17.86		
m.8639T>G	Missense variant	*MT-ATP6*	MODERATE	p.I38S	aTc/aGc	12.84		
m.8725A>T	Missense variant	*MT-ATP6*	MODERATE	p.T67S	Acc/Tcc	11.76		
m.8783G>A	Missense variant	*MT-ATP6*	MODERATE	p.G86E	gGa/gAa	12.13		
m.8836A>T	Missense variant	*MT-ATP6*	MODERATE	p.M104L	Atg/Ttg	11.3		
m.8860G>A	Missense variant	*MT-ATP6*	MODERATE	p.A112T	Gca/Aca	15.33		
m.8864T>G	Missense variant	*MT-ATP6*	MODERATE	p.V113G	gTg/gGg	12.26		
m.8887A>G	Missense variant	*MT-ATP6*	MODERATE	p.I121V	Att/Gtt	10.42		
m.8965A>C	Missense variant	*MT-ATP6*	MODERATE	p.I147L	Atc/Ctc	23.08		
m.9252T>G	Missense variant	*MT-CO3*	MODERATE	p.W16G	Tga/Gga	10.2		
m.9294G>A	Missense variant	*MT-CO3*	MODERATE	p.G30S	Ggc/Agc	25.26	COSM1155700 & COSM1155701	Endometrium tumor
m.9387G>C	Missense variant	*MT-CO3*	MODERATE	p.V61L	Gta/Cta	16.33		
m.9447T>G	Missense variant	*MT-CO3*	MODERATE	p.Y81D	Tac/Gac	10.95		
m.9475A>G	Missense variant	*MT-CO3*	MODERATE	p.E90G	gAa/gGa	10.71		
m.9512C>G	Stop-gained	*MT-CO3*	HIGH	p.Y102X	taC/taG	20		
m.9583C>A	Missense variant	*MT-CO3*	MODERATE	p.P126H	cCc/cAc	10		
m.9631T>A	Missense variant	*MT-CO3*	MODERATE	p.V142E	gTa/gAa	30.86		
m.9646C>G	Missense variant	*MT-CO3*	MODERATE	p.A147G	gCt/gGt	30.95		
m.9763T>C	Missense variant	*MT-CO3*	MODERATE	p.F186S	tTc/tCc	17.95		
m.9770T>G	Missense variant	*MT-CO3*	MODERATE	p.I188M	atT/atG	12.87		
m.9785C>G	Stop-gained	*MT-CO3*	HIGH	p.Y193X	taC/taG	16.67		
m.9800T>A	Missense variant	*MT-CO3*	MODERATE	p.F198L	ttT/ttA	17.69		
m.9865T>G	Missense variant	*MT-CO3*	MODERATE	p.I220S	aTc/aGc	11.86		
m.9899T>G	Missense variant	*MT-CO3*	MODERATE	p.H231Q	caT/caG	13.14	rs41345446	
m.9937T>C	Missense variant	*MT-CO3*	MODERATE	p.F244S	tTt/tCt	11.11		
m.9946T>G	Missense variant	*MT-CO3*	MODERATE	p.V247G	gTg/gGg	10.23		

m.9952G>C	Missense variant	*MT-CO3*	MODERATE	p.W249S	tGa/tCa	16.67		
m.10086A>C	Missense variant	*MT-ND3*	MODERATE	p.N10H	Aac/Cac	16.67	rs28358274	
m.10096T>C	Missense variant	*MT-ND3*	MODERATE	p.L13P	cTa/cCa	10.53		
m.10111T>A	Missense variant	*MT-ND3*	MODERATE	p.M18K	aTa/aAa	37.36		
m.10115T>A	Missense variant	*MT-ND3*	MODERATE	p.I19M	atT/atA	11.76		
m.10165C>G	Missense variant	*MT-ND3*	MODERATE	p.P36R	cCt/cGt	12		
m.10203G>C	Missense variant	*MT-ND3*	MODERATE	p.V49L	Gtc/Ctc	14.74		
m.10239A>C	Missense variant	*MT-ND3*	MODERATE	p.T61P	Acc/Ccc	16.67		
m.10399C>T	Missense variant	*MT-ND3*	MODERATE	p.T114I	aCc/aTc	12.5		
m.10401G>A	Missense variant	*MT-ND3*	MODERATE	p.E115K	Gaa/Aaa	11.11	rs28719882	
m.10518C>G	Missense variant	*MT-ND4L*	MODERATE	p.L17V	Cta/Gta	10		
m.10536C>G	Missense variant	*MT-ND4L*	MODERATE	p.R23G	Cgc/Ggc	12.36		
m.10593A>T	Missense variant	*MT-ND4L*	MODERATE	p.I42F	Att/Ttt	10.34		
m.10640T>G	Missense variant	*MT-ND4L*	MODERATE	p.N57K	aaT/aaG	45.87	rs386419955	
m.10676C>G	Missense variant	*MT-ND4L*	MODERATE	p.C69W	tgC/tgG	33.33		
m.10711T>A	Missense variant	*MT-ND4L*	MODERATE	p.I81N	aTc/aAc	35.01		
m.10774C>G	Missense variant	*MT-ND4*	MODERATE	p.I5M	atC/atG	14.29		
m.10790T>G	Missense variant	*MT-ND4*	MODERATE	p.L11V	Tta/Gta	11.11		
m.10829T>G	Missense variant	*MT-ND4*	MODERATE	p.W24G	Tga/Gga	10.71		
m.10885T>A	Missense variant	*MT-ND4*	MODERATE	p.F42L	ttT/ttA	18.18		
m.10895A>T	Missense variant	*MT-ND4*	MODERATE	p.N46Y	Aac/Tac	13.33		
m.10928T>G	Missense variant	*MT-ND4*	MODERATE	p.S57A	Tcc/Gcc	19.62		
m.11019A>C	Missense variant	*MT-ND4*	MODERATE	p.E87A	gAa/gCa	15.22		
m.11021C>A	Missense variant	*MT-ND4*	MODERATE	p.P88T	Cca/Aca	10		
m.11069A>T	Missense variant	*MT-ND4*	MODERATE	p.I104F	Atc/Ttc	12.5		
m.11140C>G	Missense variant	*MT-ND4*	MODERATE	p.I127M	atC/atG	12.42		
m.11145C>T	Missense variant	*MT-ND4*	MODERATE	p.T129I	aCc/aTc	13.89		
m.11183C>T	Missense variant	*MT-ND4*	MODERATE	p.R142C	Cgc/Tgc	17.39		
m.11322A>C	Missense variant	*MT-ND4*	MODERATE	p.N188T	aAc/aCc	11.36		
m.11330G>C	Missense variant	*MT-ND4*	MODERATE	p.A191P	Gcc/Ccc	17.9		
m.11423G>T	Stop-gained	*MT-ND4*	HIGH	p.E222X	Gaa/Taa	11.11		
m.11445T>G	Stop-gained	*MT-ND4*	HIGH	p.M229X	aTa/aGa	10.86		
m.11514C>T	Missense variant	*MT-ND4*	MODERATE	p.P252L	cCc/cTc	12.68		
m.11675C>T	Missense variant	*MT-ND4*	MODERATE	p.P306S	Ccc/Tcc	12.75		
m.11700T>A	Missense variant	*MT-ND4*	MODERATE	p.I314N	aTt/aAt	12		
m.11751A>T	Missense variant	*MT-ND4*	MODERATE	p.N331I	aAc/aTc	11.76		
m.11765C>T	Missense variant	*MT-ND4*	MODERATE	p.R336C	Cgc/Tgc	13.33		
m.11777C>G	Missense variant	*MT-ND4*	MODERATE	p.R340G	Cgc/Ggc	17.39	rs28384199	Leigh syndrome
m.11778G>A	Missense variant	*MT-ND4*	MODERATE	p.R340H	cGc/cAc	14.29	rs199476112	Lebers optic atrophy; MIM: 516003

m.11874C>G	Missense variant	*MT-ND4*	MODERATE	p.T372S	aCt/aGt	10		
m.11924T>C	Missense variant	*MT-ND4*	MODERATE	p.S389P	Tca/Cca	33.33		
m.12122A>C	Missense variant	*MT-ND4*	MODERATE	p.T455P	Acc/Ccc	18.18		
m.12347A>C	Missense variant	*MT-ND5*	MODERATE	p.H4P	cAc/cCc	15.22		
m.12373A>T	Missense variant	*MT-ND5*	MODERATE	p.T13S	Act/Tct	24.78		
m.12467T>G	Missense variant	*MT-ND5*	MODERATE	p.F44C	tTt/tGt	10.34		
m.12499A>T	Missense variant	*MT-ND5*	MODERATE	p.M55L	Atg/Ttg	16.86		
m.12523A>G	Missense variant	*MT-ND5*	MODERATE	p.I63V	Atc/Gtc	41.31		
m.12569T>A	Missense variant	*MT-ND5*	MODERATE	p.L78Q	cTa/cAa	17.77	COSM1155523	Skin tumor
m.12763G>T	Missense variant	*MT-ND5*	MODERATE	p.G143C	Ggc/Tgc	15.79		
m.12812A>C	Missense variant	*MT-ND5*	MODERATE	p.Y159S	tAc/tCc	10.43		
m.12841A>G	Missense variant	*MT-ND5*	MODERATE	p.I169V	Att/Gtt	12.11		
m.12884T>C	Missense variant	*MT-ND5*	MODERATE	p.I183T	aTc/aCc	14.07		
m.12951C>G	Missense variant	*MT-ND5*	MODERATE	p.N205K	aaC/aaG	11.56		
m.12968C>G	Missense variant	*MT-ND5*	MODERATE	p.T211S	aCc/aGc	22.54		
m.12986T>A	Missense variant	*MT-ND5*	MODERATE	p.L217H	cTc/cAc	15.62		
m.13005A>T	Missense variant	*MT-ND5*	MODERATE	p.K223N	aaA/aaT	12		
m.13117A>C	Missense variant	*MT-ND5*	MODERATE	p.I261L	Atc/Ctc	15		
m.13142A>T	Missense variant	*MT-ND5*	MODERATE	p.N269I	aAt/aTt	16.67		
m.13162C>G	Missense variant	*MT-ND5*	MODERATE	p.L276V	Cta/Gta	11.76		
m.13186A>T	Missense variant	*MT-ND5*	MODERATE	p.T284S	Acc/Tcc	12.44		
m.13198G>C	Missense variant	*MT-ND5*	MODERATE	p.A288P	Gca/Cca	14.43		
m.13293C>G	Missense variant	*MT-ND5*	MODERATE	p.I319M	atC/atG	10.17		
m.13343A>G	Stop-gained	*MT-ND5*	HIGH	p.K336X	aAa/aGa	16		
m.13350A>C	Missense variant	*MT-ND5*	MODERATE	p.M338I	atA/atC	13.04		
m.13363T>A	Missense variant	*MT-ND5*	MODERATE	p.S343T	Tcc/Acc	10.42		
m.13391A>G	Missense variant	*MT-ND5*	MODERATE	p.N352S	aAt/aGt	11.76		
m.13485A>T	Missense variant	*MT-ND5*	MODERATE	p.M383I	atA/atT	11.22	rs28359176	
m.13495A>C	Missense variant	*MT-ND5*	MODERATE	p.T387P	Aca/Cca	29.5		
m.13510A>C	Missense variant	*MT-ND5*	MODERATE	p.K392Q	Aaa/Caa	10.34		
m.13511A>G	Stop-gained	*MT-ND5*	HIGH	p.K392X	aAa/aGa	13.99		
m.13556G>C	Missense variant	*MT-ND5*	MODERATE	p.W407S	tGa/tCa	10.47	COSM1720929	
m.13579G>T	Missense variant	*MT-ND5*	MODERATE	p.A415S	Gct/Tct	11.5		
m.13726G>C	Missense variant	*MT-ND5*	MODERATE	p.A464P	Gca/Cca	11.67		
m.13765C>G	Missense variant	*MT-ND5*	MODERATE	p.P477A	Ccc/Gcc	11.13		
m.13808T>A	Missense variant	*MT-ND5*	MODERATE	p.L491H	cTc/cAc	10.42		
m.13823T>C	Missense variant	*MT-ND5*	MODERATE	p.L496P	cTa/cCa	10.88		
m.14211C>A	Missense variant	*MT-ND6*	MODERATE	p.V155F	Gtt/Ttt	11.76		
m.14256T>A	Missense variant	*MT-ND6*	MODERATE	p.I140F	Att/Ttt	12		
m.14270A>G	Missense variant	*MT-ND6*	MODERATE	p.I135T	aTt/aCt	33.52		

m.14363A>T	Missense variant	*MT-ND6*	MODERATE	p.L104Q	cTg/cAg	14.78		
m.14427C>A	Missense variant	*MT-ND6*	MODERATE	p.G83W	Ggg/Tgg	38.19		
m.14478C>A	Missense variant	*MT-ND6*	MODERATE	p.V66F	Gtc/Ttc	10		
m.14556A>T	Missense variant	*MT-ND6*	MODERATE	p.C40S	Tgt/Agt	15.38		
m.14777A>C	Missense variant	*MT-CYB*	MODERATE	p.M11L	Ata/Cta	17.43		
m.14790A>G	Missense variant	*MT-CYB*	MODERATE	p.N15S	aAc/aGc	23.08		
m.14843T>C	Missense variant	*MT-CYB*	MODERATE	p.F33L	Ttc/Ctc	10.7		
m.14847G>T	Missense variant	*MT-CYB*	MODERATE	p.G34V	gGc/gTc	18.61	COSM1138282 & COSM1138283	Kidney tumor
m.14883C>G	Missense variant	*MT-CYB*	MODERATE	p.T46S	aCc/aGc	10		
m.14927A>G	Missense variant	*MT-CYB*	MODERATE	p.T61A	Acc/Gcc	18.24	rs201551481	
m.14990C>G	Missense variant	*MT-CYB*	MODERATE	p.L82V	Ctt/Gtt	14.72		
m.15030T>G	Missense variant	*MT-CYB*	MODERATE	p.F95C	tTc/tGc	19.29		
m.15078A>G	Missense variant	*MT-CYB*	MODERATE	p.E111G	gAa/gGa	10.59		
m.15097T>G	Missense variant	*MT-CYB*	MODERATE	p.I117M	atT/atG	22.01		
m.15108T>C	Missense variant	*MT-CYB*	MODERATE	p.L121P	cTt/cCt	10.51		
m.15129T>G	Missense variant	*MT-CYB*	MODERATE	p.F128C	tTc/tGc	10.71		
m.15200G>T	Missense variant	*MT-CYB*	MODERATE	p.A152S	Gcc/Tcc	18.75		
m.15240G>C	Missense variant	*MT-CYB*	MODERATE	p.W165S	tGa/tCa	13.95		
m.15255T>G	Missense variant	*MT-CYB*	MODERATE	p.V170G	gTa/gGa	41.38		
m.15402C>G	Missense variant	*MT-CYB*	MODERATE	p.T219S	aCc/aGc	10.26		
m.15462T>G	Missense variant	*MT-CYB*	MODERATE	p.L239W	tTa/tGa	17.24		
m.15502C>G	Missense variant	*MT-CYB*	MODERATE	p.D252E	gaC/gaG	21.43		
m.15545C>A	Missense variant	*MT-CYB*	MODERATE	p.H267N	Cac/Aac	14.29		
m.15645T>G	Missense variant	*MT-CYB*	MODERATE	p.I300S	aTc/aGc	10.85		
m.15653A>C	Missense variant	*MT-CYB*	MODERATE	p.M303L	Ata/Cta	15.57		
m.15659C>T	Missense variant	*MT-CYB*	MODERATE	p.P305S	Ccc/Tcc	15.38		

Supplementary table 17: Position of SNVs, their consequences, and heteroplasmy percentage in single myeloid cells from 3 AML patients.

Substitution	Consequence	Gene	Impact	Amino acid change	HET%	Codons	Existing variants	Phenotype data
m.3397A>T	Missense variant	*MT-ND1*	MODERATE	p.M31L	15.62	Ata/Tta		
m.3524C>G	Missense variant	*MT-ND1*	MODERATE	p.T73S	96.61	aCc/aGc		
m.3574C>A	Missense variant	*MT-ND1*	MODERATE	p.P90T	47.69	Ccc/Acc		
m.3669A>C	Missense variant	*MT-ND1*	MODERATE	p.W121C	20.59	tgA/tgC		
m.3812A>C	Missense variant	*MT-ND1*	MODERATE	p.Q169P	15.79	cAa/cCa		
m.3820C>A	Missense variant	*MT-ND1*	MODERATE	p.L172I	50	Ctc/Atc		
m.3947A>T	Missense variant	*MT-ND1*	MODERATE	p.E214V	27.12	gAa/gTa		
m.3967G>T	Missense variant	*MT-ND1*	MODERATE	p.A221S	15.79	Gcc/Tcc		
m.4212A>T	Missense variant	*MT-ND1*	MODERATE	p.M302I	13.46	atA/atT		
m.4222T>A	Missense variant	*MT-ND1*	MODERATE	p.S306T	59.32	Tcc/Acc		
m.4227A>T	Missense variant	*MT-ND1*	MODERATE	p.M307I	11.63	atA/atT		
m.4509T>C	Missense variant	*MT-ND2*	MODERATE	p.F14L	23.91	Ttt/Ctt		
m.4516G>A	Missense variant	*MT-ND2*	MODERATE	p.G16D	12.2	gGc/gAc		
m.4578A>G	Missense variant	*MT-ND2*	MODERATE	p.M37V	25	Atg/Gtg		
m.4629G>A	Missense variant	*MT-ND2*	MODERATE	p.E54K	76.97	Gaa/Aaa		
m.4703T>G	Missense variant	*MT-ND2*	MODERATE	p.N78K	93.87	aaT/aaG		
m.4707C>A	Missense variant	*MT-ND2*	MODERATE	p.L80I	16.28	Ctc/Atc		
m.4719T>G	Missense variant	*MT-ND2*	MODERATE	p.W84G	85.62	Tga/Gga		
m.4808C>G	Missense variant	*MT-ND2*	MODERATE	p.F113L	11.76	ttC/ttG		
m.4813T>C	Missense variant	*MT-ND2*	MODERATE	p.V115A	17.65	gTc/gCc		
m.4886C>G	Missense variant	*MT-ND2*	MODERATE	p.I139M	40	atC/atG		
m.5925T>G	Missense variant	*MT-CO1*	MODERATE	p.F8V	91.86	Ttc/Gtc		
m.5927C>G	Missense variant	*MT-CO1*	MODERATE	p.F8L	55.81	ttC/ttG		
m.5939C>G	Missense variant	*MT-CO1*	MODERATE	p.H12Q	48.78	caC/caG		
m.5942A>C	Missense variant	*MT-CO1*	MODERATE	p.K13N	10.26	aaA/aaC		
m.5952A>G	Missense variant	*MT-CO1*	MODERATE	p.T17A	11.76	Aca/Gca	rs879232447	
m.6069G>T	Missense variant	*MT-CO1*	MODERATE	p.V56F	12.9	Gtt/Ttt		
m.6171C>G	Missense variant	*MT-CO1*	MODERATE	p.P90A	12.12	Ccc/Gcc		
m.6223C>T	Missense variant	*MT-CO1*	MODERATE	p.P107L	31.03	cCc/cTc		
m.6270G>C	Missense variant	*MT-CO1*	MODERATE	p.G123R	11.02	Gga/Cga		
m.6273A>G	Missense variant	*MT-CO1*	MODERATE	p.T124A	59.52	Aca/Gca		
m.6409T>C	Missense variant	*MT-CO1*	MODERATE	p.I169T	21.21	aTc/aCc		
m.6413T>G	Missense variant	*MT-CO1*	MODERATE	p.N170K	23.91	aaT/aaG		
m.6451T>G	Missense variant	*MT-CO1*	MODERATE	p.L183R	12.5	cTc/cGc		
m.6511C>G	Missense variant	*MT-CO1*	MODERATE	p.A203G	12.9	gCt/gGt		
m.6771C>T	Missense variant	*MT-CO1*	MODERATE	p.H290Y	14.29	Cac/Tac		

m.6797C>A	Missense variant	*MT-CO1*	MODERATE	p.D298E	12.2	gaC/gaA		
m.6801G>T	Missense variant	*MT-CO1*	MODERATE	p.D300Y	30.19	Gac/Tac		
m.6861G>A	Missense variant	*MT-CO1*	MODERATE	p.V320M	17.95	Gta/Ata		
m.6897A>T	Missense variant	*MT-CO1*	MODERATE	p.M332L	15.22	Atg/Ttg		
m.6915G>C	Missense variant	*MT-CO1*	MODERATE	p.V338L	15.38	Gtg/Ctg		
m.6990C>G	Missense variant	*MT-CO1*	MODERATE	p.L363V	61.36	Cta/Gta		
m.7005C>T	Missense variant	*MT-CO1*	MODERATE	p.H368Y	10.26	Cac/Tac		
m.7152A>G	Missense variant	*MT-CO1*	MODERATE	p.M417V	14.08	Ata/Gta		
m.7195T>C	Missense variant	*MT-CO1*	MODERATE	p.L431P	45	cTc/cCc		
m.7236G>C	Missense variant	*MT-CO1*	MODERATE	p.D445H	88.3	Gat/Cat		
m.7240C>A	Missense variant	*MT-CO1*	MODERATE	p.A446E	25.35	gCa/gAa		
m.7393G>T	Missense variant	*MT-CO1*	MODERATE	p.G497V	51.52	gGa/gTa		
m.7590C>G	Missense variant	*MT-CO2*	MODERATE	p.A2G	47.83	gCa/gGa		
m.7653T>C	Missense variant	*MT-CO2*	MODERATE	p.F23S	15.31	tTt/tCt		
m.7764A>C	Missense variant	*MT-CO2*	MODERATE	p.E60A	76.09	gAa/gCa		
m.7787C>A	Missense variant	*MT-CO2*	MODERATE	p.L68M	21.95	Ctg/Atg		
m.7813C>G	Missense variant	*MT-CO2*	MODERATE	p.I76M	44.12	atC/atG		
m.7991C>G	Missense variant	*MT-CO2*	MODERATE	p.L136V	14.63	Ctt/Gtt		
m.8054C>G	Missense variant	*MT-CO2*	MODERATE	p.Q157E	10.42	Caa/Gaa		
m.8064T>C	Missense variant	*MT-CO2*	MODERATE	p.L160S	29.23	tTg/tCg		
m.8154G>A	Missense variant	*MT-CO2*	MODERATE	p.G190E	15.92	gGg/gAg		
m.8694A>C	Missense variant	*MT-ATP6*	MODERATE	p.Q56H	31.25	caA/caC		
m.8707C>G	Missense variant	*MT-ATP6*	MODERATE	p.H61D	12.24	Cac/Gac		
m.8708A>C	Missense variant	*MT-ATP6*	MODERATE	p.H61P	40	cAc/cCc		
m.8711A>C	Missense variant	*MT-ATP6*	MODERATE	p.N62T	23.44	aAc/aCc		
m.8794C>G	Missense variant	*MT-ATP6*	MODERATE	p.H90D	21.88	Cac/Gac	COSM1138408 & COSM488775	Kidney tumor
m.8795A>T	Missense variant	*MT-ATP6*	MODERATE	p.H90L	37.78	cAc/cTc		
m.8836A>G	Missense variant	*MT-ATP6*	MODERATE	p.M104V	11.36	Atg/Gtg		
m.8965A>T	Missense variant	*MT-ATP6*	MODERATE	p.I147F	86.67	Atc/Ttc		
m.9140C>T	Missense variant	*MT-ATP6*	MODERATE	p.A205V	68	gCt/gTt	rs878972895	
m.9194A>G	Missense variant	*MT-ATP6*	MODERATE	p.H223R	19.35	cAc/cGc		
m.9234A>G	Missense variant	*MT-CO3*	MODERATE	p.M10V	10.26	Ata/Gta		
m.9277C>A	Missense variant	*MT-CO3*	MODERATE	p.A24D	19.44	gCc/gAc		
m.9314C>A	Missense variant	*MT-CO3*	MODERATE	p.H36Q	15.62	caC/caA		
m.9402A>G	Missense variant	*MT-CO3*	MODERATE	p.T66A	65.62	Aca/Gca		
m.9409A>C	Missense variant	*MT-CO3*	MODERATE	p.Q68P	22.22	cAa/cCa		
m.9414C>A	Missense variant	*MT-CO3*	MODERATE	p.H70N	13.08	Cac/Aac		
m.9515C>A	Missense variant	*MT-CO3*	MODERATE	p.H103Q	45.71	caC/caA		
m.9607C>T	Missense variant	*MT-CO3*	MODERATE	p.T134M	47.73	aCa/aTa		

m.9777G>A	Missense variant	*MT-CO3*	MODERATE	p.G191S	24.59	Ggc/Agc		
m.9925G>C	Missense variant	*MT-CO3*	MODERATE	p.W240S	47.62	tGa/tCa		
m.9972A>G	Missense variant	*MT-CO3*	MODERATE	p.I256V	13.86	Atc/Gtc		
m.10173T>C	Missense variant	*MT-ND3*	MODERATE	p.C39R	44	Tgc/Cgc		
m.10198C>G	Missense variant	*MT-ND3*	MODERATE	p.A47G	10.64	gCc/gGc		
m.10206C>T	Missense variant	*MT-ND3*	MODERATE	p.P50S	16.22	Cct/Tct		
m.10213C>G	Missense variant	*MT-ND3*	MODERATE	p.S52C	15.07	tCc/tGc		
m.10284C>T	Missense variant	*MT-ND3*	MODERATE	p.P76S	35.48	Cca/Tca		
m.10483A>C	Missense variant	*MT-ND4L*	MODERATE	p.Y5S	45.16	tAc/tCc		
m.10619C>G	Missense variant	*MT-ND4L*	MODERATE	p.N50K	19.35	aaC/aaG		
m.10621C>T	Missense variant	*MT-ND4L*	MODERATE	p.T51I	20	aCc/aTc		
m.10635G>T	Missense variant	*MT-ND4L*	MODERATE	p.A56S	42.42	Gcc/Tcc		
m.10665T>G	Missense variant	*MT-ND4L*	MODERATE	p.F66V	35.56	Ttt/Gtt		
m.10718C>G	Missense variant	*MT-ND4L*	MODERATE	p.N83K	17.31	aaC/aaG		
m.10725G>A	Missense variant	*MT-ND4L*	MODERATE	p.G86S	21.82	Ggc/Agc		
m.10726G>C	Missense variant	*MT-ND4L*	MODERATE	p.G86A	32.73	gGc/gCc		
m.10776T>A	Missense variant	*MT-ND4*	MODERATE	p.V6D	84.68	gTc/gAc		
m.10833T>A	Missense variant	*MT-ND4*	MODERATE	p.I25N	14.63	aTc/aAc		
m.10899A>G	Missense variant	*MT-ND4*	MODERATE	p.N47S	14.29	aAc/aGc		
m.11093G>C	Missense variant	*MT-ND4*	MODERATE	p.A112P	11.76	Gcc/Ccc	COSM1155502	Endometrium tumor
m.11178C>G	Missense variant	*MT-ND4*	MODERATE	p.P140R	25	cCa/cGa		
m.11303A>T	Missense variant	*MT-ND4*	MODERATE	p.T182S	13.95	Act/Tct		
m.11364C>G	Missense variant	*MT-ND4*	MODERATE	p.A202G	28.12	gCt/gGt		
m.11427C>A	Missense variant	*MT-ND4*	MODERATE	p.A223D	12.9	gCc/gAc		
m.11433T>G	Missense variant	*MT-ND4*	MODERATE	p.I225S	16.67	aTc/aGc		
m.11442C>G	Missense variant	*MT-ND4*	MODERATE	p.S228W	54.17	tCa/tGa		
m.11498A>T	Missense variant	*MT-ND4*	MODERATE	p.T247S	13.89	Aca/Tca		
m.11526A>T	Missense variant	*MT-ND4*	MODERATE	p.H256L	23.81	cAc/cTc		
m.11594C>G	Missense variant	*MT-ND4*	MODERATE	p.Q279E	23.28	Caa/Gaa		
m.11617T>A	Missense variant	*MT-ND4*	MODERATE	p.I286M	38.1	atT/atA		
m.11632C>A	Missense variant	*MT-ND4*	MODERATE	p.I291M	15.56	atC/atA		
m.11687A>C	Missense variant	*MT-ND4*	MODERATE	p.T310P	11.36	Acc/Ccc		
m.11699A>C	Missense variant	*MT-ND4*	MODERATE	p.I314L	21.62	Att/Ctt		
m.11797A>C	Missense variant	*MT-ND4*	MODERATE	p.Q346H	32.91	caA/caC		
m.11813C>T	Missense variant	*MT-ND4*	MODERATE	p.L352F	12.9	Ctc/Ttc		
m.11893A>T	Missense variant	*MT-ND4*	MODERATE	p.E378D	36.84	gaA/gaT		
m.12077C>T	Missense variant	*MT-ND4*	MODERATE	p.H440Y	15.56	Cac/Tac	COSM6716735 & COSM6716736	Large intestine tumor
m.12389C>T	Missense variant	*MT-ND5*	MODERATE	p.P18L	44.12	cCc/cTc		
m.12393C>A	Missense variant	*MT-ND5*	MODERATE	p.I19M	78.95	atC/atA		

m.12442G>A	Missense variant	*MT-ND5*	MODERATE	p.V36M	10.87	Gta/Ata		
m.12452T>C	Missense variant	*MT-ND5*	MODERATE	p.I39T	12.28	aTt/aCt		
m.12500T>A	Missense variant	*MT-ND5*	MODERATE	p.M55K	28.95	aTg/aAg	COSM1155521	Endometrium tumor
m.12534A>C	Missense variant	*MT-ND5*	MODERATE	p.W66C	46.94	tgA/tgC		
m.12548C>A	Missense variant	*MT-ND5*	MODERATE	p.T71N	58.54	aCc/aAc		
m.12643T>C	Missense variant	*MT-ND5*	MODERATE	p.F103L	71.43	Ttc/Ctc		
m.12654A>T	Missense variant	*MT-ND5*	MODERATE	p.W106C	21.62	tgA/tgT	rs386829162	
m.12662A>T	Missense variant	*MT-ND5*	MODERATE	p.N109I	82.15	aAc/aTc		
m.12788C>A	Missense variant	*MT-ND5*	MODERATE	p.S151Y	11.43	tCc/tAc		
m.12808T>C	Missense variant	*MT-ND5*	MODERATE	p.W158R	35.29	Tga/Cga		
m.12818G>C	Missense variant	*MT-ND5*	MODERATE	p.R161P	39.02	cGa/cCa		
m.12821C>A	Missense variant	*MT-ND5*	MODERATE	p.A162E	10.42	gCa/gAa		
m.12853C>G	Missense variant	*MT-ND5*	MODERATE	p.L173V	24.24	Cta/Gta		
m.12854T>G	Missense variant	*MT-ND5*	MODERATE	p.L173R	53.85	cTa/cGa	COSM488735	Kidney tumour
m.12933A>T	Missense variant	*MT-ND5*	MODERATE	p.Q199H	58.79	caA/caT		
m.13204G>T	Missense variant	*MT-ND5*	MODERATE	p.V290F	11.11	Gtc/Ttc	COSM488743	Kidney tumour
m.13297C>G	Missense variant	*MT-ND5*	MODERATE	p.Q321E	10.42	Caa/Gaa		
m.13298A>C	Missense variant	*MT-ND5*	MODERATE	p.Q321P	62.5	cAa/cCa		
m.13357A>T	Missense variant	*MT-ND5*	MODERATE	p.M341L	20.07	Atg/Ttg		
m.13520T>G	Missense variant	*MT-ND5*	MODERATE	p.I395S	80.18	aTc/aGc		
m.13546A>C	Missense variant	*MT-ND5*	MODERATE	p.T404P	77.22	Aca/Cca		
m.13757C>A	Missense variant	*MT-ND5*	MODERATE	p.P474H	24.24	cCc/cAc		
m.13769T>C	Missense variant	*MT-ND5*	MODERATE	p.F478S	76.77	tTc/tCc		
m.13771C>A	Missense variant	*MT-ND5*	MODERATE	p.Q479K	13.51	Caa/Aaa		
m.13937A>T	Missense variant	*MT-ND5*	MODERATE	p.H534L	30.95	cAc/cTc		
m.14051C>A	Missense variant	*MT-ND5*	MODERATE	p.S572Y	13.04	tCc/tAc		
m.14159C>A	Missense variant	*MT-ND6*	MODERATE	p.R172L	27.08	cGg/cTg		
m.14178T>C	Missense variant	*MT-ND6*	MODERATE	p.I166V	40.79	Att/Gtt	rs28357671	
m.14238A>G	Missense variant	*MT-ND6*	MODERATE	p.Y146H	18.75	Tat/Cat		
m.14292C>G	Missense variant	*MT-ND6*	MODERATE	p.E128Q	10.45	Gaa/Caa		
m.14482C>G	Missense variant	*MT-ND6*	MODERATE	p.M64I	79.22	atG/atC	rs199476108	
m.14656A>C	Missense variant	*MT-ND6*	MODERATE	p.F6L	48.72	ttT/ttG		
m.14782A>C	Missense variant	*MT-CYB*	MODERATE	p.K12N	42.11	aaA/aaC		
m.14889G>A	Missense variant	*MT-CYB*	MODERATE	p.G48E	10.26	gGa/gAa		
m.14901C>A	Missense variant	*MT-CYB*	MODERATE	p.A52D	26.67	gCc/gAc		
m.14907A>G	Missense variant	*MT-CYB*	MODERATE	p.H54R	14.75	cAc/cGc		
m.14915C>G	Missense variant	*MT-CYB*	MODERATE	p.P57A	54.76	Cca/Gca		
m.14928C>G	Missense variant	*MT-CYB*	MODERATE	p.T61S	36.96	aCc/aGc		
m.14999A>T	Missense variant	*MT-CYB*	MODERATE	p.N85Y	12.9	Aat/Tat		
m.15023T>A	Missense variant	*MT-CYB*	MODERATE	p.C93S	37.5	Tgc/Agc		

m.15185A>T	Missense variant	*MT-CYB*	MODERATE	p.T147S	71.43	Aca/Tca
m.15309T>G	Missense variant	*MT-CYB*	MODERATE	p.I188S	18.84	aTt/aGt
m.15617G>T	Missense variant	*MT-CYB*	MODERATE	p.V291F	41.3	Gtc/Ttc
m.15623G>C	Missense variant	*MT-CYB*	MODERATE	p.A293P	25.64	Gcc/Ccc
m.15664C>G	Missense variant	*MT-CYB*	MODERATE	p.I306M	54.35	atC/atG
m.15665C>G	Missense variant	*MT-CYB*	MODERATE	p.L307V	12.77	Ctc/Gtc
m.15668C>G	Missense variant	*MT-CYB*	MODERATE	p.H308D	32.69	Cat/Gat
m.15884G>T	Missense variant	*MT-CYB*	MODERATE	p.A380S	24.07	Gcc/Tcc
m.3932C>A	Stop-gained	*MT-ND1*	HIGH	p.S209X	72.06	tCa/tAa
m.5057C>A	Stop-gained	*MT-ND2*	HIGH	p.Y196X	23.4	taC/taA
m.5905T>G	Stop-gained&start-lost	*MT-CO1*	HIGH	p.M1X	60	aTg/aGg
m.6535C>G	Stop-gained	*MT-CO1*	HIGH	p.T211X	61.54	aCa/aGa
m.6596C>G	Stop-gained	*MT-CO1*	HIGH	p.Y231X	26.19	taC/taG
m.7705T>G	Stop-gained	*MT-CO2*	HIGH	p.Y40X	56.52	taT/taG
m.11097C>G	Stop-gained	*MT-ND4*	HIGH	p.T113X	18.07	aCa/aGa
m.12432C>G	Stop-gained	*MT-ND5*	HIGH	p.Y32X	48.57	taC/taG

Supplementary table 18: Position of SVs and their heteroplasmy percentage in bulk myeloid cells from 3 MDS patients.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Deletions	4937-4938	*MT-ND2*	1	1.89
	5390-5392	*MT-ND2*	2	4.38
	11959-11961	*MT-ND4*	2	20.65
	11962-11964	*MT-ND4*	2	5.73
	12638-12639	*MT-ND5*	1	3.64
	14951-14952	*MT-CYB*	1	2.94
	7183-7186	*MT-CO1*	3	2.33
	11490-11491	*MT-ND4*	1	3.45
	11959-11961	*MT-ND4*	2	6.45
	12046-12048	*MT-ND4*	2	6.84
	12638-12639	*MT-ND5*	1	17.74
	14641-14644	*MT-CYB*	3	4.55
	2638-2647	*MT-RNR2*	8	2.97
Inversions	10326-10393	*MT-ND4*	68	1.61
Insertions	158-158	D-loop	1	5
	1547-1547	*MT-RNR1*	1	8.7
	4852-4852	*MT-ND2*	4	16.95
	4930-4930	*MT-ND2*	1	11.29
	5387-5387	*MT-ND2*	2	8.19
	5391-5391	*MT-ND2*	1	19.83
	9037-9037	*MT-ATP6*	2	4.48
	12039-12039	*MT-ND4*	4	3.08
	12040-12040	*MT-ND4*	5	1.05
	12041-12041	*MT-ND4*	1	6.06
	14125-14125	*MT-ND5*	7	2.3
	16069-16069	D-loop	3	6.52
	16251-16251	D-loop	3	7.41
	3791-3791	*MT-ND1*	1	5.71
	5128-5128	*MT-ND2*	1	11.11
	7185-7185	*MT-CO1*	3	5.85
	7189-7189	*MT-CO1*	1	5.84
	10147-10147	*MT-ND3*	2	14.75
	11712-11712	*MT-ND4*	2	15.38
	12680-12680	*MT-ND4*	3	26.42
	14053-14053	*MT-ND5*	1	1.52
	14125-14125	*MT-ND5*	7	2.08

	16251-16251	D-loop	3	9.8
	6049-6049	*MT-CO1*	1	3.27

Supplementary table 19: Position of SVs and their heteroplasmy percentage in single myeloid cells from 3 MDS patients.

Type of SVs	**Breakpoints**	**Size (nt)**	**Gene**	**HET%**
Deletions	5315–5316	1	*MT-ND2*	8.33
	4878–4879	1	*MT-ND2*	1.08
	4849–4850	1	*MT-ND2*	1.87
	4780–4781	1	*MT-ND2*	0.81
	1869–1870	1	*MT-RNR2*	15.38
	16264–16265	1	D-loop	1.45
	16234–16235	1	D-loop	2.74
	16199–16200	1	D-loop	5.03
	16194–16196	2	D-loop	4.51
	15900–15901	1	*MT-TT*	1.62
	15524–15527	3	*MT-CYB*	18.03
	12228–12423	195	*MT-ND4*	25.00
	12076–12461	385	*MT-ND4*	28.57
	10841–10842	1	*MT-ND4*	3.85
	10626–10627	1	*MT-ND4L*	2.86
	10360–10362	2	*MT-ND3*	2.06
Inversions	4627–4791	164	*MT-ND2*	0.82
	72–432	360	D-loop	11.76
	6587–6589	134	*MT-CO1*	26.86
	5854–5939	85	*MT-TY*	10.53
	4914–4975	61	*MT-ND2*	1.35
	4890–4966	76	*MT-ND2*	3.95
	4883–4975	92	*MT-ND2*	1.14
	4634–4851	219	*MT-ND2*	31.37
	2432–2811	379	*MT-RNR2*	6.45
	2347–2430	83	*MT-RNR2*	7.41
	1925–1980	55	*MT-RNR2*	18.75
	15910–16088	188	*MT-TT ...MT-TP*	3.33
	1562–1650	90	*MT-RNR1*	20.00
	14138–14598	472	*MT-ND5 ... MT-ND6*	71.43
	12562–12735	173	*MT-ND5*	37.50
	12470–12657	187	*MT-ND5*	40.00
	12292–12511	219	*MT-TL2 ...MT-ND5*	60.00
	12009–12084	75	*MT-ND4*	44.44
	11561–11643	82	*MT-ND4*	1.85
	11477–11584	109	*MT-ND4*	12.21

Insertions	227–230	3	D-loop	11.76
	1628–1631	3	*MT-RNR2*	19.23
	4700–4700	1	*MT-ND2*	0.92
	6477–6477	24	*MT-CO1*	0.62
	1960–1960	9	*MT-RNR2*	10.00
	4622–4622	1	*MT-ND2*	2.78
	4623–4623	4	*MT-ND2*	41.98
	4626–4626	6	*MT-ND2*	36.97
	4628–4628	3	*MT-ND2*	6.47
	4794–4794	1	*MT-ND2*	1.53
	4847–4847	4	*MT-ND2*	2.22
	4855–4855	1	*MT-ND2*	1.34
	4859–4859	2	*MT-ND2*	1.31
	4865–4865	1	*MT-ND2*	1.36
	4889–4889	10	*MT-ND2*	5.88
	4890–4890	5	*MT-ND2*	4.92
	4894–4894	2	*MT-ND2*	2.02
	4973–4973	3	*MT-ND2*	5.88
	4974–4974	7	*MT-ND2*	4.00
	4975–4975	5	*MT-ND2*	10.00
	6377–6377	6	*MT-CO1*	23.33
	6438–6438	10	*MT-CO1*	1.65
	6444–6444	5	*MT-CO1*	9.24
	6589–6589	1	*MT-CO1*	6.71
	6721–6721	2	*MT-CO1*	31.75
	6723–6723	10	*MT-CO1*	8.99
	13051–13051	2	*MT-ND5*	14.29
	11658–11658	39	*MT-ND4*	2.35
	11497–11497	6	*MT-ND4*	7.75
	11509–11509	5	*MT-ND4*	14.68
	11533–11533	3	*MT-ND4*	1.63
	11559–11559	19	*MT-ND4*	1.11
	11579–11579	4	*MT-ND4*	3.66
	11583–11583	2	*MT-ND4*	6.05
	11643–11643	9	*MT-ND4*	1.19
	11656–11656	4	*MT-ND4*	1.2
	11657–11657	11	*MT-ND4*	1.23
	11679–11679	3	*MT-ND4*	3.85
	11680–11680	10	*MT-ND4*	7.38
	11706–11706	2	*MT-ND4*	2.35

	11763–11763	8	*MT-ND4*	16
	11767–11767	6	*MT-ND4*	11.32
	5842–5842	4	*MT-TY*	10
	6085–6085	3	*MT-CO1*	5.56
	6299–6299	2	*MT-CO1*	5.71
	80–80	3	D-loop	4.17
	1926–1926	1	*MT-RNR2*	6.25
	2054–2054	1	*MT-RNR2*	1.68
	2415–2415	2	*MT-RNR2*	4.26
	2422–2422	2	*MT-RNR2*	4.82
	2754–2754	10	*MT-RNR2*	2.9
	6945–6945	1	*MT-CO1*	2.2
	15506–15506	4	*MT-CYB*	5.56
	15522–15522	2	*MT-CYB*	11.76
	15525–15525	2	*MT-CYB*	18.6
	15648–15648	8	*MT-CYB*	4.41
	15649–15649	14	*MT-CYB*	6.9
	15650–15650	12	*MT-CYB*	2.9
	15883–15883	1	*MT-CYB*	6.76
	15898–15898	1	*MT-TT*	30
	15904–15904	1	*MT-TT*	40.68
	16205–16205	3	D-loop	1.73
	16272–16272	10	D-loop	30.77
	16276–16276	1	D-loop	13.98
	4503–4503	1	*MT-ND2*	11.11
Tandem duplications	11471–11763	292	*MT-ND4*	42.86
	11509–11670	162	*MT-ND4*	41.13
	11512–11673	161	*MT-ND4*	2.63
	9409–12697	3288	*MT-CO3*	36.96
	6888–7447	559	*MT-CO1*	14.28
	4627–4975	348	*MT-ND2*	76.47
	4787–4877	90	*MT-ND2*	0.81
	6430–6581	151	*MT-CO1*	1.20

Supplementary table 20: Position of SNVs, their consequences, and heteroplasmy percentage in bulk myeloid cells from 3 MDS patients.

Substitution	Consequence	Impact	Gene	Amino acid substitution	Codons	HET%	Existing variants	Phenopte data
m.3322C>A	Missense variant	MODERATE	*MT-ND1*	p.L6I	Ctc/Atc	10.88		
m.3406C>G	Missense variant	MODERATE	*MT-ND1*	p.R34G	Cgc/Ggc	17.33		
m.3420C>G	Missense variant	MODERATE	*MT-ND1*	p.N38K	aaC/aaG	13.56		
m.3459C>G	Missense variant	MODERATE	*MT-ND1*	p.D51E	gaC/gaG	11.32		
m.3474C>G	Missense variant	MODERATE	*MT-ND1*	p.F56L	ttC/ttG	17.16		
m.3536T>C	Missense variant	MODERATE	*MT-ND1*	p.L77S	tTa/tCa	10.58		
m.3593T>G	Missense variant	MODERATE	*MT-ND1*	p.V96G	gTc/gGc	18.45		
m.3602A>G	Missense variant	MODERATE	*MT-ND1*	p.N99S	aAc/aGc	13.55		
m.3700G>T	Missense variant	MODERATE	*MT-ND1*	p.A132S	Gca/Tca	10.26		
m.3945C>G	Missense variant	MODERATE	*MT-ND1*	p.I213M	atC/atG	54.55		
m.4024A>G	Missense variant	MODERATE	*MT-ND1*	p.T240A	Aca/Gca	14.37		
m.4697C>G	Missense variant	MODERATE	*MT-ND2*	p.F76L	ttC/ttG	10.53		
m.4966G>C	Missense variant	MODERATE	*MT-ND2*	p.S166T	aGt/aCt	10.44		
m.4985A>C	Missense variant	MODERATE	*MT-ND2*	p.Q172H	caA/caC	10.96		
m.5053C>A	Missense variant	MODERATE	*MT-ND2*	p.P195Q	cCg/cAg	10.94		
m.5212T>G	Missense variant	MODERATE	*MT-ND2*	p.L248R	cTc/cGc	18.28		
m.5236C>A	Missense variant	MODERATE	*MT-ND2*	p.P256Q	cCg/cAg	11.11		
m.5300C>G	Missense variant	MODERATE	*MT-ND2*	p.I277M	atC/atG	12.93		
m.5362A>C	Missense variant	MODERATE	*MT-ND2*	p.Y298S	tAc/tCc	16.41		
m.5909C>G	Missense variant	MODERATE	*MT-CO1*	p.F2L	ttC/ttG	11.11		
m.6024C>A	Missense variant	MODERATE	*MT-CO1*	p.L41M	Ctg/Atg	50.16		
m.6189C>A	Missense variant	MODERATE	*MT-CO1*	p.R96S	Cgc/Agc	17.65		
m.6656C>G	Missense variant	MODERATE	*MT-CO1*	p.F251L	ttC/ttG	10.98		
m.6737A>C	Missense variant	MODERATE	*MT-CO1*	p.M278I	atA/atC	17.05		
m.6768G>T	Missense variant	MODERATE	*MT-CO1*	p.A289S	Gca/Tca	12.38		
m.6783A>T	Missense variant	MODERATE	*MT-CO1*	p.T294S	Aca/Tca	13.48		
m.6840G>T	Missense variant	MODERATE	*MT-CO1*	p.A313S	Gct/Tct	15.28		
m.7215C>A	Stop-gained	HIGH	*MT-CO1*	p.R438X	Cga/Aga	10.87		
m.7325A>C	Missense variant	MODERATE	*MT-CO1*	p.E474D	gaA/gaC	22.7		
m.7372T>G	Stop-gained	HIGH	*MT-CO1*	p.M490X	aTa/aGa	10.34		
m.7421A>T	Missense variant	MODERATE	*MT-CO1*	p.E506D	gaA/gaT	13.33		
m.7657T>A	Missense variant	MODERATE	*MT-CO2*	p.H24Q	caT/caA	15.04		
m.7695T>A	Missense variant	MODERATE	*MT-CO2*	p.L37Q	cTa/cAa	14.56		
m.7784A>C	Missense variant	MODERATE	*MT-CO2*	p.I67L	Atc/Ctc	17.22		
m.7814G>T	Missense variant	MODERATE	*MT-CO2*	p.A77S	Gcc/Tcc	16.13	COSM1155680	Endometrium tumour
m.7815C>G	Missense variant	MODERATE	*MT-CO2*	p.A77G	gCc/gGc	11.76		

m.7845C>G	Stop-gained	HIGH	*MT-CO2*	p.T87X	aCa/aGa	15.34	
m.7909C>G	Stop-gained	HIGH	*MT-CO2*	p.Y108X	taC/taG	19.35	
m.7936C>G	Missense variant	MODERATE	*MT-CO2*	p.I117M	atC/atG	10.86	
m.7985C>G	Missense variant	MODERATE	*MT-CO2*	p.R134G	Cga/Gga	13.1	
m.8022T>G	Missense variant	MODERATE	*MT-CO2*	p.I146S	aTt/aGt	32.43	
m.8066C>A	Missense variant	MODERATE	*MT-CO2*	p.H161N	Cac/Aac	24.95	
m.8187G>C	Missense variant	MODERATE	*MT-CO2*	p.G201A	gGa/gCa	10.56	
m.8247T>C	Missense variant	MODERATE	*MT-CO2*	p.M221T	aTa/aCa	15.87	
m.8259T>A	Missense variant	MODERATE	*MT-CO2*	p.F225Y	tTt/tAt	13.27	
m.8783G>A	Missense variant	MODERATE	*MT-ATP6*	p.G86E	gGa/gAa	10.11	
m.8836A>T	Missense variant	MODERATE	*MT-ATP6*	p.M104L	Atg/Ttg	11.32	
m.8864T>G	Missense variant	MODERATE	*MT-ATP6*	p.V113G	gTg/gGg	14.44	
m.8870T>C	Missense variant	MODERATE	*MT-ATP6*	p.M115T	aTa/aCa	10.4	
m.9188A>G	Missense variant	MODERATE	*MT-ATP6*	p.Y221C	tAc/tGc	13.62	
m.9387G>C	Missense variant	MODERATE	*MT-CO3*	p.V61L	Gta/Cta	15.48	
m.9447T>G	Missense variant	MODERATE	*MT-CO3*	p.Y81D	Tac/Gac	13.33	
m.9488C>G	Missense variant	MODERATE	*MT-CO3*	p.F94L	ttC/ttG	10.34	
m.9489G>C	Missense variant	MODERATE	*MT-CO3*	p.A95P	Gca/Cca	11.54	
m.9512C>G	Stop-gained	HIGH	*MT-CO3*	p.Y102X	taC/taG	19.05	
m.9631T>A	Missense variant	MODERATE	*MT-CO3*	p.V142E	gTa/gAa	25.11	
m.9646C>G	Missense variant	MODERATE	*MT-CO3*	p.A147G	gCt/gGt	31.58	
m.9710A>C	Missense variant	MODERATE	*MT-CO3*	p.L168F	ttA/ttC	11.34	
m.9770T>G	Missense variant	MODERATE	*MT-CO3*	p.I188M	atT/atG	20.77	
m.9785C>A	Stop-gained	HIGH	*MT-CO3*	p.Y193X	taC/taA	10.39	
m.9818C>G	Missense variant	MODERATE	*MT-CO3*	p.H204Q	caC/caG	11.48	rs2854139
m.9865T>G	Missense variant	MODERATE	*MT-CO3*	p.I220S	aTc/aGc	13.83	
m.9899T>G	Missense variant	MODERATE	*MT-CO3*	p.H231Q	caT/caG	12.62	rs41345446
m.9909T>C	Missense variant	MODERATE	*MT-CO3*	p.F235L	Ttc/Ctc	13.92	rs28690056
m.10111T>A	Missense variant	MODERATE	*MT-ND3*	p.M18K	aTa/aAa	44.44	
m.10203G>C	Missense variant	MODERATE	*MT-ND3*	p.V49L	Gtc/Ctc	11.02	
m.10536C>G	Missense variant	MODERATE	*MT-ND4L*	p.R23G	Cgc/Ggc	10.91	
m.10593A>T	Missense variant	MODERATE	*MT-ND4L*	p.I42F	Att/Ttt	12.62	
m.10640T>G	Missense variant	MODERATE	*MT-ND4L*	p.N57K	aaT/aaG	45.69	rs386419955
m.10676C>G	Missense variant	MODERATE	*MT-ND4L*	p.C69W	tgC/tgG	13.41	
m.10711T>A	Missense variant	MODERATE	*MT-ND4L*	p.I81N	aTc/aAc	39.14	
m.11019A>C	Missense variant	MODERATE	*MT-ND4*	p.E87A	gAa/gCa	10.53	
m.11145C>T	Missense variant	MODERATE	*MT-ND4*	p.T129I	aCc/aTc	10.58	
m.11330G>C	Missense variant	MODERATE	*MT-ND4*	p.A191P	Gcc/Ccc	20.22	
m.11435G>C	Missense variant	MODERATE	*MT-ND4*	p.A226P	Gct/Cct	12.66	
m.11445T>G	Stop-gained	HIGH	*MT-ND4*	p.M229X	aTa/aGa	13.77	

m.11514C>T	Missense variant	MODERATE	*MT-ND4*	p.P252L	cCc/cTc	12.04		
m.11675C>T	Missense variant	MODERATE	*MT-ND4*	p.P306S	Ccc/Tcc	12.31		
m.11848C>A	Stop-gained	HIGH	*MT-ND4*	p.S363X	agC/agA	20.95		
m.11924T>C	Missense variant	MODERATE	*MT-ND4*	p.S389P	Tca/Cca	31.19		
m.12373A>T	Missense variant	MODERATE	*MT-ND5*	p.T13S	Act/Tct	19.21		
m.12457G>A	Missense variant	MODERATE	*MT-ND5*	p.A41T	Gca/Aca	16.44	COSM1155520	Endometrium tumour
m.12499A>T	Missense variant	MODERATE	*MT-ND5*	p.M55L	Atg/Ttg	19.39		
m.12523A>G	Missense variant	MODERATE	*MT-ND5*	p.I63V	Atc/Gtc	38.59		
m.12569T>A	Missense variant	MODERATE	*MT-ND5*	p.L78Q	cTa/cAa	14.22	COSM1155523	Endometrium tumour
m.12788C>A	Missense variant	MODERATE	*MT-ND5*	p.S151Y	tCc/tAc	10.47		
m.12841A>G	Missense variant	MODERATE	*MT-ND5*	p.I169V	Att/Gtt	10.47		
m.12951C>G	Missense variant	MODERATE	*MT-ND5*	p.N205K	aaC/aaG	13.92		
m.12968C>G	Missense variant	MODERATE	*MT-ND5*	p.T211S	aCc/aGc	13.25		
m.13045A>T	Missense variant	MODERATE	*MT-ND5*	p.M237L	Ata/Tta	12.32		
m.13142A>T	Missense variant	MODERATE	*MT-ND5*	p.N269I	aAt/aTt	11.11		
m.13198G>C	Missense variant	MODERATE	*MT-ND5*	p.A288P	Gca/Cca	20.63		
m.13444T>G	Missense variant	MODERATE	*MT-ND5*	p.S370A	Tca/Gca	54.91		
m.13495A>C	Missense variant	MODERATE	*MT-ND5*	p.T387P	Aca/Cca	31.52		
m.13511A>G	Stop-gained	HIGH	*MT-ND5*	p.K392X	aAa/aGa	10.56		
m.13556G>C	Missense variant	MODERATE	*MT-ND5*	p.W407S	tGa/tCa	12.11	COSM1720929	Skin tumour
m.13579G>T	Missense variant	MODERATE	*MT-ND5*	p.A415S	Gct/Tct	10.84		
m.13790A>G	Missense variant	MODERATE	*MT-ND5*	p.Y485C	tAc/tGc	12.82		
m.13823T>C	Missense variant	MODERATE	*MT-ND5*	p.L496P	cTa/cCa	12.86		
m.14363A>T	Missense variant	MODERATE	*MT-ND6*	p.L104Q	cTg/cAg	11.35		
m.14427C>A	Missense variant	MODERATE	*MT-ND6*	p.G83W	Ggg/Tgg	43.9		
m.14556A>T	Missense variant	MODERATE	*MT-ND6*	p.C40S	Tgt/Agt	12.26		
m.14927A>G	Missense variant	MODERATE	*MT-CYB*	p.T61A	Acc/Gcc	22.52	rs201551481	
m.14962C>G	Missense variant	MODERATE	*MT-CYB*	p.D72E	gaC/gaG	11.11		
m.14990C>G	Missense variant	MODERATE	*MT-CYB*	p.L82V	Ctt/Gtt	20		
m.15030T>G	Missense variant	MODERATE	*MT-CYB*	p.F95C	tTc/tGc	17.65		
m.15097T>G	Missense variant	MODERATE	*MT-CYB*	p.I117M	atT/atG	14.45		
m.15108T>C	Missense variant	MODERATE	*MT-CYB*	p.L121P	cTt/cCt	13.94		
m.15255T>G	Missense variant	MODERATE	*MT-CYB*	p.V170G	gTa/gGa	32.33		
m.15502C>G	Missense variant	MODERATE	*MT-CYB*	p.D252E	gaC/gaG	17.25		
m.15653A>C	Missense variant	MODERATE	*MT-CYB*	p.M303L	Ata/Cta	12.68		

Supplementary table 21: Position of SNVs, their consequences, and heteroplasmy percentage in single myeloid cells obtained from 3 MDS patients.

Substitution	Consequence	Gene	Impact	Amino acid change	HET%	Codons	Existing variants	Phenopte data
m.3310C>T	Missense variant	*MT-ND1*	MODERATE	p.P2S	30.56	Ccc/Tcc		
m.3395A>G	Missense variant	*MT-ND1*	MODERATE	p.Y30C	12.12	tAt/tGt		
m.3524C>G	Missense variant	*MT-ND1*	MODERATE	p.T73S	10.14	aCc/aGc		
m.3841T>C	Missense variant	*MT-ND1*	MODERATE	p.W179R	58.65	Tga/Cga		
m.3844C>A	Missense variant	*MT-ND1*	MODERATE	p.P180T	30.65	Ccc/Acc		
m.3867C>A	Missense variant	*MT-ND1*	MODERATE	p.I187M	38.89	atC/atA		
m.3880G>C	Missense variant	*MT-ND1*	MODERATE	p.E192Q	50.68	Gag/Cag		
m.3910G>T	Stop-gained	*MT-ND1*	HIGH	p.E202X	50	Gaa/Taa		
m.3997A>C	Missense variant	*MT-ND1*	MODERATE	p.I231L	38.37	Att/Ctt		
m.4049A>C	Missense variant	*MT-ND1*	MODERATE	p.D248A	21.95	gAc/gCc		
m.4093A>T	Missense variant	*MT-ND1*	MODERATE	p.T263S	68.42	Acc/Tcc		
m.4117T>A	Missense variant	*MT-ND1*	MODERATE	p.L271M	23.26	Tta/Ata		
m.4227A>T	Missense variant	*MT-ND1*	MODERATE	p.M307I	28.57	atA/atT		
m.4495T>C	Missense variant	*MT-ND2*	MODERATE	p.I9T	17.44	aTc/aCc		
m.4518A>G	Missense variant	*MT-ND2*	MODERATE	p.T17A	15.09	Aca/Gca		
m.4593C>A	Missense variant	*MT-ND2*	MODERATE	p.P42T	16.28	Cca/Aca		
m.4697C>G	Missense variant	*MT-ND2*	MODERATE	p.F76L	23.44	ttC/ttG		
m.4710T>C	Missense variant	*MT-ND2*	MODERATE	p.S81P	21.88	Tcc/Ccc		
m.4732A>C	Missense variant	*MT-ND2*	MODERATE	p.N88T	19.35	aAt/aCt		
m.4767A>C	Missense variant	*MT-ND2*	MODERATE	p.M100L	44.19	Ata/Cta		
m.4839C>G	Missense variant	*MT-ND2*	MODERATE	p.L124V	71.96	Ctg/Gtg		
m.4897A>G	Missense variant	*MT-ND2*	MODERATE	p.Y143C	32.39	tAc/tGc		
m.4905T>A	Missense variant	*MT-ND2*	MODERATE	p.S146T	12	Tct/Act		
m.5169T>A	Stop-gained	*MT-ND2*	HIGH	p.W234X	10.14	Tga/Aga		
m.5201T>G	Missense variant	*MT-ND2*	MODERATE	p.I244M	21.95	atT/atG		
m.5302T>G	Missense variant	*MT-ND2*	MODERATE	p.I278S	12.5	aTc/aGc		
m.5420T>A	Missense variant	*MT-ND2*	MODERATE	p.F317L	30.16	ttT/ttA		
m.5946A>T	Missense variant	*MT-CO1*	MODERATE	p.I15F	12.12	Att/Ttt		
m.5991G>T	Missense variant	*MT-CO1*	MODERATE	p.G30C	10.71	Ggc/Tgc		
m.6052A>C	Missense variant	*MT-CO1*	MODERATE	p.N50T	68.42	aAc/aCc		
m.6199A>T	Missense variant	*MT-CO1*	MODERATE	p.N99I	45.33	aAc/aTc		
m.6340C>A	Missense variant	*MT-CO1*	MODERATE	p.T146N	78.26	aCc/aAc		
m.6373C>G	Missense variant	*MT-CO1*	MODERATE	p.S157C	14.55	tCt/tGt		
m.6376T>A	Missense variant	*MT-CO1*	MODERATE	p.I158N	21.52	aTc/aAc		
m.6378T>A	Missense variant	*MT-CO1*	MODERATE	p.L159M	47.89	Tta/Ata		
m.6496C>A	Missense variant	*MT-CO1*	MODERATE	p.S198Y	21.01	tCt/tAt	COSM5656133 & COSM5656134	**Hematopoietic and**

								lymphoid tissue tumor
m.6511C>G	Missense variant	*MT-CO1*	MODERATE	p.A203G	12.5	gCt/gGt		
m.6519A>C	Missense variant	*MT-CO1*	MODERATE	p.I206L	35.82	Atc/Ctc		
m.6552A>T	Missense variant	*MT-CO1*	MODERATE	p.T217S	11.76	Acc/Tcc		
m.6579G>A	Stop-gained	*MT-CO1*	HIGH	p.G226X	11.11	Gga/Aga		
m.6724T>G	Missense variant	*MT-CO1*	MODERATE	p.V274G	26.79	gTc/gGc		
m.6727G>C	Missense variant	*MT-CO1*	MODERATE	p.W275S	37.5	tGa/tCa		
m.6732A>G	Missense variant	*MT-CO1*	MODERATE	p.M277V	44.07	Atg/Gtg		
m.6777A>G	Missense variant	*MT-CO1*	MODERATE	p.M292V	11.43	Ata/Gta		
m.6786G>A	Missense variant	*MT-CO1*	MODERATE	p.V295M	14.29	Gta/Ata		
m.6801G>T	Missense variant	*MT-CO1*	MODERATE	p.D300Y	43.93	Gac/Tac		
m.6938C>A	Missense variant	*MT-CO1*	MODERATE	p.I345M	19.66	atC/atA		
m.7008G>C	Missense variant	*MT-CO1*	MODERATE	p.D369H	33.9	Gac/Cac		
m.7060T>C	Missense variant	*MT-CO1*	MODERATE	p.V386A	26.67	gTa/gCa		
m.7088C>A	Missense variant	*MT-CO1*	MODERATE	p.H395Q	26.32	caC/caA		
m.7093T>C	Missense variant	*MT-CO1*	MODERATE	p.F397S	80.95	tTt/tCt		
m.7185C>G	Missense variant	*MT-CO1*	MODERATE	p.Q428E	12.31	Caa/Gaa		
m.7244C>G	Stop-gained	*MT-CO1*	HIGH	p.Y447X	17	taC/taG		
m.7285C>A	Missense variant	*MT-CO1*	MODERATE	p.S461Y	12.82	tCt/tAt		
m.7387T>C	Missense variant	*MT-CO1*	MODERATE	p.L495P	15.67	cTa/cCa		
m.7592C>A	Missense variant	*MT-CO2*	MODERATE	p.H3N	33.33	Cat/Aat		
m.7657T>A	Missense variant	*MT-CO2*	MODERATE	p.H24Q	16.67	caT/caA		
m.7691T>G	Missense variant	*MT-CO2*	MODERATE	p.F36V	78.95	Ttc/Gtc		
m.7779G>C	Missense variant	*MT-CO2*	MODERATE	p.W65S	24.27	tGa/tCa		
m.7860A>C	Missense variant	*MT-CO2*	MODERATE	p.D92A	11.94	gAt/gCt		
m.7879A>C	Missense variant	*MT-CO2*	MODERATE	p.K98N	25.58	aaA/aaC		
m.7914A>G	Missense variant	*MT-CO2*	MODERATE	p.Y110C	12.2	tAc/tGc		
m.8390T>A	Stop-gained	*MT-ATP8*	HIGH	p.W9X	20	Tgg/Agg		
m.8735T>C	Missense variant	*MT-ATP6*	MODERATE	p.L70P	13.89	cTt/cCt		
m.9035T>A	Missense variant	*MT-ATP6*	MODERATE	p.L170H	26.04	cTc/cAc		
m.9103T>A	Missense variant	*MT-ATP6*	MODERATE	p.F193I	35	Ttc/Atc		
m.9200A>C	Missense variant	*MT-ATP6*	MODERATE	p.N225T	18.75	aAc/aCc		
m.9270C>G	Missense variant	*MT-CO3*	MODERATE	p.L22V	90.6	Ctc/Gtc		
m.9315T>G	Missense variant	*MT-CO3*	MODERATE	p.F37V	34.69	Ttc/Gtc		
m.9384G>C	Missense variant	*MT-CO3*	MODERATE	p.D60H	19.18	Gat/Cat	COSM1138427 & COSM1138428	Kidney tumour
m.9517C>T	Missense variant	*MT-CO3*	MODERATE	p.S104F	12.5	tCc/tTc		
m.9651C>G	Missense variant	*MT-CO3*	MODERATE	p.H149D	53.85	Cat/Gat		
m.9718T>C	Missense variant	*MT-CO3*	MODERATE	p.L171P	60.53	cTc/cCc		
m.9853C>G	Missense variant	*MT-CO3*	MODERATE	p.T216S	85.11	aCt/aGt		

m.9861T>G	Missense variant	*MT-CO3*	MODERATE	p.F219V	72.58	Ttc/Gtc		
m.9960C>G	Missense variant	*MT-CO3*	MODERATE	p.L252V	16.98	Ctg/Gtg		
m.9983A>C	Missense variant	*MT-CO3*	MODERATE	p.W259C	12.9	tgA/tgC		
m.10117T>A	Missense variant	*MT-ND3*	MODERATE	p.I20N	12.5	aTt/aAt		
m.10151A>T	Missense variant	*MT-ND3*	MODERATE	p.M31I	15.62	atA/atT		
m.10201G>T	Missense variant	*MT-ND3*	MODERATE	p.R48L	25	cGc/cTc		
m.10204T>C	Missense variant	*MT-ND3*	MODERATE	p.V49A	60.71	gTc/gCc		
m.10206C>T	Missense variant	*MT-ND3*	MODERATE	p.P50S	35	Cct/Tct		
m.10261A>C	Missense variant	*MT-ND3*	MODERATE	p.E68A	41.86	gAa/gCa		
m.10392G>T	Missense variant	*MT-ND3*	MODERATE	p.D112Y	29.03	Gac/Tac		
m.10396G>T	Missense variant	*MT-ND3*	MODERATE	p.W113L	18.18	tGa/tTa		
m.10484C>G	Stop-gained	*MT-ND4L*	HIGH	p.Y5X	47.62	taC/taG		
m.10615T>C	Missense variant	*MT-ND4L*	MODERATE	p.L49P	15.56	cTc/cCc		
m.10683G>T	Missense variant	*MT-ND4L*	MODERATE	p.A72S	12.5	Gcg/Tcg		
m.10740C>T	Missense variant	*MT-ND4L*	MODERATE	p.H91Y	14.67	Cat/Tat		
m.10759A>T	Missense variant	*MT-ND4L*	MODERATE	p.Q97L	10.64	cAa/cTa		
m.10836A>T	Missense variant	*MT-ND4*	MODERATE	p.N26I	10	aAc/aTc		
m.11097C>G	Stop-gained	*MT-ND4*	HIGH	p.T113X	11.58	aCa/aGa		
m.11155C>G	Missense variant	*MT-ND4*	MODERATE	p.I132M	14	atC/atG		
m.11195G>T	Missense variant	*MT-ND4*	MODERATE	p.G146C	18	Ggc/Tgc		
m.11256A>T	Missense variant	*MT-ND4*	MODERATE	p.Y166F	19.8	tAc/tTc		
m.11303A>T	Missense variant	*MT-ND4*	MODERATE	p.T182S	29.11	Act/Tct		
m.11465T>A	Missense variant	*MT-ND4*	MODERATE	p.L236M	11.43	Tta/Ata		
m.11559G>A	Stop-gained	*MT-ND4*	HIGH	p.W267X	48.48	tGa/tAa		
m.11579T>A	Missense variant	*MT-ND4*	MODERATE	p.S274T	41.67	Tcc/Acc	COSM1155512	Endometrium tumour
m.11595A>G	Missense variant	*MT-ND4*	MODERATE	p.Q279R	10.26	cAa/cGa		
m.11618G>C	Missense variant	*MT-ND4*	MODERATE	p.A287P	17.14	Gca/Cca		
m.11638C>G	Missense variant	*MT-ND4*	MODERATE	p.H293Q	13.39	caC/caG		
m.11682G>C	Missense variant	*MT-ND4*	MODERATE	p.S308T	20.83	aGc/aCc		
m.11771C>G	Missense variant	*MT-ND4*	MODERATE	p.H338D	16.36	Cac/Gac	COSM6716765 & COSM6716766	Large intestine tumour
m.11773C>G	Missense variant	*MT-ND4*	MODERATE	p.H338Q	15.69	caC/caG		
m.11948G>T	Missense variant	*MT-ND4*	MODERATE	p.G397W	87.73	Gga/Tga	COSM1155518	Endometrium tumour
m.11993A>T	Missense variant	*MT-ND4*	MODERATE	p.T412S	12.12	Acc/Tcc		
m.12137T>G	Incomplete terminal codon variant & coding sequence variant	*MT-ND4*	LOW	p.X460	21.26	T/G		
m.12427T>A	Missense variant	*MT-ND5*	MODERATE	p.S31T	14.71	Tca/Aca		
m.12441T>G	Stop-gained	*MT-ND5*	HIGH	p.Y35X	16.2	taT/taG		
m.12538T>A	Stop-gained	*MT-ND5*	HIGH	p.W68X	23.21	Tga/Aga		
m.12593C>A	Missense variant	*MT-ND5*	MODERATE	p.S86Y	75	tCc/tAc		

m.12631T>G	Missense variant	*MT-ND5*	MODERATE	p.S99A	10.53	Tcc/Gcc		
m.12655T>C	Missense variant	*MT-ND5*	MODERATE	p.Y107H	13.51	Tat/Cat		
m.12771G>C	Missense variant	*MT-ND5*	MODERATE	p.E145D	96.61	gaG/gaC	COSM1155528	Endometrium tumour
m.12795G>T	Missense variant	*MT-ND5*	MODERATE	p.L153F	18.37	ttG/ttT		
m.12867C>G	Missense variant	*MT-ND5*	MODERATE	p.I177M	34.91	atC/atG		
m.12868G>T	Missense variant	*MT-ND5*	MODERATE	p.G178C	81.5	Ggc/Tgc		
m.12875T>C	Missense variant	*MT-ND5*	MODERATE	p.I180T	31.25	aTc/aCc		
m.13210G>A	Missense variant	*MT-ND5*	MODERATE	p.A292T	13.33	Gcc/Acc		
m.13248C>A	Missense variant	*MT-ND5*	MODERATE	p.F304L	42.86	ttC/ttA		
m.13320C>G	Missense variant	*MT-ND5*	MODERATE	p.H328Q	15.91	caC/caG		
m.13362C>G	Missense variant	*MT-ND5*	MODERATE	p.C342W	12.24	tgC/tgG		
m.13475T>C	Missense variant	*MT-ND5*	MODERATE	p.L380S	75	tTa/tCa		
m.13539A>C	Missense variant	*MT-ND5*	MODERATE	p.M401I	11.76	atA/atC		
m.13592C>A	Missense variant	*MT-ND5*	MODERATE	p.T419K	14.29	aCa/aAa		
m.13705C>A	Missense variant	*MT-ND5*	MODERATE	p.L457M	68.12	Ctg/Atg		
m.13942A>G	Missense variant	*MT-ND5*	MODERATE	p.T536A	11.59	Aca/Gca	rs200657506	
m.14172T>A	Missense variant	*MT-ND6*	MODERATE	p.I168F	12.12	Att/Ttt		
m.14176A>C	Missense variant	*MT-ND6*	MODERATE	p.I166M	46.97	atT/atG		
m.14177A>T	Missense variant	*MT-ND6*	MODERATE	p.I166N	20	aTt/aAt		
m.14179A>C	Stop-gained	*MT-ND6*	HIGH	p.Y165X	50.28	taT/taG		
m.14234T>C	Missense variant	*MT-ND6*	MODERATE	p.D147G	10.94	gAt/gGt		
m.14397A>C	Missense variant	*MT-ND6*	MODERATE	p.L93V	11.32	Tta/Gta		
m.14805A>G	Missense variant	*MT-CYB*	MODERATE	p.D20G	10.42	gAc/gGc		
m.14834T>A	Stop-gained	*MT-CYB*	HIGH	p.W30X	58.46	Tga/Aga		
m.14853T>G	Missense variant	*MT-CYB*	MODERATE	p.L36R	15.38	cTc/cGc		
m.14886C>T	Missense variant	*MT-CYB*	MODERATE	p.T47M	16.13	aCa/aTa		
m.15017T>A	Missense variant	*MT-CYB*	MODERATE	p.F91I	24.14	Ttt/Att		
m.15022C>A	Missense variant	*MT-CYB*	MODERATE	p.I92M	11.11	atC/atA		
m.15039T>A	Missense variant	*MT-CYB*	MODERATE	p.I98N	25.56	aTc/aAc		
m.15053T>C	Missense variant	*MT-CYB*	MODERATE	p.Y103H	74.42	Tat/Cat		
m.15080A>T	Missense variant	*MT-CYB*	MODERATE	p.T112S	17.24	Acc/Tcc		
m.15486C>G	Missense variant	*MT-CYB*	MODERATE	p.P247R	17.14	cCa/cGa		
m.15535C>A	Missense variant	*MT-CYB*	MODERATE	p.N263K	40	aaC/aaA	rs28357371	
m.15536A>C	Missense variant	*MT-CYB*	MODERATE	p.T264P	42.5	Acc/Ccc		
m.15843T>G	Stop-gained	*MT-CYB*	HIGH	p.M366X	50.88	aTa/aGa		

Supplementary table 22: The names and nucleotide sequences of the primers.

Primer names	**Sequence**
Th forward primer	5'-GGTATACGCCACGCTGAAGG-3'
Th reverse primer	5'-TAGCCACAGTACCGTTCCAGA-3'
Actb forward primer	5'-CTGTGTGGATTGGTGGCTTCTAT-3'
Actb reverse primer	5'-GTAACAGTCCGCCTAGAAGCAT-3'
Gapdh forward primer	5'-AGGTCGGTGTGAACGGATTTG-3'
Gapdh reverse primer	5'-TGTAGACCATGTAGTTGAGGTCA-3'
5741 forward primer	5’-TGCAGGAGCATCAGTAGAC-3’
13144 reverse primer	5’-ATGACAAATCCTGCAAAGATG-3’
mt-*Nd4* forward primer	5’-AACGGATCCACAGCCGTA-3’
mt-*Nd4* reverse primer	5’-AGTCCTCGGGCCCATGATT-3’
D-loop forward primer	5’-AATCTACCATCCTCCGTGAAACC-3’
D-loop reverse primer	5’-TCAGTTTAGCTACCCCCAAGTTTAA-3’
MTL-F1	5’- AAA GCA CAT ACC AAG GCC AC -3’
MTL-F2	5’- TAT CCG CCA TCC CAT ACA TT -3’
MTL-R1	5’- TTG GCT CTC CTT GCA AAG TT -3’
MTL-R2	5’- AAT GTT GAG CCG TAG ATG CC -3’