Supplementary Table 1: Mutations detected in parental and highly metastatic NSCLC cell lines A549 (A) and HTB56 (B) by SNP analysis

A

A549

	R0 - low metastatic			R3 - high metastatic		
Chr.	**SNP Alteration**	**Cytoband Start**	**Cytoband End**	**SNP Alteration**	**Cytoband Start**	**Cytoband End**
1	duplication	q21.1	q44	duplication	q21.1	q44
2	duplication	p25.3	p21	duplication	p25.3	p21
3	duplication	p26.3	q29	duplication	p26.3	q29
5	duplication	p15.33	q35.3	duplication	p15.33	q35.3
7	duplication	p22.3	q36.3	duplication	p22.3	q36.3
8	duplication	p23.3	q24.3	duplication	p23.3	q24.3
9	CNN-LOH	p24.3	p21.3	CNN-LOH	p24.3	p21.3
9	homozyg. deletion	p21.3	p21.3	homozyg. deletion	p21.3	p21.3
9	CNN-LOH	p21.3	q34.3	CNN-LOH	p21.3	q34.3
10	duplication	p15.3	q26.3	duplication	p15.3	q26.3
11	duplication	p15.5	q14.3	duplication	p15.5	q14.3
12	CNN-LOH	p13.33	q24.33	CNN-LOH	p13.33	q24.33
14	duplication	q11.2	q32.33	duplication	q11.2	q32.33
15	duplication	q11.1	q11.2	duplication	q11.1	q11.2
15	duplication	q12	q14	duplication	q12	q14
15	duplication	q21.2	q21.3	duplication	q21.2	q21.3
15	duplication	q21.3	q24.1	duplication	q21.3	q24.1
15	duplication	q24.2	q26.3	duplication	q24.2	q26.3
16	duplication	p13.3	q24.3	duplication	p13.3	q24.3
17	duplication	p13.3	q25.3	duplication	p13.3	q25.3
19	amplification	p12	q13.31	amplification	p12	q13.31
19	duplication	q13.31	q13.43	duplication	q13.31	q13.43
20	duplication	p13	p11.1	duplication	p13	p11.1
20	CNN-LOH	p11.1	q13.33	CNN-LOH	p11.1	q13.33
21	heterozyg. deletion	q21.1	q21.1	heterozyg. deletion	q21.1	q21.1

B

HTB56

	R0 - low metastatic			R3 - high metastatic		
Chr.	**SNP Alteration**	**Cytoband Start**	**Cytoband End**	**SNP Alteration**	**Cytoband Start**	**Cytoband End**
1	duplication	p32.1	p31.3	duplication	p32.1	p31.3
1	duplication	p31.1	p31.1	duplication	p31.1	p31.1
1	duplication	p31.1	p31.1	duplication	p31.1	p31.1
1	duplication	p22.2	p21.2	duplication	p22.2	p21.2
1	duplication	q21.1	q31.3	duplication	q21.1	q31.3
2	duplication	p24.3	p16.1	duplication	p24.3	p16.1
2	duplication	q36.3	q36.3	duplication	q36.3	q36.3
2	heterozyg. deletion	q36.3	q37.3	heterozyg. deletion	q36.3	q37.3
2	duplication	q37.3	q37.3	duplication	q37.3	q37.3
3	duplication	q11.2	q13.31	duplication	q11.2	q13.31
4	CNN-LOH	p16.3	q35.2	CNN-LOH	p16.3	q35.2
5	duplication	p15.33	p12	duplication	p15.33	p12
5	amplification	p14.3	p14.1	amplification	p14.3	p14.1
5	amplification	q11.2	q12.1	amplification	q11.2	q12.1
5	duplication	q23.2	q35.3	duplication	q23.2	q35.3
6	CNN-LOH	p25.3	p12.2	CNN-LOH	p25.3	p12.2
6	duplication	p12.2	p12.1	amplification	p12.2	p12.1
7	duplication	p22.3	p12.1	duplication	p22.3	p12.1
7	-	-	-	amplification	q31.2	q31.2
8	CNN-LOH	p23.3	q11.21	CNN-LOH	p23.3	q11.21
8	amplification	q11.1	q12.1	amplification	q11.1	q12.1
8	duplication	q12.1	q22.2	duplication	q12.1	q22.2
8	amplification	q21.3	q21.3	amplification	q21.3	q21.3
8	amplification	q23.1	q23.1	amplification	q23.1	q23.1
9	heterozyg. deletion	p24.3	p21.1	heterozyg. deletion	p24.3	p21.1
9	duplication	p13.2	q13	duplication	p13.2	q13
9	amplification	q34.12	q34.3	duplication	q34.12	q34.3
10	CNN-LOH	p15.3	q11.21	CNN-LOH	p15.3	q11.21
10	duplication	q21.1	q24.33	duplication	q21.1	q24.33
11	duplication	p15.5	q14.2	duplication	p15.5	q14.2
11	amplification	q23.3	q24.1	amplification	q23.3	q24.1
12	amplification	p12.1	p11.1	amplification	p12.1	p11.1
12	amplification	q14.2	q21.1	duplication	q14.2	q21.1
13	amplification	q14.3	q21.1	amplification	q14.3	q21.1
13	amplification	q31.3	q31.3	amplification	q31.3	q31.3
13	amplification	q32.1	q32.3	amplification	q32.1	q32.3

13	amplification	q33.2	q33.2	amplification	q33.2	q33.2
14	duplication	q11.2	q32.33	duplication	q11.2	q32.33
15	duplication	q11.2	q26.3	duplication	q11.2	q26.3
16	CNN-LOH	p13.3	p12.1	CNN-LOH	p13.3	p12.1
16	duplication	p11.2	q24.3	duplication	p11.2	q24.3
17	CNN-LOH	q11.1	q25.3	CNN-LOH	q11.1	q25.3
18	duplication	p11.32	p11.31	duplication	p11.32	p11.31
18	duplication	p11.31	p11.2	duplication	p11.31	p11.2
20	CNN-LOH	p13	p11.1	CNN-LOH	p13	p11.1
20	amplification	q11.1	q11.22	amplification	q11.1	q11.22
21	heterozyg. deletion	p11.2	q21.1	heterozyg. deletion	p11.2	q21.1
21	CNN-LOH	q21.1	q22.3	CNN-LOH	q21.1	q22.3
22	CNN-LOH	q11.1	q13.33	CNN-LOH	q11.1	q13.33

Supplementary Table 2: Mutations detected in parental and highly metastatic NSCLC cell lines A549 and HTB56 by Exome sequencing

A

mutations detected (*n*)

	A549		HTB-56	
	R0	**R3**	**R0**	**R3**
genomic mutations				
pathogenic	19	19	12	13
likely pathogenic	174	177	126	127
likely benign	11	11	11	13
uncertain significance	40	41	29	32
sum	244	248	178	185

B

mutations detected only in R3 in comparison to R0

A549

Chr.	Position	Gene Region	Gene Symbol	Protein Variant	Translation Impact	Function Prediction
1	215793557	Exonic	KCTD3	p.R682K	missense	Activating
2	179642589	Exonic	TTN	p.R1395P	missense	
2	213403226	Exonic	ERBB4	p.W10L	missense	Activating
6	32169135	Exonic	NOTCH4	p.L1300M	missense	Damaging

HTB-56

Chr.	Position	Gene Region	Gene Symbol	Protein Variant	Translation Impact	Function Prediction
1	17085995	Exonic	MST1L	p.A301fs	frameshift	
10	32760107	Exonic	CCDC7	p.R209H	missense	Damaging
11	65374871	Exonic	MAP3K11	p.F453L	missense	Activating
14	33293794	Exonic	AKAP6	p.P2259A	missense	Activating
16	5041924	Exonic	SEC14L5	p.R187H	missense	Damaging
17	80478115	Exonic	FOXK2	p.K118fs	frameshift	
19	43865320	Exonic	CD177	p.K263fs	frameshift	

Supplementary Table 3: Conversion rate uniquely mapped reads

Sample	uniquely mapped reads	conversion rate
A549_0R_rep1	1.69E+07	99.29
A549_0R_rep2	2.52E+07	99.82
A549_1R	2.97E+07	99.83
A549_2R	2.99E+07	99.86
A549_3R_rep1	9.97E+06	99.01
A549_3R_rep2	3.50E+07	99.89
A3R_d6_250	1.56E+07	99.82
A3R d6_1uM	2.28E+07	99.66
A3R_d13_250nM	2.18E+07	99.40
A3R_d13_1uM	1.24E+07	99.19
HTB56_0R_rep1	1.79E+07	99.52
HTB56_0R_rep2	2.44E+07	99.80
HTB56_2R	1.43E+07	99.82
HTB56_3R_rep1	2.18E+07	99.54
HTB56_3R_rep2	1.54E+07	99.85
H3R_d6_250	2.57E+07	99.38
H3R_d13_250	2.06E+07	99.75

Table S3: **Conversion rate of methylation calls from uniquely mapped reads** The conversion rate was calculated from all extracted DNA methylation calls of the uniquely mapped reads as provided by the bismark methylation extractor software output. The conversion rate is depicted as the percentage of non-methylated cytosines in non-CpG context.