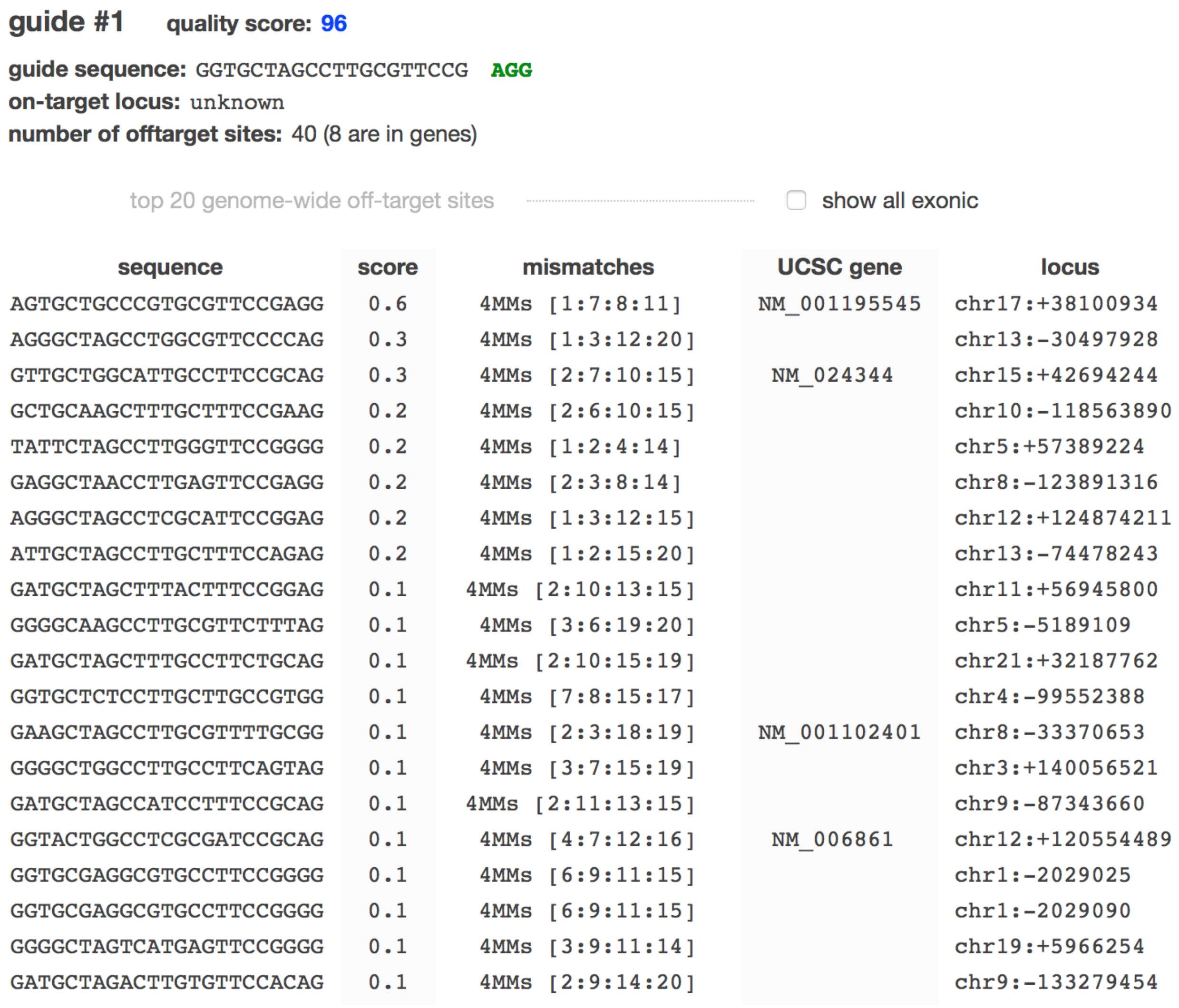
SUPPLEMENTAL FIGURES



guide #1 **quality score:** 96

guide sequence: GGTGCTAGCCTTGCGTTCCG AGG

on-target locus: unknown

number of offtarget sites: 40 (8 are in genes)

sequence	score	mismatches	UCSC gene	locus
AGTGCTGCCCGTGCGTTCCGAGG	0.6	4MMs [1:7:8:11]	NM_001195545	chr17:+38100934
AGGGCTAGCCTGGCGTTCCCCAG	0.3	4MMs [1:3:12:20]		chr13:-30497928
GTTGCTGGCATTGCCTTCCGCAG	0.3	4MMs [2:7:10:15]	NM_024344	chr15:+42694244
GCTGCAAGCTTTGCTTTCCGAAG	0.2	4MMs [2:6:10:15]		chr10:-118563890
TATTCTAGCCTTGGGTTCCGGGG	0.2	4MMs [1:2:4:14]		chr5:+57389224
GAGGCTAACCTTGAGTTCCGAGG	0.2	4MMs [2:3:8:14]		chr8:-123891316
AGGGCTAGCCTCGCATTCCGGAG	0.2	4MMs [1:3:12:15]		chr12:+124874211
ATTGCTAGCCTTGCTTTCCAGAG	0.2	4MMs [1:2:15:20]		chr13:-74478243
GATGCTAGCTTTACTTTCCGGAG	0.1	4MMs [2:10:13:15]		chr11:+56945800
GGGGCAAGCCTTGCGTTCTTTAG	0.1	4MMs [3:6:19:20]		chr5:-5189109
GATGCTAGCTTTGCCTTCTGCAG	0.1	4MMs [2:10:15:19]		chr21:+32187762
GGTGCTCTCCTTGCTTGCCGTGG	0.1	4MMs [7:8:15:17]		chr4:-99552388
GAAGCTAGCCTTGCGTTTTGCGG	0.1	4MMs [2:3:18:19]	NM_001102401	chr8:-33370653
GGGGCTGGCCTTGCCTTCAGTAG	0.1	4MMs [3:7:15:19]		chr3:+140056521
GATGCTAGCCATCCTTTCCGCAG	0.1	4MMs [2:11:13:15]		chr9:-87343660
GGTACTGGCCTCGCGATCCGCAG	0.1	4MMs [4:7:12:16]	NM_006861	chr12:+120554489
GGTGCGAGGCGTGCCTTCCGGGG	0.1	4MMs [6:9:11:15]		chr1:-2029025
GGTGCGAGGCGTGCCTTCCGGGG	0.1	4MMs [6:9:11:15]		chr1:-2029090
GGGGCTAGTCATGAGTTCCGGGG	0.1	4MMs [3:9:11:14]		chr19:+5966254
GATGCTAGACTTGTGTTCCACAG	0.1	4MMs [2:9:14:20]		chr9:-133279454

Supplemental Figure I. Output from CRISPR Design server.

Processing input tag: GGTGCTAGCCTTGCGTTCCGNGG
Search in target database: hg38
Length: 23
searching for no indel hits allowing up to 2 mismatch(es) ... Done
searching for 1b-deletion hits allowing up to 1 mismatch(es) .... Done
searching for 1b-insertion hits allowing up to 1 mismatch(es) .... Done

View raw search results in txt file

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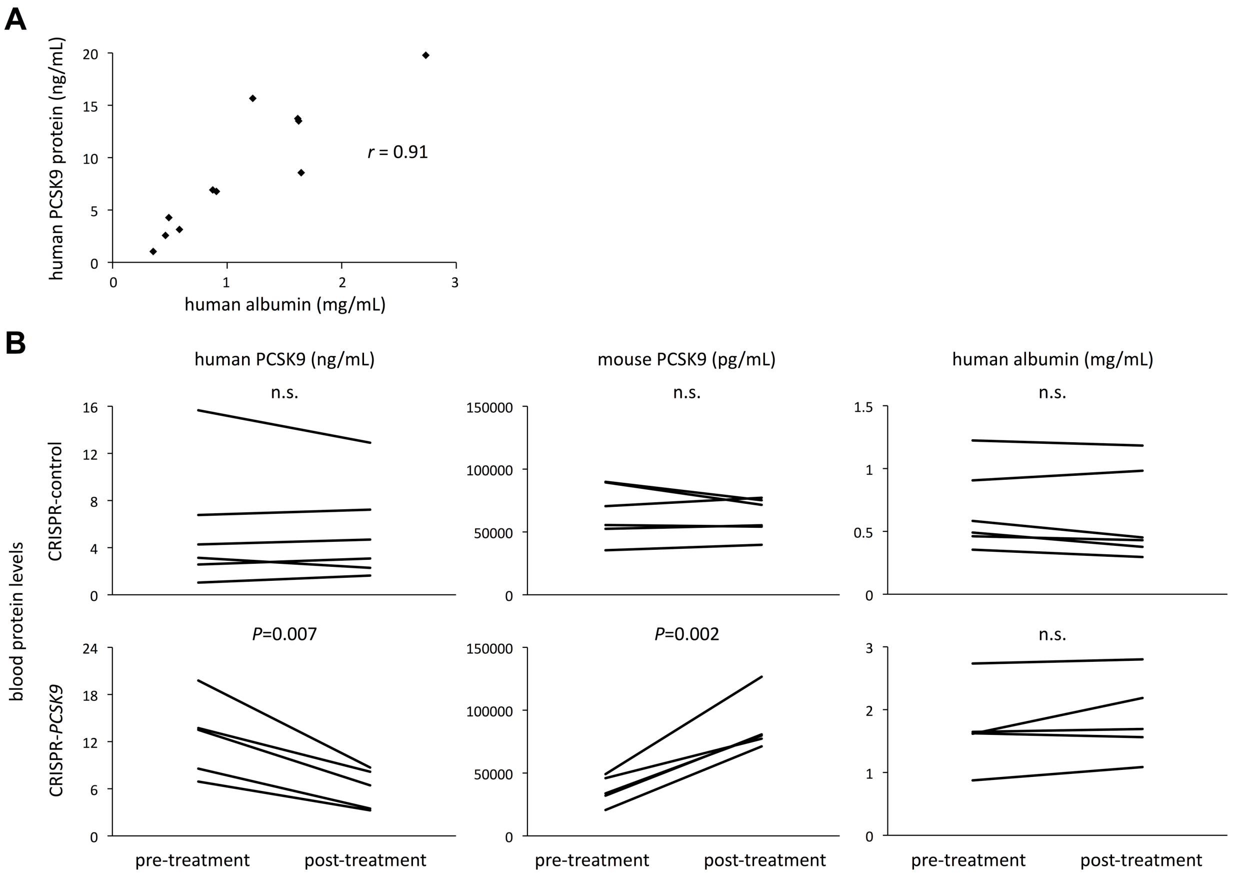
Result	Query type	Mismatch	Hit ends in RG	chr position	Strand	Cut site	Score
GGTGCTAGCCTTGCGTTCCGAGG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	No indel	0	Yes	Chr1:55039960-55039982	+	55039976	0
^GTGCTAGCCTTGCGTTCCGAGG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del 19, or Del 20	0	Yes	Chr1:55039961-55039982	+	55039976	0.63
GT^GCTAGCCTTGCGTTCCGAGG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del 18	1	Yes	Chr1:55039961-55039982	+	55039976	0.79
GGTGC^AGCCTTGCTTTCCGAGG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del 15	1	Yes	Chr5:168269438-168269459	-	168269444	2.62
GGTGCTAGCCTTGCGTTCC^GAG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del 1	1	Yes	Chr1:55039960-55039981	+	55039975	26.51
GGTGCTAGCCTTGCGTTCCG^AG -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del PAM 3	1	Yes	Chr1:55039960-55039981	+	55039975	40.51
GGTGCTAGCCTTGCGTTCCGA^G -- hit GGTGCTAGCCTTGCGTTCCGNGG -- query	Del PAM 1, or Del PAM 2	0	Yes	Chr1:55039960-55039981	+	55039975	20.51
TGGTGCTAGCCTTGCGTTCCGAGG -- hit GNGTGCTAGCCTTGCGTTCCGNGG -- query	Ins 19	1	Yes	Chr1:55039959-55039982	+	55039976	0.95
TGGTGCTAGCCTTGCGTTCCGAGG -- hit GGNTGCTAGCCTTGCGTTCCGNGG -- query	Ins 18	1	Yes	Chr1:55039959-55039982	+	55039976	0.97
GGTGCTAGCCTTGCGTTCCGAGGA -- hit GGTGCTAGCCTTGCGTTCCGNNGG -- query	Ins PAM 2, or Ins PAM 3	1	No	Chr1:55039960-55039983	+	55039977	40.7
GGTGCTAGCCTTGCGTTCCGAGGA -- hit GGTGCTAGCCTTGCGTTCCGNGNG -- query	Ins PAM 1	1	No	Chr1:55039960-55039983	+	55039977	40.7

Supplemental Figure II. Output from COSMID server.



Supplemental Figure III. Pre-treatment and post-treatment human PCSK9 protein, mouse PCSK9 protein, and human albumin levels in the blood. **A**, Pre-treatment human PCSK9 and albumin levels in individual mice are highly correlated. *r* is the Pearson correlation coefficient. **B**, Pre-treatment and post-treatment levels in individual mice in the two treatment groups. *P* values were calculated with the paired t-test.