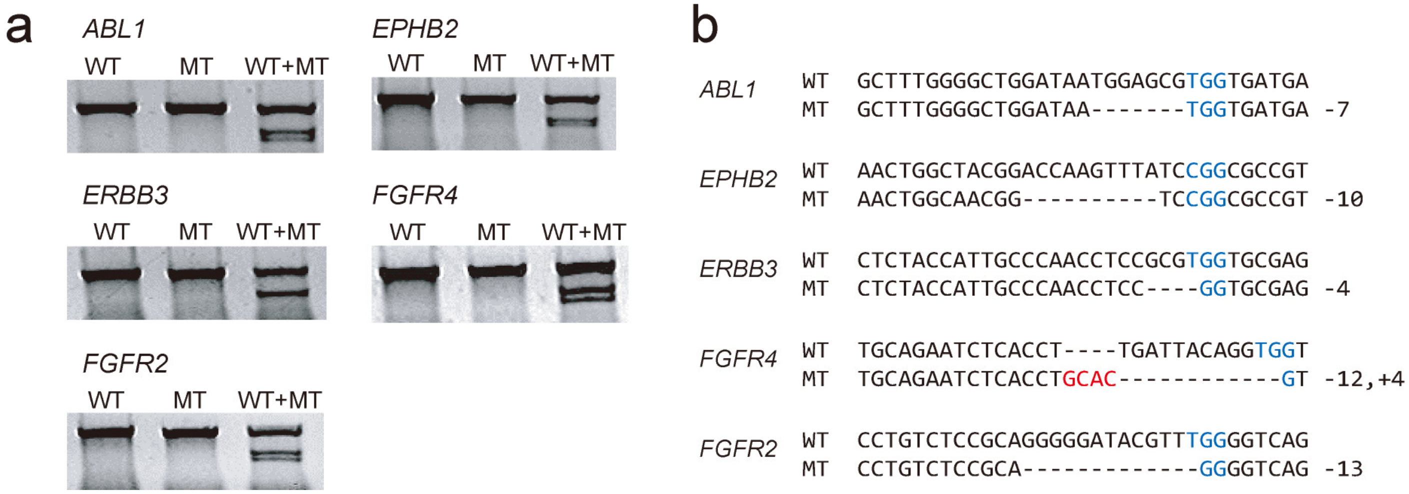
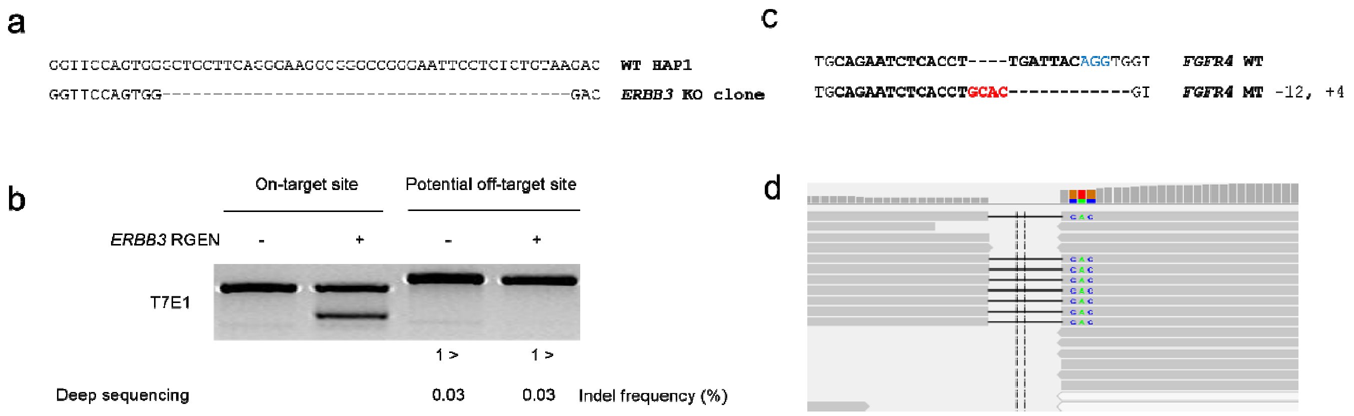


Supplementary Figure 1

Analysis of gene KO clones via T7E1 assay and DNA sequencing.

(a) T7E1 assay confirming gene knockout in clonal populations of HAP1 haploid cells. WT, wild-type; MT, mutant; WT+MT, a 1:1 mixture of WT and MT PCR amplicons. (b) DNA sequences of wild-type and mutant clones. The PAM is shown in blue. Inserted bases are shown in red.



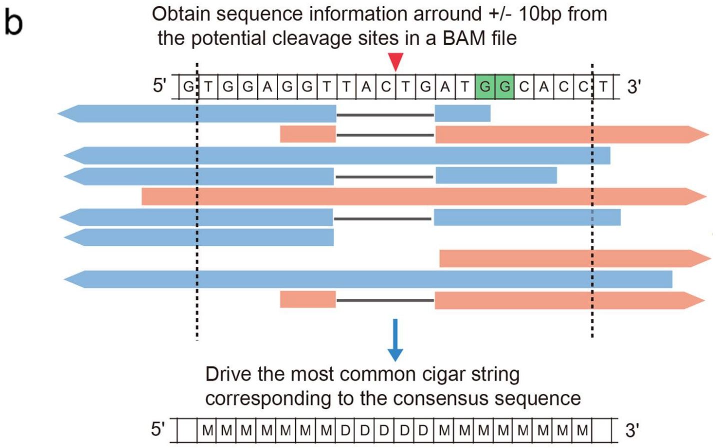
Supplementary Figure 2

Analysis of off-target effects in gene KO clones via WGS.

(a) Small deletion in the ERBB3 KO clone confirmed by Sanger sequencing. (b) RGEN-mediated mutagenesis at the on-target and potential off-target sites. Mutation frequencies (%) were measured using T7E1 and targeted deep sequencing. (c) The on-target mutant sequence in the FGFR4 KO clone. The PAM sequence is shown in blue and inserted bases are shown in red. (d) Integrative Genomics Viewer (IGV) image at the FGFR4 on-target site.

a

	Number of sites with no bulge	Number of sites with a bulge
ABL1	766,196	14,506
EPHB2	381,542	2,524
ERBB3	363,617	2,424
FGFR2	436,084	2,037
FGFR4	1,303,358	8,395



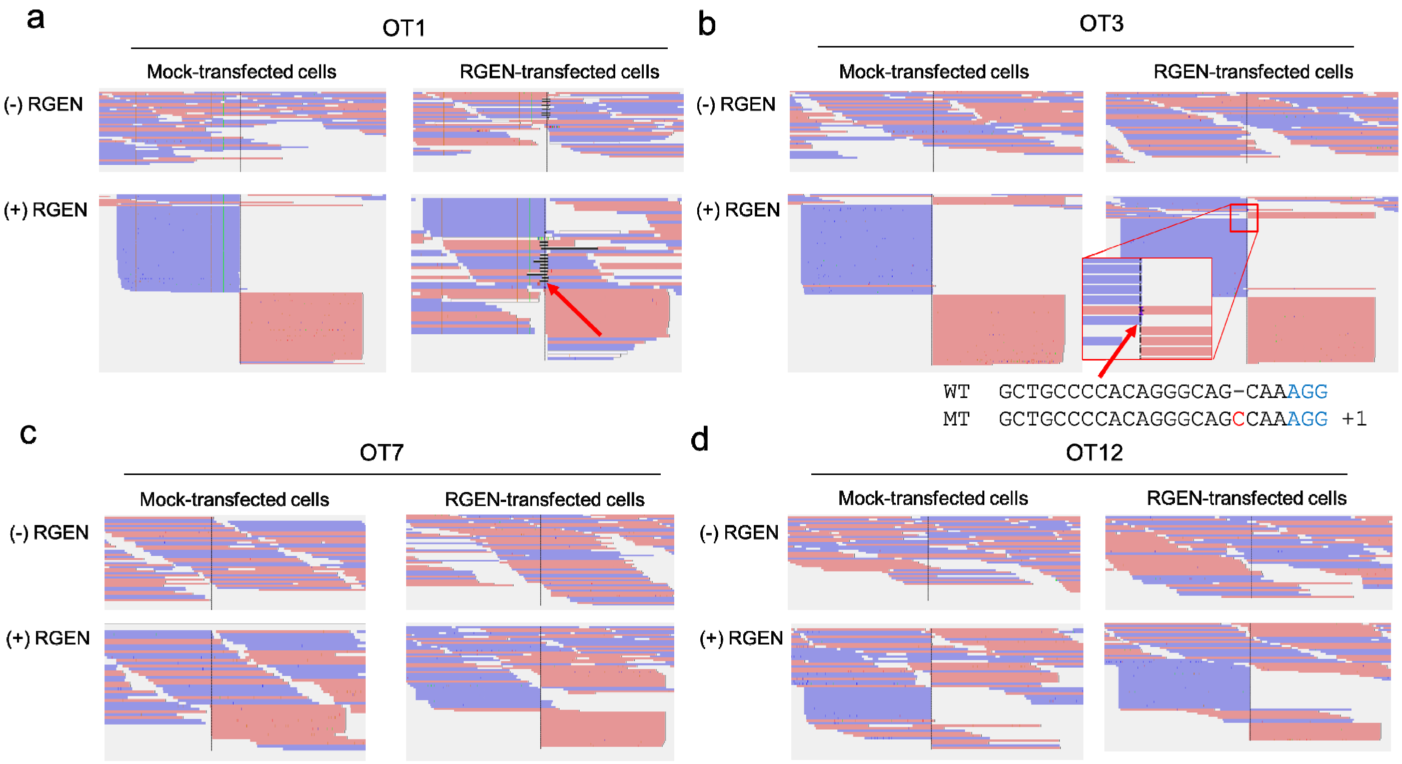
c On-target sites

ABL1	WT	MMMMMMMMMMMMMMMMMMMM
ABL1	MT	MMMMDDDDDDDMMMMMMMMM
EPHB2	WT	MMMMMMMMMMMMMMMMMMMM
EPHB2	MT	MDDDDDDDDDDSSSSSSSMM
ERBB3	WT	MMMMMMMMMMMMMMMMMMMM
ERBB3	MT	MMMMMMMMMMDDDDMMMMMM
FGFR2	WT	MMMMMMMMMMMMMMMMMMMM
FGFR2	MT	MDDDDDDDDDDDDDSSSMMM
FGFR4	WT	MMMMMMMMMMMMMMMMMMMM
FGFR4	MT	MMMMMMDDDDDDDDSSSSSS

Supplementary Figure 3

Examination of potential off-target sites.

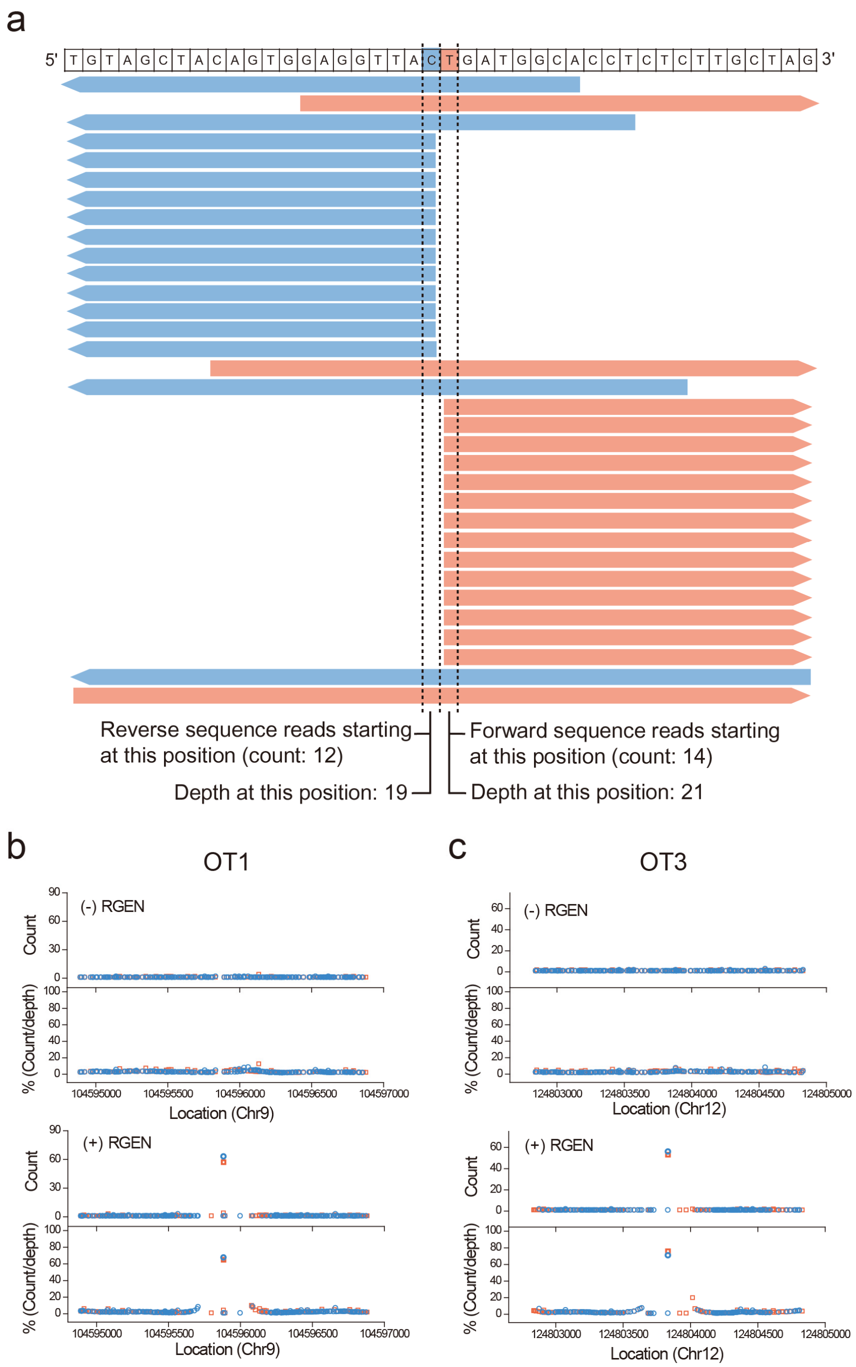
(a) The number of potential off-target sites that differ from on-target sites by up to 8 nucleotides or by 2 nucleotides with a DNA or RNA bulge of up to 5 nucleotides in length. (b) Schematic of consensus sequence generation. (c) On-target mutations in five KO clones identified by consensus sequence comparison.



Supplementary Figure 4

RGEN-induced digenome sequencing to capture off-target sites.

(a-d) Representative IGV images obtained using the HBB-specific RGEN at the potential off-target sites OT1 (a), OT3 (b), OT7 (c), and OT12 (d). An indel is indicated by an arrow (a) or shown in a box (b).



Reverse sequence reads starting at this position (count: 12)

Depth at this position: 19

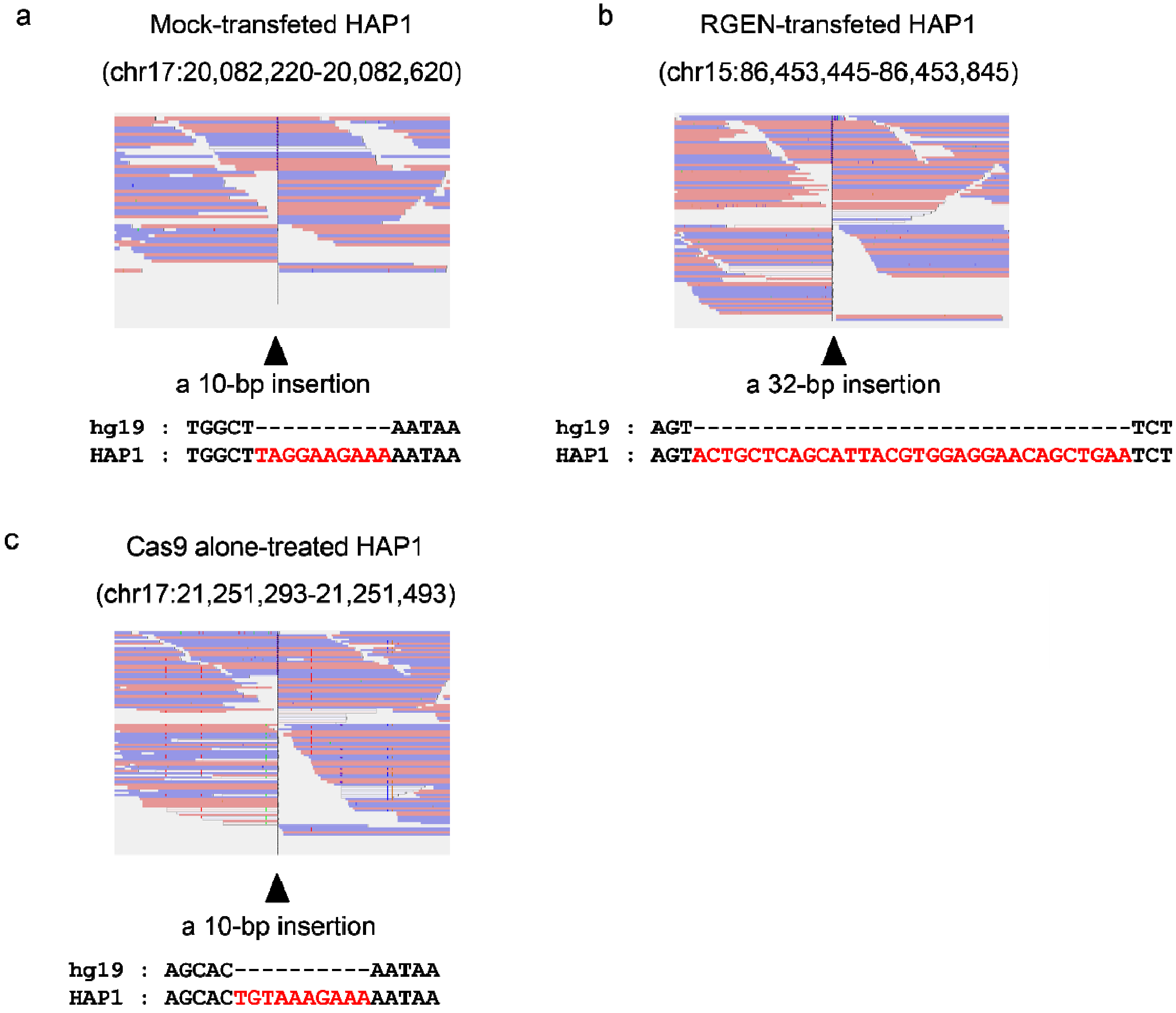
Forward sequence reads starting at this position (count: 14)

Depth at this position: 21

Supplementary Figure 5

5′-end plot.

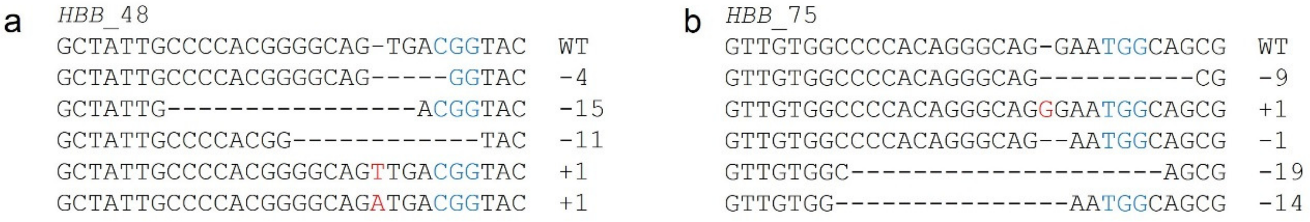
(a) An IGV image at a nuclease cleavage site. (b, c) 5’ End plots showing the absolute and relative number of sequence reads with the same 5’ end across nucleotide positions at the OT1 (b) and OT3 (c) sites.



Supplementary Figure 6

False positive positions captured in the intact genome sequences.

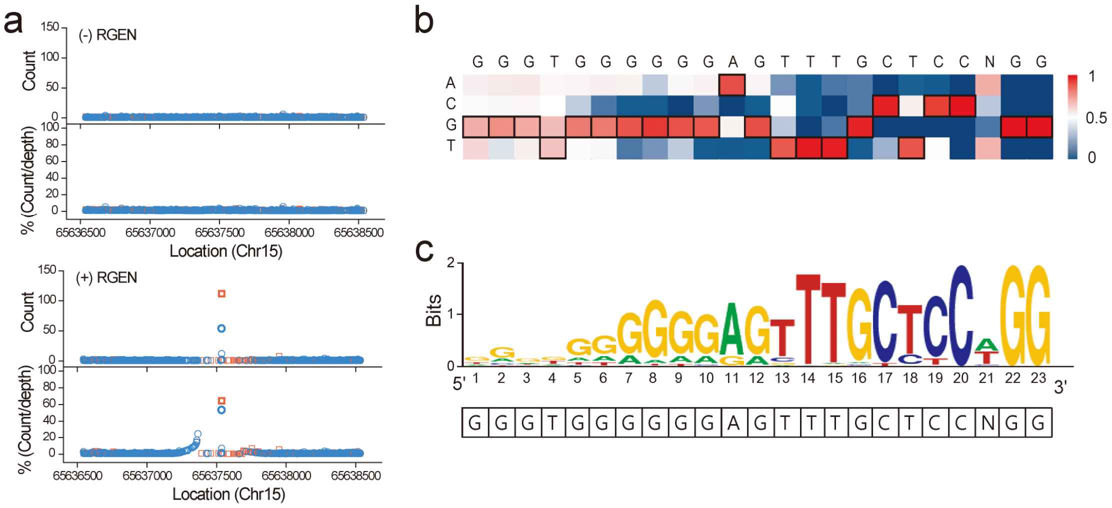
(a-c) Representative IGV images around false-positive sites that resulted from naturally-occurring indels in HAP1 cells.



Supplementary Figure 7

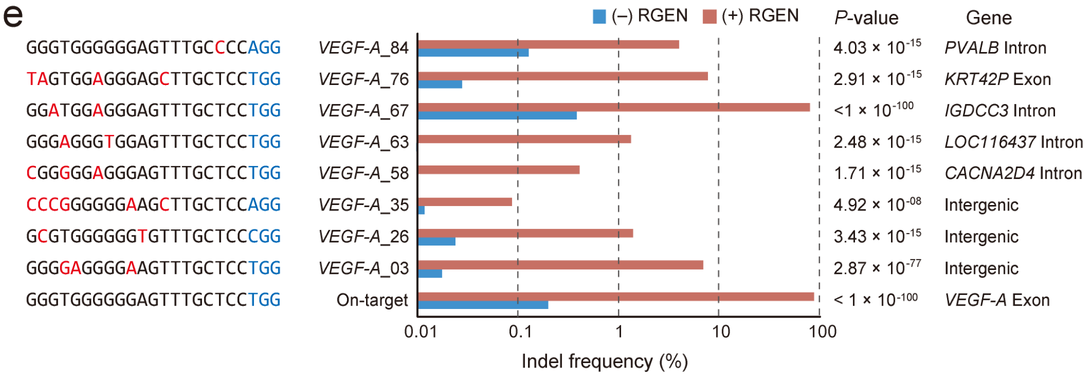
Indel sequences induced by the *HBB* RGEN at newly validated off-target sites.

(a, b) Off-target indels were detected by targeted deep sequencing. Inserted nucleotides are shown in red and the PAM sequence is shown in blue.



d

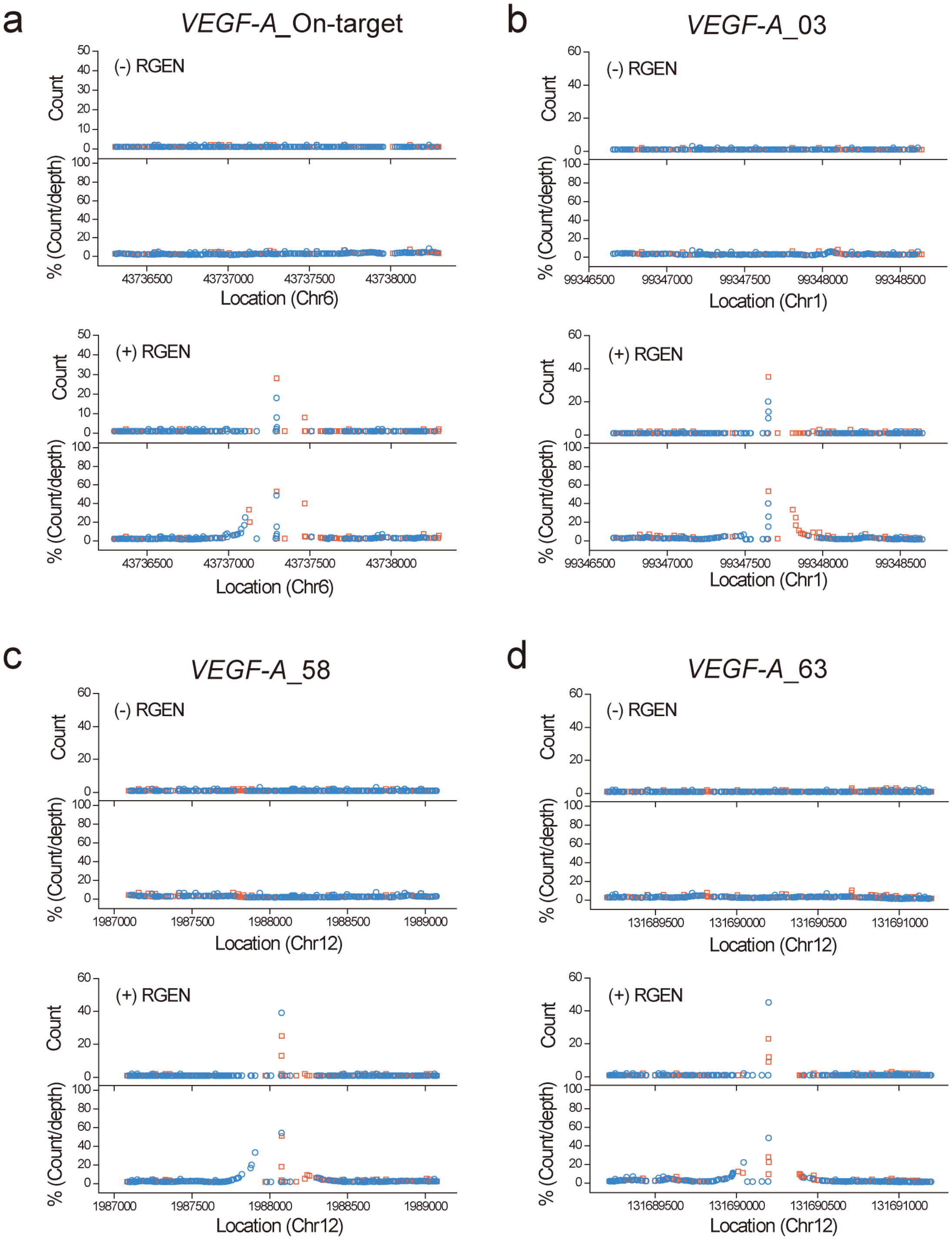
Total		Digenome-captured sites		Sites not captured by digenome sequencing	
Number of mismatches	Number of sites	Total number	Number of validated sites	Total number	Number of validated sites
0	1	1	1	0	0
1	1	1	1	0	0
2	4	3	3	1	0
3	32	5	2	27	0
4	283	12	1	271	N.D.
5	2,176	7	0	2,169	N.D.
6	13,892	6	1	13,886	N.D.



Supplementary Figure 8

Off-target sites of the *VEGFA* RGEN captured by Digenome-seq.

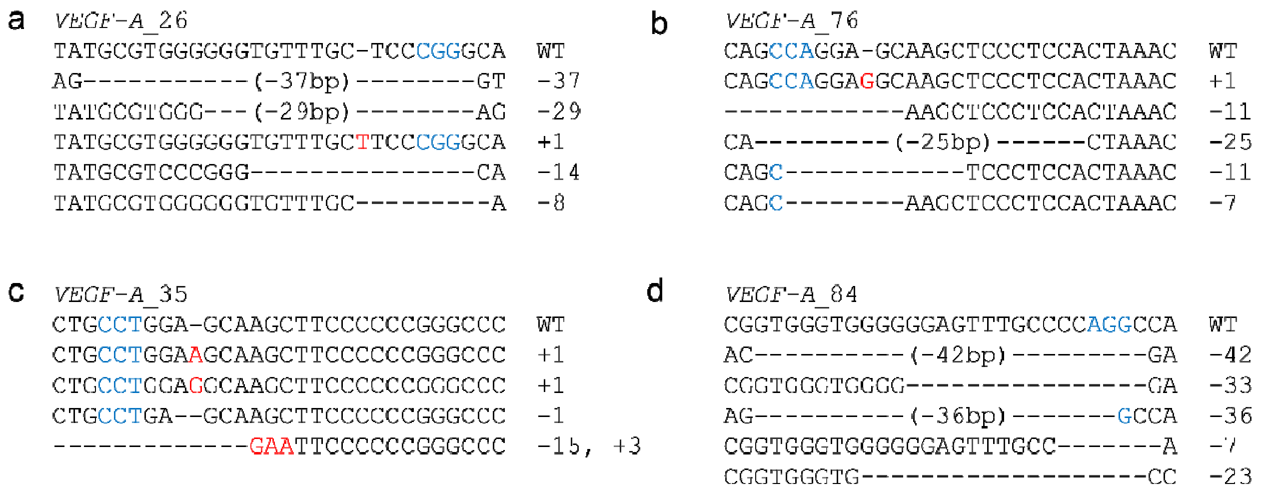
(a) 5’ End plots at the one of VEGF-A off-target site. (b) Heatmap comparing digenome-captured sites with the on-target site. Dark red and dark blue correspond to 100% and 0% matches, respectively, at a given position. (c) Sequence logo obtained via WebLogo using DNA sequences at digenome-captured sites. (d) Summary of Digenome-seq and targeted deep sequencing. N.D., not determined. (e) Off-target sites validated by targeted deep sequencing. Blue and red bars represent indel frequencies obtained using mock-transfected HAP1 cells and the VEGF-A RGEN-transfected HAP1 cells, respectively. (Left) DNA sequences of on-target and off-target sites. Mismatched bases are shown in red. The PAM is shown in blue. (Right) P value was calculated by the Fisher exact test. Additional deep sequencing results can be found in Supplementary Table 3.



Supplementary Figure 9

RGEN-induced digenome sequencing to capture off-target sites of the *VEGFA*-targeting RGEN.

(a-d) 5' End plots showing the absolute and relative number of sequence reads with the same 5' end across nucleotide positions in on-target (a) and off-target region (b-d).



Supplementary Figure 10

Indel sequences induced by the *VEGFA* RGEN at newly validated off-target sites.

(a-d) Off-target indels were detected by targeted deep sequencing. Inserted nucleotides are shown in red and the PAM sequence is shown in blue.

Supplementary Information

Digenome-Seq: Genome-wide Profiling of CRISPR/Cas9 Off-target Effects in Human Cells

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Supplemental Tables

Supplementary Table 1. Analysis of indels in gene knockout clones.

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Supplementary Table 6. List of primers.

Supplemental Notes

Supplementary Table 1. Analysis of indels in gene knockout clones.

			Knockout clone					
	WT (Experiment 1)	WT (Experiment 2)	*ABL1* (Experiment 1)	*ABL1* (Experiment 2)	*EPHB2*	*ERBB3*	*FGFR2*	*FGFR4*
Raw indel calls	331,325	337,993	322,090	323,620	316,917	319,022	309,976	312,553
Indels not present in the indel database	38,009	40,874	37,376	38,282	36,232	36,642	34,323	34,841
Haploid indels	29,159	30,851	29,707	30,005	28,779	29,142	27,202	27,961
KO clone-specific indels	2,226	2,968	2,910	3,250	2,107	2,196	2,026	2,061
Candidate indels at homologous sites	N/A	N/A	84	73	9	17	17	15
Confirmed by Sanger sequencing	N/A	N/A	0	0	0	1	0	0

Supplementary Table 2. Digenome-captured off-target candidate sites.

Intact genome										
	Forward strand				Reverse strand					
chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene	DNAsequence
chr17	20082420	14	32	43.8	20082419	11	27	40.7	Intergenic	GCTGATTTTGGTTGGCTAATAAA
chr17	21251093	10	35	28.6	21251092	17	49	34.7	Intergenic	CAGGTGGTAGTGAGCACAATAAA

RGEN-transfected genome										
	Forward strand				Reverse strand					
chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene	DNAsequence
chr12	84900444	11	38	28.9	84900443	10	34	29.4	Intergenic	GGGGCCGTGGGGTTTAACTGATA
chr15	86453645	10	48	20.8	86453644	13	60	21.7	Intergenic	CTCTGGCTCTTCAGAGTTCTTTT
chr17	21251093	14	46	30.4	21251092	20	55	36.4	Intergenic	CAGGTGGTAGTGAGCACAATAAA

Cas9 alone-treated genome										
	Forward strand				Reverse strand					
chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene	DNAsequence
chr17	21251093	12	59	20.3	21251092	20	88	22.7	Intergenic	CAGGTGGTAGTGAGCACAATAAA

HBB Mock-transfected digenome

		Forward strand				Reverse strand						
	chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene		DNAsequence
On-target	chr11	5248215	43	48	89.6	5248214	52	57	91.2	Exonic	*HBB*	CTTGCCCCACAGGGCAGTAACGG
HBB_1	chr1	38230668	31	38	81.6	38230667	25	32	78.1	Exonic	*EPHA10*	CTCTGTCTCGCGCTGCTTTTGGG
HBB_2	chr1	177593980	34	55	61.8	177593979	55	76	72.4	Intergenic		TCTACCCCACATGGCAGTAATGG
HBB_3	chr1	191839022	12	29	41.4	191839021	10	25	40	Intergenic		CCATAGCACTCTTTAAAAAAAGC
HBB_4	chr2	91869721	15	74	20.3	91869720	15	74	20.3	Intergenic		CTTACCTCACAGGGCAGTGAGAG
HBB_5	chr2	112686732	63	85	74.1	112686731	10	32	31.2	Exonic	*MERTK*	GGTCCCGGGAATAGCGGGTAAGG
HBB_6	chr2	188075775	14	36	38.9	188075774	20	42	47.6	Intergenic		ATGCAAGTCCAATATCCAGT GGG
HBB_7	chr2	211832279	29	56	51.8	211832278	11	36	30.6	Intergenic		TAAGCCCCACACAGCAGTTAAGG
HBB_8	chr2	240591539	30	37	81.1	240591538	25	32	78.1	Intergenic		ACAGCCCCACAGGGCACTAGAGG
HBB_9	chr3	3662556	49	54	90.7	3662555	42	47	89.4	Intergenic		AAAGCCCCACAGGGTAGTAGAGG
HBB_10	chr3	19957634	38	54	70.4	19957633	38	54	70.4	Intronic	*EFHB*	GCTACCCCACAGGGCATTAGGGG
HBB_11	chr3	104567551	13	30	43.3	104567550	16	33	48.5	Intergenic		ATGAAAGTCCAATATCCAGT GGG
HBB_12	chr4	45763604	29	36	80.6	45763603	45	52	86.5	Intergenic		GCTGCCCCACATGACAGAAATGG
HBB_13	chr4	48091817	26	37	70.3	48091816	49	60	81.7	Exonic	*TXK*	ACTCGTCTCCGATATCCAGT TGG
HBB_14	chr4	55979545	52	81	64.2	55979544	30	59	50.8	Exonic	*KDR*	GGTGTAACCCGGAGTGACCAAGG
HBB_15	chr4	67338877	14	37	37.8	67338876	20	43	46.5	Intergenic		TTTGACCCACAGGGCAGTAATGG
HBB_16	chr4	125564266	14	32	43.8	125564265	10	28	35.7	Intergenic		CCCTCCCCACAGGGCAGTGAGAG
HBB_17	chr4	148531374	38	43	88.4	148531373	32	37	86.5	Intergenic		GTTACCTCACAGAGCAGAAAGGG
HBB_18	chr4	151226685	20	55	36.4	151226684	19	55	34.5	Intronic	*LRBA*	TCTGCCCCACAAGACTGTAAAGG
HBB_19	chr4	165593737	27	56	48.2	165593736	26	56	46.4	Intronic	*MIR5684*	TATGCTCCACAGGGTAGTAATGA
HBB_20	chr5	14347051	46	62	74.2	14347050	48	63	76.2	Intronic	*TRIO*	CATACCCCACAGGTCAGT-AAGG
HBB_21	chr5	26107853	13	43	30.2	26107852	13	43	30.2	Intergenic		AATACCCCACAGGGAAGTGATGG
HBB_22	chr5	131423385	38	55	69.1	131423384	25	42	59.5	Intergenic		TCTGCCCCACAGGCCAGGAAGGG
HBB_23	chr6	23709579	29	52	55.8	23709578	14	37	37.8	Intergenic		GAAGCCCTACAGGGCAGCAATGG
HBB_24	chr6	50041372	38	49	77.6	50041371	60	71	84.5	Intergenic		TCTGCCCCACATGGCAGTAATGA
HBB_25	chr6	80093919	34	51	66.7	80093918	36	53	67.9	Intergenic		TGAGTTCTCCAATATCCAGT TGG
HBB_26	chr6	85738203	51	58	87.9	85738202	29	35	82.9	Intergenic		ACTGCCCCACAGGGAAGTAATAG
HBB_27	chr6	156371508	14	34	41.2	156371507	13	33	39.4	Intergenic		CATGCTCCACAGAGCAGCAAAGG
HBB_28	chr8	41296595	37	45	82.2	41296594	40	47	85.1	Intergenic		TCAGCCCCACAGGTCAGCAATGG
HBB_29	chr8	134024458	22	50	44	134024457	16	44	36.4	Intergenic		ATTACCCCACAGGGCAGCCAAGG
HBB_30	chr9	78341070	19	36	52.8	78341069	44	62	71	Intergenic		TGTTACCCCCAGGGAAGTAT AGG
OT1	chr9	104595883	57	64	89.1	104595882	63	69	91.3	Intergenic		TCAGCCCCACAGGGCAGTAAGGG
HBB_32	chr9	134609673	26	38	68.4	134609672	28	40	70	Intronic	*RAPGEF1*	TTTGCCCCTCAGGGCAGCTAAGG
HBB_33	chr9	134994964	21	28	75	134994963	29	36	80.6	Intergenic		CCTGCCCCACAGGGCAATTATGG
HBB_34	chr10	71843328	33	38	86.8	71843327	46	52	88.5	Intronic	*H2AFY2*	CATGGCCAGGAAGAGAAGGCTGG
HBB_35	chr10	72286450	21	32	65.6	72286449	25	36	69.4	Intronic	*PALD1*	CAAGCCCCACAGGGCAGACAGGG
HBB_36	chr10	73555691	25	53	47.2	73555690	18	46	39.1	Exonic	*CDH23*	CAGGCCCCACAGGACAGGAAGGG
HBB_37	chr10	73563394	13	31	41.9	73563393	17	34	50	Intronic	*CDH23*	AGTGCCACACAGGGCAGTAT AGG
HBB_38	chr10	111569275	12	29	41.4	111569274	22	39	56.4	Intergenic		ATGCAAGTCCAATATCCAGT GGG
HBB_39	chr11	3125346	24	43	55.8	3125345	18	36	50	Intronic	*OSBPL5*	CTGGCCCCACAGGGCAGGTAGGG

HBB_40	chr11	30888494	10	37	27	30888493	11	38	28.9	Intronic	*DCDC5*	ACTTCCCCACAGGGCAGAAGTGG
HBB_41	chr11	59611432	28	34	82.4	59611431	58	64	90.6	Exonic	*GIF*	CGGCCAGATTCATGGCAATCAGG
HBB_42	chr11	76387498	22	28	78.6	76387497	36	42	85.7	Intergenic		GCTGCCCCTCAGGGAAGTAT GGG
HBB_43	chr11	104908796	11	37	29.7	104908795	12	38	31.6	Intergenic		ATGCAAGTCCAATATCCAGT AGG
HBB_44	chr11	125807920	11	42	26.2	125807919	15	46	32.6	Intergenic		ATAGCCCCATAGGGCAGAAT AGG
HBB_45	chr12	27234755	51	75	68	27234754	19	43	44.2	Intronic	*C12orf71*	GATGCCTCACAGGACAGGAAGGG
HBB_46	chr12	40327469	41	49	83.7	40327468	32	40	80	Intronic	*SLC2A13*	GCTATGGTTCCTGAACGGCCTGG
HBB_47	chr12	54421218	17	49	34.7	54421217	10	42	23.8	Intronic	*HOXC4*	TCCAGCCAGAAAGAGAAGGCTGG
HBB_48	chr12	66309907	11	42	26.2	66309906	18	49	36.7	Intronic	*HMGA2*	ATTGCCCCACGGGGCAGTGACGG
OT3	chr12	124803834	53	54	98.1	124803833	56	58	96.6	Intergenic		GCTGCCCCACAGGGCAGCAAAGG
HBB_50	chr13	44886376	44	58	75.9	44886375	48	62	77.4	Intergenic		GGAGCCCCACAGGGCAGAGAGGG
HBB_51	chr14	36889538	47	50	94	36889537	55	58	94.8	Intergenic		GTTATCCCACAGGACAGTGAGGG
HBB_52	chr14	49319039	15	49	30.6	49319038	19	53	35.8	Intergenic		ATTACCCCACAGGACAGAAATAG
HBB_53	chr14	59445901	27	50	54	59445900	21	44	47.7	Intergenic		TCTTCCCCAATATCCAGT-- AGG
HBB_54	chr14	94585327	51	52	98.1	94585326	28	29	96.6	Intergenic		ATGGCCCCACAAGGCAGAAATGG
HBB_55	chr15	29983547	42	56	75	29983546	37	51	72.5	Intergenic		CCAGCCCCACAGGGCAGTAAAGG
HBB_56	chr15	46598129	47	48	97.9	46598128	54	55	98.2	Intergenic		GTTGCCCCTCAGGACAGTACAGG
HBB_57	chr15	88488821	13	48	27.1	88488820	18	53	34	Intronic	*NTRK3*	CCTGCCCCACAGGGCAGCCAAGG
HBB_58	chr15	99709337	19	37	51.4	99709336	17	33	51.5	Intronic	*TTC23*	TGTGCCCCACAGGG-AGTGAAGG
HBB_59	chr16	49082904	27	30	90	49082903	42	46	91.3	Intergenic		GCAGCCCCACAGGTCAGTGAGGG
HBB_60	chr17	8370253	24	26	92.3	8370252	49	51	96.1	ExoniC	*NDEL1*	TTGCTCCCACAGGGCAGTAACGG
HBB_61	chr18	745994	58	59	98.3	745993	45	46	97.8	ExoniC	*YES1*	AAAATACCTCGTTGATTTCCAGG
HBB_62	chr18	6663844	23	39	59	6663843	23	39	59	Intergenic		GTTGCCCCACTGGGGAGAAAAGG
HBB_63	chr18	42330301	23	43	53.5	42330300	14	34	41.2	Intronic	*SETBP1*	ATAGCCTCACAGGGCAGAGAGGG
HBB_64	chr19	8560462	21	49	42.9	8560461	11	37	29.7	Intronic	*PRAM1*	AAATCCCCACAGGGCAGT-AAGG
HBB_65	chr19	29880768	40	52	76.9	29880767	26	38	68.4	Intronic	*LOC284395*	TGTGCCCCACAGG-CAGTAATGG
HBB_66	chr19	34262013	18	32	56.2	34262012	13	27	48.1	Intronic	*CHST8*	CTTGCTCCACAGGGCAGGTATGG
HBB_67	chr19	37539042	28	54	51.9	37539041	12	36	33.3	Intergenic		CTTGCACCACAGAGCACTAAGGG
HBB_68	chr19	50010010	14	41	34.1	50010009	15	42	35.7	Intergenic		ATTGCCCCCCAGGTCAGTAGGGG
HBB_69	chr20	17385713	12	35	34.3	17385712	15	38	39.5	Intronic	*PCSK2*	GTTGCCCC---ACGCAGTAT GGG
HBB_70	chr20	39992928	33	52	63.5	39992927	17	36	47.2	Intronic	*EMILIN3*	AGTGGCCCCCAGGGCAGTGAGGG
HBB_71	chr20	58136220	10	37	27	58136219	23	50	46	Intergenic		TTTACCCCACAGGGCATTTAAGG
HBB_72	chr22	17230623	44	48	91.7	17230622	52	56	92.9	Intergenic		TGTGCCCCACAGAGCACTAAGGG
HBB_73	chr22	26043758	16	31	51.6	26043757	11	26	42.3	Intronic	*ADRBK2*	AAAATACCTCATTAATTTCCAGG
HBB_74	chr22	35537395	31	37	83.8	35537394	32	38	84.2	Intergenic		AGTGCCCCACAGGGGAGAAATGG
HBB_75	chrX	75006257	22	33	66.7	75006256	30	41	73.2	Intergenic		GTGGCCCCACAGGGCAGGAATGG

HBB RGEN-transfected digenome											
	Forward strand				Reverse strand						
chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene		DNAsequence
chr1	8926618	14	43	32.6	8926617	11	40	27.5	Intronic	*ENO1*	AGAGCCCCACAGGGCAGTAAGCC
chr1	17346702	19	34	55.9	17346701	47	62	75.8	Intronic	*SDHB*	GGTCCCCACAGGGTCAGTAAGGG
chr1	34925501	26	45	57.8	34925500	31	50	62	Intergenic		AGTTGCCCACAGGCCAGTAAGAG
chr1	38230668	23	41	56.1	38230667	21	39	53.8	Exonic	*EPHA10*	CTCTGTCTCGCGCTGCTTTTGGG
chr1	38682359	14	35	40	38682358	18	39	46.2	Intergenic		TACTGCCCCACAGGCAGTAACTG
chr1	64639008	12	47	25.5	64639007	18	53	34	Intronic	*ROR1*	CTATCTCACCAATATCCAGTGGG
chr1	167513585	10	32	31.2	167513584	10	22	45.5	Intronic	*CRFG1*	CTACCATGATTGGAAATCTCAGT
chr1	177593980	36	56	64.3	177593979	52	72	72.2	Intergenic		TCTACCCCACATGGCAGTAATGG
chr2	112686732	62	83	74.7	112686731	17	39	43.6	Exonic	*MERTK*	GGTCCCGGGAATAGCGGGTAAGG
chr2	188075775	26	45	57.8	188075774	30	49	61.2	Intergenic		ATGCAAGTCCAATATCCAGTGGG
chr2	211832279	32	46	69.6	211832278	16	30	53.3	Intergenic		TAAGCCCCACACAGCAGTTAAGG
chr2	240591539	40	48	83.3	240591538	30	38	78.9	Intergenic		ACAGCCCCACAGGGCACTAGAGG
chr3	3662556	49	51	96.1	3662555	46	48	95.8	Intergenic		AAAGCCCCACAGGGTAGTAGAGG
chr3	5619889	20	42	47.6	5619888	10	32	31.2	Intergenic		CTAGCTCCACAGGACAGTAATAG
chr3	14489594	25	63	39.7	14489593	19	57	33.3	Exonic	*SLC6A6*	CCTGCCTCACAGGGTAGTAATGA
chr3	19957634	57	69	82.6	19957633	55	67	82.1	Intronic	*EFHB*	GCTACCCCACAGGGCATTAGGGG
chr3	37982828	12	40	30	37982827	13	41	31.7	Intronic	*CTDSPL*	ATACCCCACAGGGAGAGTAAAGG
chr3	46414440	14	40	35	46414439	20	46	43.5	Exonic	*CCR5*	TGACATCAATTATTATACATCGG
chr3	104567551	21	52	40.4	104567550	27	58	46.6	Intergenic		ATGAAAGTCCAATATCCAGTGGG
chr3	128713852	15	69	21.7	128713851	23	77	29.9	Intergenic		ATAGCCCCACAGGGCAGGTTAGG
chr3	128713853	25	59	42.4	128713852	35	69	50.7	Intergenic		TAGCCCCACAGGGCAGGTTAGGG
chr3	138703033	35	51	68.6	138703032	25	41	61	Intergenic		ACTGTCCCACAGAGCAGTAAAGA
chr3	170245123	32	59	54.2	170245122	19	46	41.3	Intronic	*SLC7A14*	CAAGACCACAGAGCAGTAAGTGG
chr4	677375	15	38	39.5	677374	17	40	42.5	Intronic	*MFSD7*	CCACCCCCACAGGGCAGTCTTGG
chr4	45763604	34	43	79.1	45763603	20	30	66.7	Intergenic		GCTGCCCCACATGACAGAAATGG
chr4	48091817	25	35	71.4	48091816	65	76	85.5	Exonic	*TXK*	ACTCGTCTCCGATATCCAGTTGG
chr4	55979545	66	86	76.7	55979544	31	51	60.8	Exonic	*KDR*	GGTGTAACCCGGAGTGACCAAGG
chr4	67338877	16	40	40	67338876	21	45	46.7	Intergenic		TTGACCCACAGGGCCAGTAAATG
chr4	84856732	14	42	33.3	84856731	31	59	52.5	Intergenic		CTTTCCCCACAAGACAGTAAGAG
chr4	125564266	28	62	45.2	125564265	19	52	36.5	Intergenic		CCCTCCCCACAGGGCAGTGATGA
chr4	141516305	15	33	45.5	141516304	35	54	64.8	Intergenic		TTTGCCCTACAGGCCAGTAGATG
chr4	148531374	56	66	84.8	148531373	47	56	83.9	Intergenic		GTTACCTCACAGAGCAGAAAGGG
chr4	151226685	26	66	39.4	151226684	20	60	33.3	Intronic	*LRBA*	TCTGCCCCACAAGACTGTAAAGG
chr4	165593737	34	62	54.8	165593736	22	49	44.9	Intronic	*MIR5684*	TATGCTCCAGAGGGTAGTAATGA
chr5	14347051	48	67	71.6	14347050	47	59	79.7	Intronic	*TRIO*	CATACCCCACAGGTCAGTAAGGA
chr5	26107853	15	33	45.5	26107852	17	35	48.6	Intergenic		ATACCCCACAGGGACAGTGATGG
chr5	53613387	16	46	34.8	53613386	19	49	38.8	Intergenic		TCACCCCCACAGGCCAGTAAAGG
chr5	84984681	13	41	31.7	84984680	10	38	26.3	Intergenic		TTGCCCCAGAAGGGCAGTAATAG
chr5	131423385	57	90	63.3	131423384	20	53	37.7	Intergenic		TCTGCCCCACAGGCCAGGAAGGG
chr5	131876425	10	34	29.4	131876424	12	44	27.3	Intergenic		AAGAAAGAGAGAATGGAGGGTCT

chr5	132620120	10	42	23.8	132620119	19	51	37.3	Intergenic		GATGCCCCTCAGGGCAGAAGTGG
chr6	23709579	40	53	75.5	23709578	33	46	71.7	Intergenic		GAAGCCCTACAGGGCAGCAATGG
chr6	50041372	38	51	74.5	50041371	43	58	74.1	Intergenic		TCTGCCCCACATGGCAGTAATGA
chr6	80093919	36	49	73.5	80093918	41	55	74.5	Intergenic		TGAGTTCTCCAATATCCAGTTGG
chr6	85738203	55	59	93.2	85738202	27	31	87.1	Intergenic		ACTGCCCCACAGGGAAGTAATAG
chr6	156371508	26	51	51	156371507	35	60	58.3	Intergenic		CATGCTCCACAGAGCAGCAAAGG
chr7	10462259	13	44	29.5	10462258	13	45	28.9	Intergenic		GTTGCCCCAAAAGGCAGTAATGC
chr7	57716477	33	87	37.9	57716476	39	74	52.7	Intergenic		TGTGCACCACAGAGCAATAAGGG
chr7	123435167	31	65	47.7	123435166	14	48	29.2	Intergenic		ATGCAAGTCCAATATCCAGTAGG
chr8	24931381	32	66	48.5	24931380	21	56	37.5	Intergenic		AGTGCCACACACAGCAGTAAGGG
chr8	41296595	44	45	97.8	41296594	53	54	98.1	Intergenic		TCAGCCCCACAGGTCAGCAATGG
chr8	79592624	27	45	60	79592623	14	34	41.2	Intronic	*ZC2HC1A*	TGTGGCCCACAGAGCAGTAATAG
chr8	134024458	27	46	58.7	134024457	11	30	36.7	Intergenic		ATTACCCCACAGGGCAGCCAAGG
chr8	143699609	26	40	65	143699608	20	34	58.8	Intergenic		CCAGCCCCACCGGGCAGTAGATG
chr9	24439672	11	19	57.9	24439671	35	44	79.5	Intergenic		GGACTCCTCCAATATCCTGTTGG
chr9	78341070	21	43	48.8	78341069	35	57	61.4	Intergenic		TGTTACCCCCAGGGAAGTATAGG
chr9	96637408	15	61	24.6	96637407	39	86	45.3	Intergenic		ACAGCCCCACAGGGCATAAACGG
chr9	104595883	12	31	38.7	104595882	11	30	36.7	Intergenic		TCAGCCCCACAGGGCAGTAAGGG
chr9	111755408	11	48	22.9	111755407	10	47	21.3	Intronic	*CTNNAL1*	CCTGCCCTACAAGACAGTAAGAG
chr9	134609673	54	68	79.4	134609672	51	64	79.7	Intronic	*RAPGEF1*	TTTGCCCCTCAGGGCAGCTAAGG
chr9	134994964	48	60	80	134994963	55	67	82.1	Intergenic		CCTGCCCCACAGGGCAATTATGG
chr10	729165	14	57	24.6	729164	11	54	20.4	Intronic	*DIP2C*	TTCTTTCTTCAATATCCAGTAGG
chr10	43697435	22	47	46.8	43697434	17	43	39.5	Intronic	*RASGEF1A*	AAGGCCCCACAGGGCAGAGTAGG
chr10	71843328	56	61	91.8	71843327	66	73	90.4	Intronic	*H2AFY2*	CATGGCCAGGAAGAGAAGGCTGG
chr10	72286450	61	78	78.2	72286449	41	58	70.7	Intronic	*PALD1*	CAAGCCCCACAGGGCAGACAGGG
chr10	73555691	34	69	49.3	73555690	19	54	35.2	Exonic	*CDH23*	CAGGCCCCACAGGACAGGAAGGG
chr10	73563394	16	41	39	73563393	21	46	45.7	Intronic	*CDH23*	AGTGCCACACAGGGCAGTATTGA
chr10	111569275	34	67	50.7	111569274	17	49	34.7	Intergenic		ATGCAAGTCCAATATCCAGTGGG
chr11	1001396	20	49	40.8	1001395	20	49	40.8	Intronic	*AP2A2*	CCCACCCCACAGGGCAGCAGGGG
chr11	3125346	16	39	41	3125345	24	47	51.1	Intronic	*OSBPL5*	AGCCCCCACAGGGCAGGTAGGGG
chr11	5248215	12	23	52.2	5248214	15	29	51.7	Exonic	*HBB*	CTTGCCCCACAGGGCAGTAACGG
chr11	30888494	28	58	48.3	30888493	16	46	34.8	Intronic	*DCDC5*	CTTCCCCACAGGGCAGAAAGTGG
chr11	59611432	48	54	88.9	59611431	56	62	90.3	Exonic	*GIF*	CGGCCAGATTCATGGCAATCAGG
chr11	76387498	49	58	84.5	76387497	45	54	83.3	Intergenic		CTGCCCCTCAGGGACAGTATGGG
chr11	104908796	13	51	25.5	104908795	13	52	25	Intergenic		ATGCGAGTCCAATATCCAGTAGG
chr11	119259302	30	61	49.2	119259301	28	59	47.5	Intronic	*USP2-AS1*	TCATATCCCCTATATCCAGTGGG
chr11	125807920	15	49	30.6	125807919	15	49	30.6	Intergenic		ATAGCCCCATAGGGCAGAAATAG
chr12	27234755	59	86	68.6	27234754	25	52	48.1	Intronic	*C12orf71*	GATGCCTCACAGGACAGGAAGGG
chr12	40327469	41	45	91.1	40327468	39	43	90.7	Intronic	*SLC2A13*	GCTATGGTTCCTGAACGGCCTGG
chr12	50056756	35	60	58.3	50056755	22	48	45.8	Intronic	*FMNL3*	AAGGCCCCGCAGGGCAGTTTGGG
chr12	66309907	20	46	43.5	66309906	46	72	63.9	Intronic	*HMGA2*	AGTCCCCCACAGAACAGTAAGGG
chr12	93549202	71	72	98.6	93549201	59	60	98.3	Intronic	*LOC643339*	ATTGCCCCACGGGGCAGTGACGG
chr12	114081180	12	46	26.1	114081179	10	44	22.7	Intergenic		CTCCCCCACAGAGCAGTTAATGG

chr12	124803834	54	56	96.4	124803833	57	59	96.6	Intergenic		GCTGCCCCACAGGGCAGCAAAGG
chr13	44886376	54	68	79.4	44886375	81	96	84.4	Intergenic		GGAGCCCCACAGGGCAGAGAGGG
chr13	106995598	12	48	25	106995597	16	52	30.8	Intergenic		CTAGCCCCACAGGGTAGGAAAGG
chr14	36889538	50	52	96.2	36889537	60	62	96.8	Intergenic		GTTATCCCACAGGACAGTGAGGG
chr14	49319039	27	38	71.1	49319038	17	28	60.7	Intergenic		ATTACCCCACAGGACAGAAATGA
chr14	59445901	29	51	56.9	59445900	20	42	47.6	Intergenic		AGTCTTCCCCAATATCCAGTAGG
chr14	89458507	39	59	66.1	89458506	18	38	47.4	Intergenic		GAAACCCCACAGAGCAGTAATGA
chr14	94585327	59	63	93.7	94585326	42	45	93.3	Intergenic		ATGGCCCCACAAGGCAGAAATGG
chr15	29983547	56	71	78.9	29983546	42	58	72.4	Intergenic		GGAGCCCAGCAGCTTTACTGCCC
chr15	34059408	31	58	53.4	34059407	42	70	60	Intronic	*RYR3*	GTTACCACACAGAGCAGTTAAGG
chr15	46598129	57	61	93.4	46598128	66	69	95.7	Intergenic		GTTGCCCCTCAGGACAGTACAGG
chr15	66873249	20	91	22	66873248	25	95	26.3	Intergenic		AGAGCCCCACAGGACAGTCCTGG
chr15	80100573	16	73	21.9	80100572	17	74	23	Intergenic		TGCACTCTCAGATATCCAGTTGG
chr15	86453645	17	58	29.3	86453644	11	43	25.6	Intergenic		ACTGGGATGCCAAAAGAACTCTG
chr15	88488821	17	46	37	88488820	22	51	43.1	Intronic	*NTRK3*	CCTGCCCCACAGGGCAGCCAAGG
chr15	99709337	22	38	57.9	99709336	17	33	51.5	Intronic	*TTC23*	CTGTGCCCCACAGGGAGTGAGGG
chr16	585496	13	49	26.5	585495	22	58	37.9	Intronic	*CAPN15*	TTGTCCCCACAGGGCAGTGGCGG
chr16	49082904	47	54	87	49082903	51	59	86.4	Intergenic		GCAGCCCCACAGGTCAGTGAGGG
chr17	8370253	25	31	80.6	8370252	73	80	91.2	ExoniC	*NDEL1*	TTGCTCCCACAGGGCAGTAAACG
chr17	18167224	13	37	35.1	18167223	13	37	35.1	ExoniC	*SMCR7*	AATGCCCCAAAGGGCAGTTCCGG
chr17	38648014	10	35	28.6	38648013	10	35	28.6	ExoniC	*YES1*	GGTGCAGTCGCTGTTTACTGGCC
chr18	745994	61	62	98.4	745993	41	43	95.3	Intergenic		AAAATACCTCGTTGATTTCCAGG
chr18	6663844	23	46	50	6663843	25	48	52.1	Intronic	*SETBP1*	GTTGCCCCACTGGGGAGAAAAGG
chr18	42330301	30	50	60	42330300	32	52	61.5	Intronic	*PRAM1*	ATAGCCTCACAGGGCAGAGAGGG
chr19	8560462	32	64	50	8560461	24	50	48	Intronic	*PRAM1*	GGGGGTGCATTGCCTTACTGCCC
chr19	17952542	10	45	22.2	17952541	21	56	37.5	ExoniC	*JAK3*	ATGCTAATGTCTACGATTTCTGG
chr19	29880768	48	57	84.2	29880767	26	35	74.3	Intronic	*LOC284395*	CTGTGCCCCACAGGCAGTAGATG
chr19	34262013	32	55	58.2	34262012	16	39	41	Intronic	*CHST8*	CTGCTCCACAGGGCAGGTATGGG
chr19	37539042	38	70	54.3	37539041	24	56	42.9	Intergenic		CTTGCACCACAGAGCACTAAGGG
chr19	50010010	17	42	40.5	50010009	10	36	27.8	Intergenic		ATTGCCCCCCAGGTCAGTAGGGG
chr20	17385713	15	36	41.7	17385712	19	40	47.5	Intronic	*PCSK2*	CACGTTGCCCCACGCAGTATGGG
chr20	36470909	12	34	35.3	36470908	36	58	62.1	Intronic	*CTNNBL1*	TCACCCCACAGGATAGGTAAGGG
chr20	39992928	50	63	79.4	39992927	15	27	55.6	Intronic	*EMILIN3*	AGTGGCCCCCAGGGCAGTGAGGG
chr20	58136220	17	39	43.6	58136219	25	47	53.2	Intergenic		TTTACCCCACAGGGCATTTAAGG
chr21	46331408	15	48	31.2	46331407	12	45	26.7	Intronic	*ITGB2*	CATAGCCAGGAAGAGAAAGCTGG
chr22	17230623	79	86	91.9	17230622	43	49	87.8	Intergenic		TGTGCCCCACAGAGCACTAAGGG
chr22	26043758	23	41	56.1	26043757	14	32	43.8	Intronic	*ADRBK2*	AAAATACCTCATTAATTTCCAGG
chr22	35537395	29	38	76.3	35537394	47	56	83.9	Intergenic		AGTGCCCCACAGGGGAGAAATGG
chrX	224145	11	27	40.7	224144	26	42	61.9	ExoniC	*GTPBP6*	GTGGCCCCGCAGGGCAGACACGG
chrX	75006257	23	59	39	75006256	47	83	56.6	Intergenic		GTGGCCCCACAGGGCAGGAATGG
chrX	122165569	20	65	30.8	122165568	18	63	28.6	Intergenic		TCTGTCTCCCAATATCCAGTCGG
chrX	132429379	38	50	76	132429378	35	48	72.9	Intergenic		GCATCCCCACAGGGCAGTATGTG

HBB Mock-transfected digenome_0.01 X

	Forward strand				Reverse strand						
chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene		DNAsequence
chr1	177593980	31	68	45.6	177593979	52	93	55.9	Intergenic		TCTACCCCACATGGCAGTAATGG
chr4	48091817	31	65	47.7	48091816	23	60	38.3	Exonic	*TXK*	ACTCGTCTCCGATATCCAGT TGG
chr6	23709579	29	69	42	23709578	32	74	43.2	Intergenic		GAAGCCCTACAGGGCAGCAATGG
chr6	50041372	16	60	26.7	50041371	22	64	34.4	Intergenic		TCTGCCCCACATGGCAGTAATGA
chr8	24931381	42	93	45.2	24931380	13	57	22.8	Intergenic		AGTGCCACACACAGCAGTAAGGG
chr8	82872599	10	22	45.5	82872598	10	34	29.4	Intergenic		CACTTTTATTGATTATGCATTGG
chr9	104595883	58	88	65.9	104595882	67	97	69.1	Intergenic		TCAGCCCCACAGGGCAGTAAGGG
chr11	5248215	41	55	74.5	5248214	46	68	67.6	Exonic	*HBB*	CTTGCCCCACAGGGCAGTAACGG
chr11	59611432	36	76	47.4	59611431	44	85	51.8	Exonic	*GIF*	CGGCCAGATTCATGGCAATCAGG
chr12	93549202	53	83	63.9	93549201	46	71	64.8	Intronic	*LOC643339*	ATTGCCCCACGGGGCAGTGACGG
chr12	124803834	66	82	80.5	124803833	57	72	79.2	Intergenic		GCTGCCCCACAGGGCAGCAAAGG
chr14	94585327	74	118	62.7	94585326	44	63	69.8	Intergenic		ATGGCCCCACAAGGCAGAAATGG
chr15	46598129	43	76	56.6	46598128	48	86	55.8	Intergenic		GTTGCCCCTCAGGACAGTACAGG
chr17	8370253	34	42	81	8370252	75	98	76.5	ExoniC	*NDEL1*	TTGCTCCCACAGGGCAGTAACGG
chr18	745994	33	56	58.9	745993	48	79	60.8	ExoniC	*YES1*	AAAATACCTCGTTGATTTCCAGG
chr22	17230623	63	78	80.8	17230622	58	79	73.4	Intergenic		TGTGCCCCACAGAGCACTAAGGG
chrX	75006257	19	45	42.2	75006256	41	67	61.2	Intergenic		GTGGCCCCACAGGGCAGGAATGG

VEGF-A Mock-transfected digenome

		Forward strand				Reverse strand						DNAsequence
	chr.	position	count	depth	%(count/depth)	position	count	depth	%(count/depth)	gene		GGGTGGGGGGAGTTTGCTCCTGG
VEGFA_1	chr01	42740063	14	59	23.7	42740062	19	60	31.7	Intronic	*FOXJ3*	AGTTGAGGGGAGTTTA-TCCTGG
VEGFA_2	chr01	48314379	14	44	31.8	48314378	22	57	38.6	Intronic	*TRABD2B*	GGGCAGGGAAAGTTTG-TCCAGG
VEGFA_3	chr01	99347651	35	66	53	99347650	20	50	40	Intergenic		GGGGAGGGGAAGTTTGCTCCTGG
VEGFA_4	chr01	102122651	11	46	23.9	102122650	12	46	26.1	Intergenic		TGCTGAGGGGAATTTGC-CCAGG
VEGFA_5	chr01	233157354	22	58	37.9	233157353	35	71	49.3	Intronic	*PCNXL2*	GGAGGAGGGGAGTCTGCTCCAGG
VEGFA_6	chr02	66561098	16	29	55.2	66561097	47	68	69.1	Intergenic		GGGTGG-GGCAGTTTG-TCCGGG
VEGFA_7	chr02	118827653	12	52	23.1	118827652	15	50	30	Intergenic		AGATGAGGGGAGTTAG-CCCTGG
VEGFA_8	chr02	157256493	18	53	34	157256492	11	43	25.6	Intergenic		GGGGCAGGGGA-CTTGCTCCAGG
VEGFA_9	chr02	205137461	49	89	55.1	205137460	46	77	59.7	Intergenic		GGCTAGAGGGAGTTTG-CCCTGG
VEGFA_10	chr02	209437600	13	56	23.2	209437599	48	94	51.1	Intergenic		AGGGAGGGAGAATTTGCTCCTGG
VEGFA_11	chr03	8753103	23	60	38.3	8753102	46	81	56.8	Intergenic		TTTTGGAGGGAATTTG-CTCCGG
VEGFA_12	chr03	38316671	26	64	40.6	38316670	17	50	34	Intergenic		AACCTGGGGGGGCTTGCTCCTGG
VEGFA_13	chr03	55562940	28	59	47.5	55562939	18	50	36	Intronic	*SLC22A13*	TATGGGGATGGGGTTGCTCCCGG
VEGFA_14	chr03	97310666	28	54	51.9	97310665	63	96	65.6	Intronic	*EPHA6*	GTGTGGGAAGAGTTTG-TCCTGG
VEGFA_15	chr03	128284321	32	69	46.4	128284320	28	65	43.1	Intergenic		AGGTGGTGGGAGCTTGTTCCTGG
VEGFA_16	chr04	8453803	23	69	33.3	8453802	27	74	36.5	Intronic	*TRMT44*	GAGTGGGTGGAGTTTGCTACAGG
VEGFA_17	chr04	21369324	28	59	47.5	21369323	63	111	56.8	Intronic	*KCNIP4*	TCCATGGGGGAGTTTG-CTCTGG
VEGFA_18	chr04	23116018	16	51	31.4	23116017	17	53	32.1	Intergenic		CAGGGGGAGAGATTTGCTCCAGG
VEGFA_19	chr04	54967137	52	104	50	54967136	15	60	25	Intronic	*GSX2*	GGAGGTGGAAAGTTTGCTCCAGG
VEGFA_20	chr04	65046699	15	47	31.9	65046698	29	60	48.3	Intergenic		GGGTAAGGGAAGTTTG-CTCTGG
VEGFA_21	chr04	65941717	23	51	45.1	65941716	17	43	39.5	Intergenic		GGCTGGTGGGAGTTT-CTCCAGG
VEGFA_22	chr04	157417951	25	66	37.9	157417950	26	70	37.1	Intergenic		TGATGGGGAAAGTTTGC-TCAGG
VEGFA_23	chr04	190326147	10	35	28.6	190326146	10	38	26.3	Intergenic		ACAGTCGCCCCTTTGTTTTGGCC
VEGFA_24	chr05	156390	16	50	32	156389	13	51	25.5	Intronic	*PLEKHG4B*	TGCTCGGGGGAGTTTGCACCAGG
VEGFA_25	chr05	7067159	23	44	52.3	7067158	47	70	67.1	Intergenic		GAGGGTGGGGAGTTTACTCCTGG
VEGFA_26	chr05	32945275	25	55	45.5	32945274	53	89	59.6	Intergenic		GCGTGGGGGGTGTTTGCTCCCGG
VEGFA_27	chr05	56172079	23	68	33.8	56172078	12	56	21.4	Intronic	*MAP3K1*	GGTGGGGGTGGGTTTGCTCCTGG
VEGFA_28	chr05	57030872	22	54	40.7	57030871	26	57	45.6	Intergenic		TCTG-AGGGGAGTTTG-CTCTGG
VEGFA_29	chr05	139263024	19	59	32.2	139263023	36	86	41.9	Intergenic		TTGGGGGGGCAGTTTGCTCCTGG
VEGFA_30	chr05	140642769	17	53	32.1	140642768	22	58	37.9	Intergenic		CAAGGTGGGAGGATTGCTCCAGG
VEGFA_31	chr05	146236270	11	55	20	146236269	26	69	37.7	Intronic	*PPP2R2B*	TCTTTGGGAGAGTTTGCTCCAGG
VEGFA_32	chr06	42229599	51	94	54.3	42229598	41	81	50.6	Intronic	*TRERF1*	GGGGCAAGGGAGTTTG-CTCAGG
On-target	chr06	43737297	28	53	52.8	43737296	18	37	48.6	Exonic	*VEGFA*	GGGTGGGGGGAGTTTGCTCCTGG
VEGFA_34	chr06	50485682	23	64	35.9	50485681	42	88	47.7	Intergenic		ATGTGTGGGGAATTTGCTCCAGG
VEGFA_35	chr06	91365255	40	72	55.6	91365254	16	43	37.2	Intergenic		CCCGGGGGGAAGCTTGCTCCAGG
VEGFA_36	chr06	103251063	14	50	28	103251062	25	60	41.7	Intergenic		TCCATGGGG-GATTTGCTCCAGG
VEGFA_37	chr06	115347691	13	39	33.3	115347690	10	27	37	Intergenic		AACCACAGCAGTGCAGGACATCA
VEGFA_38	chr07	17819097	15	47	31.9	17819096	39	76	51.3	Intergenic		ACAACTGGGGAGTTTGCTCCTGG
VEGFA_39	chr07	31001913	15	46	32.6	31001912	10	41	24.4	Intergenic		TGGGGTGGTGAGTTG-CTCCTGG
VEGFA_40	chr07	32333724	34	56	60.7	32333723	33	61	54.1	Intronic	*PDE1C*	GAAGGGAGGAGGTTTGCTCCTGG

VEGFA_41	chr07	73254136	11	38	28.9	73254135	21	53	39.6	Intronic	*WBSCR27*	GGA-GGGTGGAGTTG-CTCCTGG
VEGFA_42	chr08	74709100	55	100	55	74709099	16	55	29.1	Intronic	*UBE2W*	GG--GGGGTGAGTTTG-TCCTGG
VEGFA_43	chr08	128303251	20	57	35.1	128303250	15	47	31.9	Intergenic		TCTTGGGGAGAGTTTGC-CCAGG
VEGFA_44	chr09	9028824	18	55	32.7	9028823	38	77	49.4	Intronic	*PTPRD*	TGACTGGGGAAGTTTGC-CCAGG
VEGFA_45	chr09	91304357	11	39	28.2	91304356	13	30	43.3	Intergenic		GGATAGTTCCATTATGACTGCCC
VEGFA_46	chr09	93925190	17	65	26.2	93925189	13	59	22	Intergenic		GGGGGTGGGGAGCATGCTCCAGG
VEGFA_47	chr09	122768852	21	62	33.9	122768851	17	58	29.3	Intergenic		TCTGGAGGA-AGTTTGC-CCAGG
VEGFA_48	chr09	123154231	11	43	25.6	123154230	15	49	30.6	Intronic	*CDK5RAP2*	AGGGTGAGGGG-CTTGCTCCAGG
VEGFA_49	chr10	25067928	49	76	64.5	25067927	17	40	42.5	Intergenic		GGGGGGAAGGAGTTTC-TCCTGG
VEGFA_50	chr10	81363268	23	52	44.2	81363267	24	46	52.2	Intergenic		CACTGAGGGGAGTTTGC-CCAGG
VEGFA_51	chr10	99376528	26	73	35.6	99376527	22	71	31	Exonic	*MORN4*	TATGAGGGGGAGTTTGC-CCAGG
VEGFA_52	chr10	132171413	20	52	38.5	132171412	35	61	57.4	Intergenic		CCCTGGGGA-AGTTTGT-CCAGG
VEGFA_53	chr11	17395396	62	87	71.3	17395395	20	30	66.7	Exonic	*NCR3LG1*	GGGGAGGCGGAGTTTG-TCCTGG
VEGFA_54	chr11	57835243	18	49	36.7	57835242	20	55	36.4	Intronic	*OR9Q1*	GAGGTGGGGTGATTTGCTCCAGG
VEGFA_55	chr11	72475898	36	62	58.1	72475897	14	39	35.9	Intronic	*STARD10*	TTCCAGGGGGAGTTTC-TCCGGG
VEGFA_56	chr11	117481208	45	75	60	117481207	11	37	29.7	Intronic	*DSCAML1*	GGGCAAGGGGAGGTTGCTCCTGG
VEGFA_57	chr11	126678277	10	47	21.3	126678276	11	45	24.4	Intronic	*KIRREL3*	GGGGAGGGGGAGTTAG-CCCTGG
VEGFA_58	chr12	1988077	25	49	51	1988076	39	72	54.2	Intronic	*CACNA2D4*	CGGGGGAGGGAGTTTGCTCCTGG
VEGFA_59	chr12	5619395	40	58	69	5619394	15	23	65.2	Intergenic		CGGAGGGGTGAGTTTG-TCCCGG
VEGFA_60	chr12	26641302	20	57	35.1	26641301	20	54	37	Intronic	*ITPR2*	AGTTTGGGGGAGTTTGCCCCAGG
VEGFA_61	chr12	51888011	11	35	31.4	51888010	49	82	59.8	Intronic	*SLC4A8*	AATAGTG--GGAGTTGCTCCTGG
VEGFA_62	chr12	107832636	24	60	40	107832635	35	79	44.3	Intronic	*BTBD11*	TCTTGGGGGGAAGTTGCTCCAGG
VEGFA_63	chr12	131690199	12	53	22.6	131690198	45	93	48.4	Intronic	*LOC116437*	GGGAGGGTGGAGTTTGCTCCTGG
VEGFA_64	chr13	31251013	28	59	47.5	31251012	34	62	54.8	Intergenic		TGTAGAGGGAGTTTTGCTCCCGG
VEGFA_65	chr14	30157649	10	42	23.8	30157648	32	68	47.1	Intronic	*MIR548AI*	TGGGGGCGGGAGTTT-CTCCTGG
VEGFA_66	chr14	61906429	17	51	33.3	61906428	31	71	43.7	Intronic	*PRKCH*	TT---GGGGGAGTTTG-CTCAGG
VEGFA_67	chr15	65637537	112	174	64.4	65637536	54	101	53.5	Intronic	*IGDCC3*	GGATGGAGGGAGTTTGCTCCTGG
VEGFA_68	chr15	67385016	42	103	40.8	67385015	62	137	45.3	Intronic	*SMAD3*	TGGTGGAGGGAGTTTG-TCCAGG
VEGFA_69	chr15	78857354	22	92	23.9	78857353	23	93	24.7	Intergenic		AGTGGTGGGGGACTTGCTCCAGG
VEGFA_70	chr15	84047385	32	107	29.9	84047384	89	179	49.7	Intergenic		GGAGTCAGGGAATTTGCTCCTGG
VEGFA_71	chr15	86453645	12	53	22.6	86453644	16	60	26.7	Intergenic		CAGAGTTCTTTTGGCATCCCAGT
VEGFA_72	chr16	8763213	36	86	41.9	8763212	11	47	23.4	Intergenic		AAGTAAGGGAAGTTTGCTCCTGG
VEGFA_73	chr17	3830416	23	63	36.5	3830415	14	61	23	Intronic	*ATP2A3*	GAGTGAGGGGGAGTTTCTCCAGG
VEGFA_74	chr17	21251093	14	56	25	21251092	14	47	29.8	Intergenic		AGCACAATAAACCAGCGAAATGG
VEGFA_75	chr17	32986325	44	73	60.3	32986324	37	72	51.4	Intergenic		GGGGGTGGGGACTTTGCTCCAGG
VEGFA_76	chr17	39796328	36	62	58.1	39796327	32	58	55.2	Exonic	*KRT42P*	TAGTGGAGGGAGCTTGCTCCTGG
VEGFA_77	chr17	66834243	28	40	70	66834242	43	56	76.8	Intergenic		GGAAGGGGGGAGTTTG-TCCTGG
VEGFA_78	chr17	80625576	41	77	53.2	80625575	40	83	48.2	Intronic	*RAB40B*	TGACGGGGGGAGTTTG-CTCTGG
VEGFA_79	chr18	366714	38	73	52.1	366713	24	54	44.4	Intronic	*COLEC12*	GGGGGCAGGGAGATTGCTCCTGG
VEGFA_80	chr19	1177850	13	61	21.3	1177849	19	68	27.9	Intergenic		AAGTGGGGGCAGTTTGC-CCAGG
VEGFA_81	chr19	8150194	21	76	27.6	8150193	16	69	23.2	Intronic	*FBN3*	GAAACGGGGGAGTTTG-CTCAGG
VEGFA_82	chr20	60265710	18	45	40	60265709	25	52	48.1	Intronic	*CDH4*	GGACGGGGGGAGTTT-CTCCAGG
VEGFA_83	chr22	18454623	12	49	24.5	18454622	23	61	37.7	Intronic	*MICAL3*	GGAAAGGAGGAGCTTGCTCCAGG

VEGFA_84	chr22	37215276	42	70	60	37215275	46	75	61.3	Intronic	*PVALB*	GGGTGGGGGGAGTTTGCCCCAGG
VEGFA_85	chrX	19185601	30	55	54.5	19185600	12	32	37.5	Intergenic		GGGAGGGGAGAGTTTGTTCCAGG
VEGFA_86	chrX	128497221	25	44	56.8	128497220	16	31	51.6	Intergenic		AGGGGTAGGGAGATTGCTCCTGG

Supplementary Table3. Analysis of targeted deep sequencing data.

HBB digenome candidates							
		(-) RGEN			(+) RGEN		
	total_count	mutated_count	Mutation frequency (%)	total_count	mutated_count	Mutation frequency (%)	P-value
On-target	61185	116	0.189588952	63683	50156	78.75885244	< 1E-100
OT1	51349	79	0.15384915	70025	60057	85.7650839	< 1E-100
OT3	183091	25	0.013654412	199889	8710	4.357418367	< 1E-100
HBB_01	17545	11	0.062695925	20839	8	0.038389558	N.A.
HBB_02	38529	12	0.031145371	49256	15	0.030453143	N.A.
HBB_04	41418	0	0	41903	2	0.004772928	0.500261476
HBB_05	38757	191	0.492814201	32199	166	0.515543961	0.67035836
HBB_06	40411	0	0	45257	0	0	1
HBB_07	35167	0	0	47871	0	0	1
HBB_08	57774	2	0.003461765	49075	0	0	N.A.
HBB_09	31317	7	0.022352077	30856	3	0.009722582	N.A.
HBB_10	11367	16	0.140758336	9520	2	0.021008403	N.A.
HBB_11	35323	14	0.039634233	35027	10	0.028549405	N.A.
HBB_12	11264	0	0	11516	0	0	1
HBB_13	46893	0	0	52131	0	0	1
HBB_14	26424	0	0	19528	0	0	1
HBB_15	38642	0	0	36839	0	0	1
HBB_16	22212	0	0	25776	0	0	1
HBB_17	44291	0	0	42975	3	0.006980803	0.119498004
HBB_18	23488	2	0.008514986	24149	0	0	N.A.
HBB_19	36328	2	0.005505395	28245	0	0	N.A.
HBB_20	35373	2	0.00565403	32759	2	0.006105192	1
HBB_21	63236	17	0.026883421	57756	17	0.029434171	0.864341049
HBB_22	56268	9	0.015994882	40123	6	0.014954016	N.A.
HBB_23	47389	7	0.01477136	44136	2	0.004531448	N.A.
HBB_24	48404	0	0	39675	0	0	1
HBB_25	53097	15	0.028250184	46620	2	0.004290004	N.A.
HBB_26	48381	0	0	37433	2	0.005342879	0.190383818
HBB_27	58663	5	0.00852326	54185	2	0.003691058	N.A.
HBB_28	42552	0	0	44982	0	0	1
HBB_29	30589	2	0.006538298	26955	0	0	N.A.
HBB_31	39360	0	0	34571	3	0.008677794	0.102308954

HBB_32	45002	0	0	46637	0	0	1
HBB_33	27230	0	0	27135	0	0	1
HBB_34	39031	0	0	37097	2	0.005391272	0.237587823
HBB_35	30568	2	0.00654279	27475	5	0.018198362	0.267147879
HBB_36	43347	0	0	39370	0	0	1
HBB_37	13314	23	0.172750488	13333	48	0.360009	0.004020371
HBB_38	49874	2	0.004010105	40049	3	0.007490824	0.661619772
HBB_39	38204	0	0	35319	0	0	1
HBB_40	23714	5	0.021084591	21595	0	0	N.A.
HBB_41	37428	2	0.005343593	31453	0	0	N.A.
HBB_42	36966	180	0.486933939	29249	128	0.437621799	N.A.
HBB_43	10295	8	0.077707625	27159	4	0.014728083	N.A.
HBB_44	12362	11	0.088982365	15008	23	0.153251599	0.167530855
HBB_45	42614	2	0.004693293	54249	0	0	N.A.
HBB_46	30496	3	0.009837356	32407	4	0.012343012	1
HBB_47	38919	4	0.010277756	34030	9	0.026447252	0.162267768
HBB_48	34028	6	0.01763	32237	53	0.16441	2.75E-11
HBB_50	37923	9	0.0237323	29751	6	0.020167389	N.A.
HBB_51	38925	2	0.005138086	49948	3	0.006006246	1
HBB_52	34425	2	0.005809731	29078	4	0.013756104	0.422497082
HBB_53	42987	0	0	45261	0	0	1
HBB_54	13262	0	0	13808	2	0.014484357	0.500436898
HBB_55	42889	15	0.034974003	41578	12	0.028861417	0.70200081
HBB_56	57333	2	0.003488392	53918	0	0	N.A.
HBB_57	18031	0	0	18682	0	0	1
HBB_58	130558	165	0.126380612	123651	123	0.099473518	N.A.
HBB_59	47878	0	0	47178	4	0.008478528	0.060716085
HBB_60	50407	24	0.047612435	50099	20	0.039920957	N.A.
HBB_61	21746	4	0.018394187	18781	2	0.01064906	N.A.
HBB_62	21888	0	0	16390	0	0	1
HBB_63	13798	4	0.028989709	17985	5	0.027800945	N.A.
HBB_64	25070	3	0.011966494	24554	2	0.008145312	N.A.
HBB_65	30863	0	0	31518	0	0	1
HBB_66	8342	0	0	7516	0	0	1
HBB_67	45962	7	0.015229973	33089	2	0.006044305	N.A.
HBB_68	40133	5	0.012458575	35452	2	0.005641431	N.A.
HBB_69	53289	0	0	42614	2	0.004693293	0.19754891

HBB_70	46369	11	0.023722746	37864	8	0.021128248	N.A.
HBB_71	7635	0	0	6803	3	0.044098192	0.104712911
HBB_72	7266	4	0.055050922	5960	0	0	N.A.
HBB_73	13156	0	0	10015	0	0	1
HBB_74	43783	11	0.025123907	35731	10	0.027986902	0.829372012
HBB_75	37874	2	0.005280667	23828	843	3.537854625	3.35E-15

VEGFA digenome candidates							
		(-) RGEN			(+) RGEN		
	total_count	mutated_count	Mutation frequency (%)	total_count	mutated_count	Mutation frequency (%)	P value
On-target	43222	86	0.198972745	14583	12731	87.30028115	< 1E-100
VEGF-A_1	43307	0	0	45090	0	0	1
VEGF-A_2	55144	12	0.021761207	33350	4	0.011994003	N.A.
VEGF-A_3	57317	10	0.017446831	33818	2339	6.916435035	2.87E-77
VEGF-A_4	6347	18	0.28359855	7126	14	0.196463654	N.A.
VEGF-A_5	46752	2	0.004277892	30672	0	0	N.A.
VEGF-A_6	44540	2	0.004490346	36846	0	0	N.A.
VEGF-A_7	50098	7	0.013972614	42630	5	0.011728829	N.A.
VEGF-A_8	45834	254	0.554173757	39704	208	0.523876687	N.A.
VEGF-A_9	42680	5	0.011715089	32185	2	0.006214075	N.A.
VEGF-A_10	42677	0	0	42681	0	0	1
VEGF-A_11	49828	0	0	42190	0	0	1
VEGF-A_12	39035	9	0.023056232	35110	10	0.028481914	0.654519017
VEGF-A_13	47309	2	0.004227525	37076	0	0	N.A.
VEGF-A_14	54625	3	0.005491991	45189	2	0.004425856	N.A.
VEGF-A_15	51509	0	0	28017	3	0.010707785	0.043753736
VEGF-A_16	41983	0	0	43092	2	0.004641233	0.50032982
VEGF-A_17	46421	0	0	45701	0	0	1
VEGF-A_18	47456	2	0.00421443	31671	3	0.009472388	0.395525157
VEGF-A_19	46579	2	0.00429378	39428	6	0.015217612	0.15412147
VEGF-A_20	55505	2	0.003603279	45194	2	0.004425366	1
VEGF-A_21	46280	4	0.008643042	44409	2	0.004503592	N.A.
VEGF-A_22	54559	4	0.007331513	42955	3	0.006984053	N.A.
VEGF-A_24	47263	3	0.00634746	38821	7	0.018031478	0.126059184
VEGF-A_25	42334	0	0	44165	2	0.004528473	0.500469242
VEGF-A_26	37644	9	0.023908193	44227	611	1.381509033	3.43E-15
VEGF-A_27	39697	0	0	31928	8	0.025056377	0.001560794
VEGF-A_28	50934	0	0	48338	0	0	1
VEGF-A_29	25603	2	0.007811585	14115	2	0.014169323	0.619324961
VEGF-A_30	51100	5	0.009784736	46049	4	0.008686399	N.A.
VEGF-A_31	44173	9	0.020374437	17307	5	0.028890044	0.555608012
VEGF-A_32	13226	0	0	14911	2	0.013412917	0.50203072
VEGF-A_34	47562	10	0.021025188	23104	4	0.017313019	N.A.
VEGF-A_35	50947	6	0.011776945	43821	38	0.086716415	4.92E-08

VEGF-A_36	51258	0	0	46352	0	0	1
VEGF-A_38	50240	0	0	29482	0	0	1
VEGF-A_39	43424	0	0	35266	0	0	1
VEGF-A_40	39187	0	0	34473	0	0	1
VEGF-A_41	51483	0	0	34379	0	0	1
VEGF-A_42	317	0	0	290	0	0	1
VEGF-A_43	48353	58	0.119951192	36714	56	0.15253037	0.21878281
VEGF-A_44	43134	48	0.111281124	35305	39	0.11046594	N.A.
VEGF-A_46	37261	0	0	34672	0	0	1
VEGF-A_47	45855	35	0.076327554	33753	33	0.097769087	0.327251419
VEGF-A_48	7398	0	0	33435	6	0.017945267	0.599985158
VEGF-A_49	36650	8	0.021828104	39908	12	0.030069159	0.511183743
VEGF-A_50	39932	55	0.137734148	22536	45	0.199680511	0.075921633
VEGF-A_51	33982	25	0.07356836	32315	31	0.095930682	0.350767187
VEGF-A_52	36453	89	0.244150001	33177	43	0.129607861	N.A.
VEGF-A_53	33959	0	0	36816	2	0.005432421	0.5010596
VEGF-A_54	38077	4	0.010505029	37175	6	0.016139879	0.544166687
VEGF-A_55	36334	0	0	39939	0	0	1
VEGF-A_56	33699	0	0	37569	2	0.005323538	0.501719931
VEGF-A_57	39853	2	0.005018443	38163	6	0.015722034	0.1709386
VEGF-A_58	22468	2	0.008901549	33868	137	0.404511633	1.71E-15
VEGF-A_59	40194	0	0	40365	0	0	1
VEGF-A_60	39259	38	0.096793092	40871	63	0.154143525	0.027959609
VEGF-A_61	39519	0	0	42299	2	0.004728244	0.500822623
VEGF-A_62	47334	8	0.01690117	28951	10	0.034541121	0.146474042
VEGF-A_63	40944	0	0	39545	519	1.312428878	2.48E-15
VEGF-A_64	48264	0	0	36917	2	0.005417558	0.187933743
VEGF-A_65	46615	0	0	41429	0	0	1
VEGF-A_66	48055	0	0	40256	0	0	1
VEGF-A_67	48810	188	0.385166974	25832	20506	79.38216166	< 1E-100
VEGF-A_68	36976	13	0.03515794	8389	10	0.119203719	0.005049085
VEGF-A_69	41602	5	0.012018653	37286	4	0.010727887	N.A.
VEGF-A_70	51812	0	0	39835	0	0	1
VEGF-A_72	45175	0	0	40952	0	0	1
VEGF-A_73	46212	6	0.012983641	39639	8	0.020182144	0.434506827
VEGF-A_75	42069	4	0.009508189	37076	2	0.005394325	N.A.
VEGF-A_76	32525	9	0.027671022	31506	2417	7.671554625	2.91E-15

VEGF-A_77	21939	2	0.009116186	26671	4	0.014997563	0.6963108
VEGF-A_78	45273	2	0.004417644	39922	6	0.015029307	0.158349614
VEGF-A_79	35841	0	0	26544	0	0	1
VEGF-A_80	52315	39	0.074548409	41427	44	0.106210925	0.121392217
VEGF-A_81	43875	0	0	36742	0	0	1
VEGF-A_82	43893	2	0.004556535	34491	3	0.008697921	0.660050746
VEGF-A_83	35349	0	0	23998	2	0.008334028	0.163607168
VEGF-A_84	36680	47	0.128135224	27281	1079	3.955133609	4.03E-15
VEGF-A_85	34973	4	0.011437395	29565	4	0.013529511	1
VEGF-A_86	34877	0	0	30964	0	0	1

HBB Mismatch up to 3							
	(-) RGEN			(+) RGEN			
	total_count	mutated_count	Mutation frequency (%)	total_count	mutated_count	Mutation frequency (%)	P value
OT4	50307	5	0.009938975	58445	2	0.003422021	N.A.
OT9	35157	0	0	47053	0	0	1
OT10	45727	0	0	61046	0	0	1
OT11	44502	0	0	58593	0	0	1
OT12	35997	4	0.011112037	48166	7	0.014533073	0.767670948
OT14	34171	3	0.008779374	42340	9	0.021256495	0.246841747

VEGF-A Mismatch up to 3							
	(-) RGEN			(+) RGEN			
	total_count	mutated_count	Mutation frequency (%)	total_count	mutated_count	Mutation frequency (%)	P value
VEGF-A_OT03	57010	0	0	61607	0	0	1
VEGF-A_OT06	61309	84	0.137010879	65247	102	0.156329027	0.379269439
VEGF-A_OT07	63963	7	0.010943827	67125	8	0.011918063	1
VEGF-A_OT08	56214	2	0.003557833	59896	4	0.006678242	0.688456067
VEGF-A_OT09	57336	13	0.022673364	62473	8	0.012805532	N.A.
VEGF-A_OT10	51528	2	0.003881385	36987	4	0.010814611	0.243748528
VEGF-A_OT12	61336	6	0.009782183	65702	3	0.004566071	N.A.
VEGF-A_OT13	53919	22	0.040801944	41558	11	0.026469031	0.292869959
VEGF-A_OT15	56961	2	0.003511174	59522	9	0.01512046	0.066123051
VEGF-A_OT16							
VEGF-A_OT18	64644	3	0.004640802	69039	11	0.015933023	0.059217714
VEGF-A_OT19	71178	5	0.007024642	76936	10	0.012997816	0.3072655
VEGF-A_OT20	55669	0	0	61025	5	0.008193363	0.063846948
VEGF-A_OT21	39669	49	0.123522146	55785	91	0.163126288	0.122768926
VEGF-A_OT23	55309	12	0.021696288	57357	17	0.029638928	0.460378093
VEGF-A_OT24	6682	8	0.119724633	7569	6	0.079270709	N.A.
VEGF-A_OT25	4023	2	0.049714144	3067	0	0	0.509309244
VEGF-A_OT26	23792	10	0.042030935	18946	10	0.05278159	0.65675112
VEGF-A_OT27	22463	10	0.044517651	19518	18	0.092222564	0.086247528
VEGF-A_OT28	28530	11	0.038555906	25474	13	0.051032425	0.543400482
VEGF-A_OT29	25731	38	0.147681785	24868	64	0.257358855	0.007174025
VEGF-A_OT30	65133	0	0	66834	5	0.007481222	0.062631062
VEGF-A_OT31	62083	52	0.083758839	59841	58	0.096923514	0.447403843
VEGF-A_OT32	67222	10	0.014876082	75368	18	0.023882815	0.259060834
VEGF-A_OT33	56981	1086	1.905898457	60706	1266	2.085461075	0.016322604
VEGF-A_OT34	57978	5	0.008623961	57522	5	0.008692326	1
VEGF-A_OT35	57101	6	0.010507697	59452	9	0.015138263	0.608335335
VEGF-A_OT37	52103	6	0.011515652	50266	12	0.023872996	0.160595325

Supplementary Table 4. List of primers.

	HBB_deep sequencing_1st PCR	
	Forward (5' to 3')	Reverse (5' to 3')
On-target	GCCTATCAGAAACCCAAGAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCAACCTCAAACAGACACCA
HBB_POT1	GCTTCAAGCCCCAATACAGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGACTGACAGCTCGGTCTGC
HBB_POT2	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCATCATGAGAATGGCAAG	TGTCATCTCGATGGCATCTATT
HBB_POT3	GGGTTCCATGAGGAAAACAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGTGAAAACTGGTTACCACATC
HBB_POT4	AGACTCCACAGCCAGGCTAC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTGTGGCTGGAGGGCTATAA
HBB_POT5	CACCCCAGTGCTCTCTCTTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCTGGGTTGGTGAAAACATC
HBB_POT6	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGTGAAAGTAGCTGGGAGGA	TTGGGAAAATACAGCCGTTC
HBB_POT7	GGGGAAATTGTTGGAAATGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGCAGGAAACAGGAAGCTGA
HBB_POT8	ATTAGCAATCCGCAGTGAGC	TAACTCTGCCCCCACTTCTG
HBB_POT9	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCTGAGAACATCAAGACGTGAA	TGCCATTGTGAGGACTTCAG
HBB_POT10	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGTAAGCCATACTCCAAGCA	GATTACAGGCCTGAGCCACT
HBB_POT11	GAGGCAGAGCTGTCCAAGAC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGGGCCTGAAAAATCAAAAG
HBB_POT12	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGAGGGGAAAGGCAAAAATA	CCAGACTCAGCCACACTGAA
HBB_POT13	GCCTGACCTAAGGTGATCCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGCAACTAGGCTTGAAATATTGA
HBB_POT14	ATGTGGCCTCCCTAACAAGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGCTGTGCTTTGGAAGTTCA
HBB_POT15	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTGGAGACACTGGCATTTG	TGAGCAGTGAGCTCAGACCA
HBB_POT16	GTGTAGGCAGGGCGAATAAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACTGTGGTCATCAGGCTTT
HBB_POT17	CACCAGTGTGGTAAGCAGGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCAGGCTGGTCTCAAACTCC
HBB_POT18	TGTTTTGATTGTTTTCCAAAAAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATCTTCCCTGACACCCAGTG
HBB_POT19	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCACACCTCCCTTTGACTTC	GGGTCCATGATAGCAACCTG
HBB_POT20	GCACGAGACCAAAACTCTCC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCCAGCATCATCCACCACTA
HBB_POT21	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTCTGCCCACCAGATTAAGG	CATGGGTAATTTATTGCATGTAGC
HBB_POT22	GGACTCTTGGGACCCATTTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACCTTTTCCACGACAAGCAC
HBB_POT23	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCATGTGCCCTGATCTCTTCA	AAACTCATTTTGCCCCACAC
HBB_POT24	CAGTTCATTCCCCATGTATTGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCCCTGCATAGAGAACATGG
HBB_POT25	GAAGAAGCACATAACTGCATTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGTTTGGTGTGTGCTTTTCG
HBB_POT26	GGAATATCACTCCGGGAACC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGCACATGTGAAGAACTGGA
HBB_POT27	ATGTGAGGTTTGGGACTTGG	TCCTAGTGGGGAATGAGGTG
HBB_POT28	TTTGTGCAAGCCAAGCAATA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACACATTCCCCTTTGCTGTC
HBB_POT29	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGACAAAACCTCACACAA	GCATCTTTCCTGCCTCAGAC
HBB_POT30	TGCTTACACAGCAAACTGACC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGGTTTGGAATTGCGTACA
HBB_POT31	CATACCCTTTCCCGTTCTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATTTCCAGGCTATGCTTCCA
HBB_POT32	CAGGGAGGCTCTAACCAGTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCAGGGGTAGAATCAGAACG
HBB_POT33	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCAGAAGAAGAAGCCTGTG	CAGCAAGTGGTAGGCATGG
HBB_POT34	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGAGCCACCATCAGTAGGC	ACACTGTGGCTCTGGCATC
HBB_POT35	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGCTGGAAGCTGCTAGTTGG	GGGCAGAGGTGTGGAAAGTA
HBB_POT36	CCTGCTGCACCCTGAACTA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCCTACTCTCGCTCCCTGTC
HBB_POT37	GTGGAAGCACCCCACTCTAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTCCCAAAGTGCTGGGATTA
HBB_POT38	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAGGCAAGTCCCTACCACCT	AACCCACCTCTTGCATCAGT
HBB_POT39	GCAAGTGCTTGGGACTGAC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCTCCTTCCTGAACAAGCTC

HBB_POT40	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAACTGACTCCCCAATGCAAC	GCTACATTTGGATGCCCAAC
HBB_POT41	GAAGGACGCTGAGTTGGAAT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTTCCTCTTCTCAGCCGTTC
HBB_POT42	GTTTTGGCAGCAGCTATGGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGAAGACCCTGTCCCAGTGA
HBB_POT43	GGGATGCTGTACACTGCAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGCAAGTCCCTTCCACCTAT
HBB_POT44	CATTCAGACATAGAGTCAACTGTGC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGCTCTGATAGCTGGAAGGA
HBB_POT45	CTTGTTTCCCTCAGCATTCC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGTGCAAGCCACCAGAAAAT
HBB_POT46	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGTCTAAATTACCTAGCAGTTCCA	AGTTGCTCAGGCCTCAAATC
HBB_POT47	AGCCTCATAGCTCAGGTCCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAGGGGGAAAGACAGAGAGAA
HBB_POT48	GGAATGGGTGACCATCAGTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAACCAGCTGCCTCAGACTT
HBB_POT49	ATGGCTGTTATTCAGGGAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGCTACCACGGTGACAGTAACA
HBB_POT50	CCCACACAGGTTTTCTCCTC	TGCCCAGGAATCTGTGTTTTC
HBB_POT51	CCACAGACAGCTTTACGGAGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCATCCTCAGAGGCAGAGTG
HBB_POT52	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGATTCCCAAACACCATGACC	GGGACAAAGATTCTTCCCTCA
HBB_POT53	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGTTTATGCCCAAGGGGAGT	TCACCTCTCCCCCAATATGA
HBB_POT54	TCCCACTGGACAGAGCTTTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGCCATAGAGAGCAGAGCA
HBB_POT55	ACAAGAAAATGGGGCCCTTA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAAGGGAGACAGGGTATCCA
HBB_POT56	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAACAGCCAAAAGCAGACAGC	TTGCCCAACTCAGATTACCA
HBB_POT57	GGGCAGAACAGTTTCAAAGG	AGCAGCCCTCTGCCTTAGTT
HBB_POT58	CAAGCGTGACCTAGAGCAGA	CAGTTTATGCCTGCCACCTC
HBB_POT59	GGGATCCTCCTAATGCTGGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAGCCTTCCTCTGTCCCTTC
HBB_POT60	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCAGAACTGAGGCCCAGAGAG	CCTAATGTGTCTCCCCTCCA
HBB_POT61	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTACAGCCTGCGAGGAATA	GGCTAGGCACTCACACACTG
HBB_POT62	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGAGTGTCTGCTCTGGGTTG	CTGGAAAGCTCTTCCTGCTG
HBB_POT63	GGAATAAGCACCTGGGTGAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCCAAACCTATCCCAGTCCA
HBB_POT64	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCTTGCTTTCAGGGACAGAA	GTCTTGAACTCCTGGCCTCA
HBB_POT65	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCAGTTCTGGAGGTTGGGAAG	TAACACCCTAACCCCCAGTG
HBB_POT66	AGATGGGTTTTTGCCATGC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTACCCTCCACTCCCAAATCC
HBB_POT67	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGGGCAATGACAGATCCAT	CTCCAGCCTTGTCCACATTT
HBB_POT68	AATCCACAGTGGCCAGAACT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCTACCCATGCAGAAAATG
HBB_POT69	CCATGCTGTTAGAGAGGGAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGTTTTCATCCTACTGATGCTTCT
HBB_POT70	TTGGGGTTTTAATGGCAGAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACGAGGAGCTGGCCTTAAA
HBB_POT71	CATGGGCTGATTTAGCTGGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCTGTTTTTGACCCTGGAAA
HBB_POT72	ACTTGGACCCCCTCTAGCTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTACCCTGGACCTTCCCTTC
HBB_POT73	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGTTGCTTGCTCCATAAT	CCCTCCAGCTGAGGTGTG
HBB_POT74	CAAGGCTGACCCTCTCTGAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACGTAGCAGCTCAGGTGAA
HBB_POT75	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAGACTGGTGGGAAGCAAGA	CTCCTGACCTCAGGTGATCC
HBB_POT76	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTGCCTTCCTCAAACACTC	ACTGGCACAATCACAGGTCA
HBB_POT77	TTGTGTAACAGCCACTCACCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTGGCAAAAGTGTTTGGAT

	HBB_deep sequencing_2nd PCR	
	Forward (5' to 3')	Reverse (5' to 3')
On-target	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGTCTTGTAACCTTGATACCAACC	
HBB_POT1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGACTCCTTCCCCCAGAAC	

Nature Methods: doi:10.1038/nmeth.3284

HBB_POT2		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCTGGAAGAGGAAGGGGATT
HBB_POT3	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCAGCAAAACAAGATCCAA	
HBB_POT4	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGTTCAAGTTGAGCTCTG	
HBB_POT5	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGCCTAAGAAGTTGGGAACC	
HBB_POT6		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGAGAAATTGGCCAAAACAA
HBB_POT7	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCTATGGAGGGACTTTGCAG	
HBB_POT8	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGAACATCTGGGAGCTGTGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACCAGGGCCCTTCATACACT
HBB_POT9		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACAAGGCAGTCAATCCAAGC
HBB_POT10		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCAGCCTGGGAATACAGATT
HBB_POT11	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCAGCATGACCTGGATGTGAG	
HBB_POT12		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCAGGACAAGAGCTCAGGAT
HBB_POT13	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTTTGCCTCCCAAAGTGCTA	
HBB_POT14	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACCATGGACCCTGACAAATG	
HBB_POT15		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGTGCACTCCAAGAATCAGC
HBB_POT16	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACCTTGCCCATACTTGCCTA	
HBB_POT17	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATCCTCCCCCAAAAGATGTC	
HBB_POT18	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCAAGCATTAGGCCTTCTT	
HBB_POT19		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGGCCGAGGTTTCTCTACTG
HBB_POT20	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCCACACTGATCTCCAGGT	
HBB_POT21		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGCATGTAGCTGGGATTTG
HBB_POT22	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGACTACAATGCCCTCAACC	
HBB_POT23		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGAAGACCCAGGAGGCTGAT
HBB_POT24	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGTGTAAGCTGAGGCGACCTT	
HBB_POT25	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAAGATGCAGAGATTCACAAATGA	
HBB_POT26	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGAGGACACAGGTCACAAT	
HBB_POT27	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGCCTTGGCAATGAGTTTAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGTGGATTCCGAAGAAAACA
HBB_POT28	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCGCTGAGACACTGACAAAC	
HBB_POT29		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCTTCCTCTGACCTGGGTTT
HBB_POT30	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTTACTTCCCCACGTCCAG	
HBB_POT31	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAAAGGGGAAGATCCCAGAG	
HBB_POT32	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGTTCCCCATTCCACTTCTC	
HBB_POT33		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGACCTCAAACATGCACTGAAAG
HBB_POT34		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTGCTGTCTCTCACCCAGTG
HBB_POT35		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAACATCCCCTCCATCTTCCT
HBB_POT36	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGTCACTTCCCACCTCATCTC	
HBB_POT37	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGAAACTTGGCTTCAGGAAA	
HBB_POT38		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTAAGGCCTGGAGTCAAAGGA
HBB_POT39	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGAGGCTACAGCTGCAGAAA	
HBB_POT40		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATTTCTGGAGGCTGGGAAGT
HBB_POT41	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGTCTCACCGTTGTTGTCG	
HBB_POT42	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCTGGTTTGTTTCAGGGAGA	
HBB_POT43		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGCAAGTCCCTTCCACCTAT
HBB_POT44	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCACTGGTTTGAAATACCACCT	

HBB_POT45	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTTGTTGTCTCCCACTGGT	
HBB_POT46		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTTGGCCAGGAATCTTTGAT
HBB_POT47	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGAGCCTGCAGGAAGCTAAC	
HBB_POT48	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGGAGGTGAGAGTCCAGTCG	
HBB_POT49	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTGTGTGGGATGCTGAGAG	
HBB_POT50	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTTCCCTAGACCTGCCTCCT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAAGGTTGGAGCTAGGCCTTC
HBB_POT51	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCATGTGCAATGGGAAGAAAA	
HBB_POT52		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGATCAGGAAGGAATGTGGA
HBB_POT53		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTGGTCCTTCCAATTTGGTG
HBB_POT54	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGTGGTATTGGGCTTGCAGAT	
HBB_POT55	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGGAGCTTGGAAGCCAATTC	
HBB_POT56		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGACCTTTCCCAAGATTGC
HBB_POT57	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTGATTTCCACCAAGCACT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAGCTCATGCACTGTGTGAA
HBB_POT58	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGTCACCTCTGGACAGAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCTCATTCTCCCAGAACAG
HBB_POT59	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGGCATCTCTTTCCTTCTC	
HBB_POT60		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGAACCCCTGTGTTGTGACT
HBB_POT61		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACACACTGAGAGGCAGCAT
HBB_POT62		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGACTCATCCCGCACTGTCTT
HBB_POT63	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTCAAAATACTGCCCCAAGA	
HBB_POT64		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTCCCAAAGTGCTGGGATTA
HBB_POT65		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTATTAGGAGGTGGGGCCTTT
HBB_POT66	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTGGAACTCCTGACCTCAA	
HBB_POT67		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTGCACTGGCTTCCTCTTTC
HBB_POT68	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGGGTCCTTTCCCTGTGACT	
HBB_POT69	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACAACATTTGGGGAGCTTTG	
HBB_POT70	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTGGGAGAGGTGTACCTGGA	
HBB_POT71	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGTGGGCCATATTTTGTGACC	
HBB_POT72	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCACTCAGGCTGCAGTAGCAC	
HBB_POT73		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAGCTTGCTGCTTCTCTGC
HBB_POT74	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCACTGTGGTTTTGTCTTCAGG	
HBB_POT75		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTCCCAAAGTGCTGGGATTA
HBB_POT76		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCCTTTCTGGAGCAGGAGTC
HBB_POT77	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGTGGTAGATGAGGATGA	

	VEGFA_deep sequencing_ 1st PCR	
	Forward (5' to 3')	Reverse (5' to 3')
VEGFA_POT1	GCATTGATTCATGTTTCATTCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGGATTTGGTACCAGACTTGG
VEGFA_POT2	GAACCCCCAGAGTGACACAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGGACACATGGTCAAGGATT
VEGFA_POT3	TGCCTACTCCAGGGTTTCTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGGCATCTCTGCCTTCATTG
VEGFA_POT4	AGCTCTCAGCAGATGGATGG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACACAAGTGGCTGGACATC
VEGFA_POT5	GATCACACCACTGCACTCCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCATGCCCTCCACTCTGTTTT
VEGFA_POT6	GCCACAGGAGATATTTGTCG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGCTGGATGCAACACTGAG
VEGFA_POT7	TCATATCTGTCTGGAGCCTTTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCCCAGTGAGTTCTCCAGATG
VEGFA_POT8	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAGGGTTCAGAAGGCATCAA	CCAGATAACCCCTTGCAGAT
VEGFA_POT9	CCTATGTGACTATTGCTGGCTA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTTGCTAATCTGGCGAGGTC
VEGFA_POT10	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTGGGCAACAGAGTGAGAT	TGTCGTGCATTTTCCAAAGA
VEGFA_POT11	GAACAACTTTTGGCATTTAGCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACGGCTACGTCCTCATCCT
VEGFA_POT12	TGGCCCAGTGCAACTTCT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTAGGGAGCTTTCCAGCTT
VEGFA_POT13	TGTGGGGTCTGCTCTATGAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGTCAGCTCTGGTTTCTGCT
VEGFA_POT14	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTTCATCTGAGTGAGTTTAGGATCT	GAGTGTCAGAACGAAATAACAGTG
VEGFA_POT15	CATGGGCAATCCTAAATCCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGATCCACGCAAAGGAAACAT
VEGFA_POT16	TGGGGAAACCGAACAATTTA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTACGCATCAAAAGGACCACA
VEGFA_POT17	TGAAGTATGTTCATCATTCCAGTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGCAAATCCTTCCCAGAGAT
VEGFA_POT18	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTGGCTGCCACATTAGATCA	TCTGCCCCAGAAGAAAACAC
VEGFA_POT19	AGCACCACGCACCTGTCT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGTAAAACGCACCAGGCTGA
VEGFA_POT20	TGAGGTATGTCAGGAGTTCTGC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAACAACAACAACAACAACAAAAA
VEGFA_POT21	CACAAGTTTAAAAACACATGTCTTAGG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACTCTCCCAAGGCCAAAGTC
VEGFA_POT22	AAGGTACAGCTGCCTCTGTTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTGGGTTCCAGCAAGTTTTC
VEGFA_POT23	ATCCTCCAGACCCCAGAATG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCAAAAGTCCAAGTCCAAA
VEGFA_POT24	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCACTGCTTGTGTCTCTCA	AGCTGGCTCCTTGATCTTTG
VEGFA_POT25	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAACATGTGCACCCACCATC	TGAAGGTACAGTCTGTGAGCTCTG
VEGFA_POT26	CCATCTCTCTTGAGGAGATTTACA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCAGATGCTTCCAGAGCAAA
VEGFA_POT27	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTAGGGCTTCTCAGCCTCA	GGAGGAAGCCTACAGACTGCT
VEGFA_POT28	AAAGTGGGACTTCAAGATTTAATTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCGAGTTTCAAAGTTGGGGAGT
VEGFA_POT29	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCTCCACATTTTCCTCAGC	TGTCTGGGCATCTCTGTTGA
VEGFA_POT30	TTCATCATATTAACAAAAGAGCAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTCTTCTTCCTGCCTCAAACTT
VEGFA_POT31	CTGTCTTGGGTTCTCCCTTG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACCGTGGCTCTCTGTCTGTC
VEGFA_POT32	CCCACCTACATGCTTCCACT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGTCACATGGGGGTCAGAGT
On-target	TCCAGATGGCACATTGTCAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACACGTCCTCACTCTCGAA
VEGFA_POT34	TCTGCTGTCTACCAGTAGTTAGGG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAGAAGGATGTGTGCAGGTT
VEGFA_POT35	TCCCTATCCAGGCTGATCTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGTCATTTGTCAAGGGTTCTG
VEGFA_POT36	TTGAAATCAAGAGAATATCCAGCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGAGATGATTTAAACTATACGGGACA
VEGFA_POT37	GGAAAAAGGGAACCTTTGGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGCCAATCCCCATTACTTTC
VEGFA_POT38	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCAATGAATTGGATTGCTT	AACTGTTCATTTCATCTAAATCAGGA
VEGFA_POT39	ACAGTTAGAGCAGGGTTTCTCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCGAGTGGTTCCTAACCTGGA
VEGFA_POT40	CACACCCCCAGTGTATGCAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTCCTTGGGTTGTACCAGA

VEGFA_POT41	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCAGGACCAAAGCAAAAACC	CAGCGTCACACACAGCCTA
VEGFA_POT42	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCATCGCCATCCTTTTTCTA	GGCCATTATCTTGTTACAAATGC
VEGFA_POT43	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGCATGCCACTAGGAGACTG	GGTATTGGTGAGGGGGTTG
VEGFA_POT44	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTGGCTAGGGTGCAGTTCT	TTGGACAACGCAGCTCTACA
VEGFA_POT45	TGTGTGAATGTGTTGGCTAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCACCTTTTGAAGAGGACCA
VEGFA_POT46	CTTCCCTCCTGCCTTCCTAC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAGGGAGGACTTGGAGGTAGG
VEGFA_POT47	CACCTCCTTGGAGGCTTATTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTGCTCTCATGAAGCCAACA
VEGFA_POT48	TCCCTTTAGACCCAGAGCAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCATTAGGCCAGACCAAATCC
VEGFA_POT49	ATATGGGGTCTCACCACGTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGACCACTGTGGAGTCCAAT
VEGFA_POT50	TGCCTTATCCTAAGGGCAGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCACAACCCCTATCCTGCAAC
VEGFA_POT51	GGCTGCAACTTACCAAAACC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGTGGGGTAGGTGGAGCTAT
VEGFA_POT52	CCTCTCTACCTCCAGGGTCA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGATGACTGGGGAAGTGCT
VEGFA_POT53	CACAGGCCTTTTTAGTCATGC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTCTGGCTTCAGAGGGTATTG
VEGFA_POT54	GAAGGCCAGTATTGGGATTGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTAATGCCTCATCCAGCAAGTT
VEGFA_POT55	GGTAGGGCTGAGTCTCTGGA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCTGGCCTGTTTTCTCAAAT
VEGFA_POT56	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGGTAGAAGGGTGGTGCAGA	GGGATAAAAGTGCAGGGTGT
VEGFA_POT57	ATGACCTGTTTTTGGCAAGC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTAGCCCTGCAGTAAGCCTGT
VEGFA_POT58	TCATAGTTCGTGGTGGGAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCTTGTGTCTTTCCTTCCA
VEGFA_POT59	GGCTTGGCAGTGGTTAAGAG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCGCAGTGAGCAGTTACGAAG
VEGFA_POT60	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAATTTCCAGATCAAGCAGAACT	AAGGCTTCATAAGACACTCTGTG
VEGFA_POT61	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGCTTTCACTCATGGACAG	CCATTCAAACAAAGAATAATCAGC
VEGFA_POT62	TCAGGTTCTTGGAGCCATTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTATTGGCACAAGCAGGAGTG
VEGFA_POT63	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGCATCAGGAGTAGCTCAG	GCACCTGCAATGTCAGAGG
VEGFA_POT64	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCCTGGAGTCATTTCCAAG	GGGCTTGATGAGGACAGAGA
VEGFA_POT65	AACATCAGCTGACAGCAACTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGAATAAAAGGGATCATGGTAGG
VEGFA_POT66	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCAGGTCGTGAGAGAAGAC	TTTCTTGCCACCTTCACTCC
VEGFA_POT67	CTGGTTTTTGGTTTGGGAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTCAGCCTCCCAAAGTTCTG
VEGFA_POT68	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGTCCCAGCAGTCTGAATTTTG	CAGCAACCCCATGATTTGAT
VEGFA_POT69	GGGATGGCTTGAGTGAGTGT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAAGCAGAGGGACAGATTGC
VEGFA_POT70	TGCTCCATTTCCCATTTTTC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCGGCATGAATGCAACAATAG
VEGFA_POT71	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGAAATGGAGCAGCAGGTT	CAAACAGTCTGCCAAGCAAG
VEGFA_POT72	CCAGCTGCAGAATGGAAGTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCATCTCAAAAACAACAGCAACA
VEGFA_POT73	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTGCATGCTGAGTGTCAAC	CACGGAAAAGCCTGTGTCTC
VEGFA_POT74	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGAGTGTCTGCTCTGGGTTG	CTGGAAAGCTCTTCCTGCTG
VEGFA_POT75	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTCCAGAGCAGCCTGAGAT	TGGGAGATAGGATCACAGAGC
VEGFA_POT76	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAGGGCAAAACAGGAGAACA	CCCTCTCCATGAAACTTTGC
VEGFA_POT77	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTAGCCATTGGGTCAGCTCT	TGTGTTCCTTGGGGTTTCAT
VEGFA_POT78	TCCAGAGGCTCTTTCTGTGG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCTGTCTGAGCCTCATCACG
VEGFA_POT79	CAGGCATGAGGGTTTTGTTT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTCTCCCAGGACATCCATA
VEGFA_POT80	GAGGAAACTGAGGCACGAAC	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAAATCCCCGCATCTGACTA
VEGFA_POT81	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGGTGCACACGTACTGGTT	GGCACCTCTGCCTACAGGA
VEGFA_POT82	GGAAGGAGTGTGGACCCAAT	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGCTATGCCATCACCAAACT
VEGFA_POT83	CCTAAGACAGAACATCGGAAGG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTGGCCTTGTGTGGAGT

VEGFA_POT84	CCTCTGGGTCCTCTCTGATG	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATCTCCCCTGTCCGTAGTGA
VEGFA_POT85	GAGATGCAGGGATTGGAAAA	GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTCCAGTGGAAGTGGGAAGA
VEGFA_POT86	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGAAGCTAGCCACCACTCCT	TCGAAGATTGCTCCATACCA
	VEGF-A deep sequencing_2nd PCR	
	Forward (5' to 3')	Reverse (5' to 3')
VEGFA_POT1	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCGGTATATCCTCCACTGAAACA	
VEGFA_POT2	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATTCTCAGCTTGCCCATGAC	
VEGFA_POT3	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTGTTGTGGGAGTTGTCCTG	
VEGFA_POT4	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATGGAGTGGGAAGGTGGTTT	
VEGFA_POT5	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCGAATGTGTGGGTAGGACA	
VEGFA_POT6	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGACAATAAGTGGCCTGTG	
VEGFA_POT7	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGAGCCTTTGTTTGACTGA	
VEGFA_POT8		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGATTTGCAGCTTGCTCTTCA
VEGFA_POT9	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGATTTGCAAAATGGGGTAA	
VEGFA_POT10		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGGTATTCACTGGGCAAATG
VEGFA_POT11	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAACCCATCACCTGCCATTA	
VEGFA_POT12	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGACTCGCCTACGGTTT	
VEGFA_POT13	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCACCCACTCAGATGCCAGTA	
VEGFA_POT14		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCTAAGGAGGGGAGTCACTG
VEGFA_POT15	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACTGGTGCAGGTCTCCAGTC	
VEGFA_POT16	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGTGGCCTGAAGTCACTGAT	
VEGFA_POT17	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCATGCAACTGTGTCAAAC	
VEGFA_POT18		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAGCTCCGGATGAAATTCTG
VEGFA_POT19	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGATTCCACTGCCTCACCAT	
VEGFA_POT20	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCCCAAGGTGTGAAACATA	
VEGFA_POT21	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGGGTAGGCCAATCCTAATG	
VEGFA_POT22	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGAAGCAGTTTTGTTCTGG	
VEGFA_POT23	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCTACCCCTTGCATCAACAT	
VEGFA_POT24		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGTGGCTGTCAGAATGGAGGT
VEGFA_POT25		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCTCTGAAAATACAGCTGGAAA
VEGFA_POT26	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGCAAAGCTAAGCAGAGATGC	
VEGFA_POT27		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATTCTGAATTGGGGGCAGTT
VEGFA_POT28	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCAAGAAGAAAAACAATCCATGA	
VEGFA_POT29		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTCCTCAGAGGGTGCTGTCT
VEGFA_POT30	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAGGCACAGTGGCTCACACTT	
VEGFA_POT31	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGTTCAGATCCAGACTCCA	
VEGFA_POT32	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCACCAACGAGGTCTCTCTC	
On-target	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAAGCAACTCCAGTCCCAAA	
VEGFA_POT34	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGACTTTGTTTTCAATGGCTTC	
VEGFA_POT35	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGTGTTTTGCAAAGCTGGAC	
VEGFA_POT36	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGTACTCTCTTGATGCTTGCACT	

VEGFA_POT37	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTTCTGTCGGGTGAATGCTT	
VEGFA_POT38		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAAGGTAACATTTGGGCAAGA
VEGFA_POT39	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGTTTCTCAGCCTTGGTCT	
VEGFA_POT40	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGCAGCCAATTCAATCAGAC	
VEGFA_POT41		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTAACATCCCAGCCACCAAC
VEGFA_POT42		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACCACCTTTTGTCAGCCTGT
VEGFA_POT43		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGAATGGGTTGGAGGTAGGA
VEGFA_POT44		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCATTTTCATTCCTTGCTT
VEGFA_POT45	ACACTCTTTCCCTACACGACGCTCTTCCGATCTAAAGGGGTATTCAGTTTTTCCA	
VEGFA_POT46	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTCCCCTTCTCCTCACTTG	
VEGFA_POT47	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCAGGGTCTTTGCACTTAC	
VEGFA_POT48	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGACCTGACTCCTTGGGATGA	
VEGFA_POT49	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTGGGCTCAAGCAATTCACT	
VEGFA_POT50	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGAAATGGAGTGGGAAGGTGA	
VEGFA_POT51	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCCCTCAAAGGTCATGTTGT	
VEGFA_POT52	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGGAGGAAGTGACGATGTGT	
VEGFA_POT53	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCTGAAAGTCCCACTCCTT	
VEGFA_POT54	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCCACATACAGCAGGAATGC	
VEGFA_POT55	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTATTAGGCCCTGGCTGAGTG	
VEGFA_POT56		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGAGGTCCATGCTGAAGATCC
VEGFA_POT57	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGTGCAGCTTTCAAGGAGTC	
VEGFA_POT58	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCTCAGCACCTGCACTTCTTG	
VEGFA_POT59	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGAGCACCAGAACCAAACAG	
VEGFA_POT60		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTTGCCCACAGAGAAAATTGC
VEGFA_POT61		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCAATGACAAGCTCCTGATTTTT
VEGFA_POT62	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCAAAGTTTGCGCTGAAGATG	
VEGFA_POT63		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGCCACAGTCGTGTCATCTTG
VEGFA_POT64		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCGATAAACAGAGGGGACTG
VEGFA_POT65	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTCTCTGGGGTACCACCATTC	
VEGFA_POT66		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCCCTCTTTCCTTCCAACCAT
VEGFA_POT67	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCAGCAGACCCACTGAGTCAA	
VEGFA_POT68		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTACAGCCCTACCAGTCCTGTG
VEGFA_POT69	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGGTCCACAACACAGGTCTCC	
VEGFA_POT70	ACACTCTTTCCCTACACGACGCTCTTCCGATCTACTACCTCCCTCTGCCAGGT	
VEGFA_POT71		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCTGCTGGGATAAGGGGTGTA
VEGFA_POT72	ACACTCTTTCCCTACACGACGCTCTTCCGATCTCCACCTCTCACAATCAAGCA	
VEGFA_POT73		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGATTCCCCAGGCCTAAAGAG
VEGFA_POT74		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGACTCATCCCGCACTGTCTT
VEGFA_POT75		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTCAGGTCAAAGGAAGCTCCAG
VEGFA_POT76		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTGCGTCAACCAGAAACACTC
VEGFA_POT77		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTTCATCTAAATAAACCCTGTGGAAAG
VEGFA_POT78	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCATCCTCCTCTGTCTCCTG	
VEGFA_POT79	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTTTCCCTAAGCAAAGGAGCA	

VEGFA_POT80	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATCTCTGCCACATCCACCTC	
VEGFA_POT81		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTATGGCTCAGGCTACACTGCT
VEGFA_POT82	ACACTCTTTCCCTACACGACGCTCTTCCGATCTTGCTGCATGTCTCTGTTCCT	
VEGFA_POT83	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCCCTTCAGGTGGTAATGAA	
VEGFA_POT84	ACACTCTTTCCCTACACGACGCTCTTCCGATCTGCATCACCAGAGTCCACAGA	
VEGFA_POT85	ACACTCTTTCCCTACACGACGCTCTTCCGATCTATTTCTCTGCACCCATGGTC	
VEGFA_POT86		GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGGTGTAGATGCAGGGGTATGA

qPCR		
	Forward (5' to 3')	Reverse (5' to 3')
HBB On-target	TTGGTCTCCTTAAACCTGTCTTG	CATGGTGCATCTGACTCCTG
HBB_OT-1	AAGGGGAAGATCCCAGAGAA	CCAACTCCCAAATTGAAAGC
HBB_OT-3	CTTCCCTAGACCTGCCTCCT	AAGGTTGGAGCTAGGCCTTC
HBB_OT-7	ACTCACTCCCAGGAGGAAAG	CTTCCCGTATCTCCCTCCAC
HBB_OT-11	GCTCTTGATAAATTGTTTGCCTCT	TGGACAAGCATTATGCCAAG

Supplementary Table 5. Indel frequencies measured by targeted deep sequencing.

HBB on-target and validated off-target sites

HAP1 cells

	Indel frequency			P-value	
	(-) RGEN	(+) RGEN gX$_{19}$	(+) RGEN ggX$_{20}$	(-) RGEN vs. (+) RGEN gX$_{19}$	(-) RGEN vs. (+) RGEN ggX$_{20}$
On-target	0.225%	33.142%	37.799%	2.34E-15	0.643
OT1	0.385%	85.541%	1.343%	1.79E-03	1
OT3	0.009%	3.143%	0.026%	3.06E-15	0.176
HBB _48	0.012%	0.088%	0.013%	< 1E-100	2.73E-15
HBB _75	0.006%	2.292%	0.009%	< 1E-100	< 1E-100

K562 cells

	Indel frequency			P-value	
	(-) RGEN	(+) RGEN gX$_{19}$	(+) RGEN ggX$_{20}$	(-) RGEN vs. (+) RGEN gX$_{19}$	(-) RGEN vs. (+) RGEN ggX$_{20}$
On-target	0.525%	41.548%	23.111%	1.88E-15	N.A.
OT1	0.701%	49.691%	0.767%	0.218	N.A.
OT3	0.012%	0.700%	0.009%	2.80E-15	N.A.
HBB _48	0.008%	0.026%	0.005%	< 1E-100	0.236
HBB _75	0.010%	0.322%	0.010%	< 1E-100	< 1E-100

VEGF-A on-target and validated off-target sites

HAP1 cells

	Indel frequency			P-value	
	(-) RGEN	(+) RGEN GX$_{19}$	(+) RGEN ggX$_{20}$	(-) RGEN vs. (+) RGEN GX$_{19}$	(-) RGEN vs. (+) RGEN ggX$_{20}$
On-target	0.055%	42.688%	32.411%	1.14E-37	6.60E-13
VEGF-A _03	0.031%	45.501%	0.151%	< 1E-100	2.90E-15
VEGF-A _26	0.015%	5.430%	0.015%	< 1E-100	< 1E-100
VEGF-A _35	0.013%	0.035%	0.021%	< 1E-100	0.507
VEGF-A _58	0.015%	18.633%	0.031%	< 1E-100	3.66E-02
VEGF-A _63	0.016%	18.383%	0.021%	2.33E-04	0.166
VEGF-A _67	0.080%	52.792%	5.456%	< 1E-100	1
VEGF-A _76	0.096%	45.392%	0.387%	< 1E-100	1.55E-15
VEGF-A _84	0.168%	3.265%	0.360%	< 1E-100	< 1E-100

K562 cells

	Indel frequency			P-value	
	(-) RGEN	(+) RGEN GX$_{19}$	(+) RGEN ggX$_{20}$	(-) RGEN vs. (+) RGEN GX$_{19}$	(-) RGEN vs. (+) RGEN ggX$_{20}$
On-target	0.077%	49.829%	4.810%	1.94E-15	1.31E-04
VEGF-A _03	0.027%	14.910%	0.011%	< 1E-100	N.A.
VEGF-A _26	0.000%	0.627%	0.008%	< 1E-100	3.96E-15
VEGF-A _35	0.011%	0.016%	0.010%	3.04E-90	N.A.
VEGF-A _58	0.000%	7.864%	0.008%	4.42E-15	0.578
VEGF-A _63	0.109%	14.741%	0.011%	0.714	N.A.
VEGF-A _67	0.093%	48.483%	2.824%	6.33E-16	0.268
VEGF-A _76	0.001%	8.070%	0.160%	7.15E-60	N.A.
VEGF-A _84	0.067%	1.292%	0.168%	< 1E-100	2.38E-15

Supplementary Table 6.Specificity ratio calculated by dividing indel frequencies

	Specificity ration (on/off)					
	HAP1			K562		
	gX19	ggX20	ggX20/gX19	gX19	ggX20	ggX20/gX19
OT1	0.39	28	72	0.84	30	36
OT3	11	1400	130	59	2700	45
HBB_48	380	2900	7.6	1600	4900	3
HBB_75	14	4100	290	130	2300	18

	Specificity ration (on/off)					
	HAP1			K562		
	GX19	ggX20	ggX20/GX19	GX19	ggX20	ggX20/GX19
VEGF-A_03	0.94	210	230	3.3	430	130
VEGF-A_26	7.9	2100	270	79	590	7.5
VEGF-A_35	1200	1500	1.3	3000	460	0.15
VEGF-A_58	2.3	1000	460	6.3	580	91
VEGF-A_63	2.3	1500	660	3.4	440	130
VEGF-A_67	0.81	5.9	7.3	1	1.7	1.7
VEGF-A_76	0.94	84	89	6.2	30	4.8
VEGF-A_84	13	90	6.9	39	29	0.74

Supplementary Note 1

HAP1 is an immortalized cell line derived from KBM7, a leukemia cell line. Unlike most other immortalized human cancer cell lines, HAP1 is nearly haploid; each chromosome is present in only a single copy except for a duplicated 30 mega-base pair (Mbp) region in Chromosome 15. Haploid cells facilitate genome analysis because sequencing depth is doubled, compared to diploid cells, and a filter can be used to remove heterozygous variants. We isolated 5 different gene knockout (KO) HAP1 cell lines in each of which a single kinase gene was disrupted by an RGEN. Genomic DNA isolated from these cells and wild-type cells was subjected to WGS via Illumina HiSeq X 10. To test the reproducibility of WGS, genomic DNA isolated from wild-type cells and the *ABL1* gene KO cells was sequenced twice. Thus, a total of 8 independent genomic DNA samples were sequenced.

We applied bioinformatics filters to discard indels that were listed in a public database, heterozygous indels that were accompanied by corresponding wild-type alleles, and those that were also called in other KO or wild-type genomes. As a result, 2,026 to 3,250 indels that were unique in each genome sequence were obtained. We note that even the wild-type genome sequence determined in duplicate yielded 2,226 or 2,968 indels that were not present in KO genome sequences and that the two (wild-type and *ABL1* KO) sets of duplicate WGS data yielded thousands of indels that were unique in each sequencing analysis. These results suggest that both WGS and variant calling are incomplete and that most indels identified using Isaac are false positives.

Supplementary Note 2

Hap1 genomic DNA was digested using Cas9 protein pre-incubated with the *HBB*-specific sgRNA at variable concentrations (0.03 to 300nM). We then used quantitative PCR to measure DNA cleavage at these sites. Both the *HBB* on-target and OT1 sites were cleaved almost completely even at a very low RGEN concentration (Fig. 2a). By contrast, the OT3 site was cleaved completely only at high RGEN concentrations. The other two sites, OT7 and OT12, were cleaved poorly even at the highest concentration.

Next, we transfected this RGEN into HAP1 cells and measured mutation frequencies using deep sequencing. As expected, the *HBB* RGEN was highly active at both the on-target and OT1 off-target sites, producing indels at frequencies of 78% and 85%, respectively (Fig. 2b). Off-target indels were also induced at the OT3 site with a frequency of 4.3% (Fig. 2b). At the other two potential off-target sites that were poorly cleaved *in vitro*, no indels were detected.