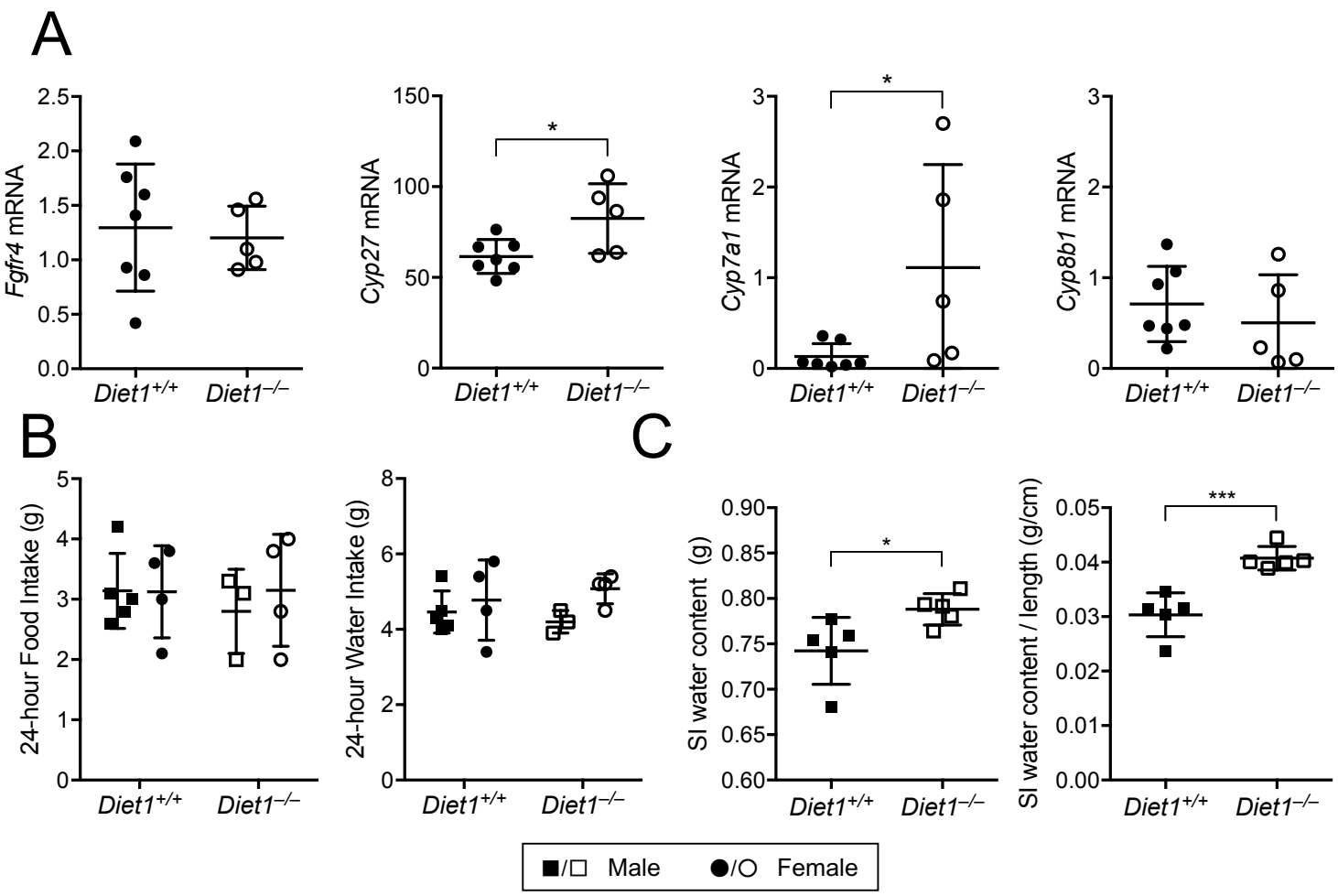
Supplemental Figure 1



***Diet1*$^{-/-}$ congenic mouse characterization (continued)**

(A) Hepatic expression of *Cyp27* and *Cyp7a1* is elevated in *Diet1*$^{-/-}$ mice, while *Cyp8b1* and *Fgfr4* expression is similar to *Diet1*$^{+/+}$ mice. Data from female mice fed on atherogenic diet for 3 weeks. N = 5–7 mice/genotype.

(B) Normal food and water intake in *Diet1*$^{-/-}$ mice compared to *Diet1*$^{+/+}$ mice assessed during single housing in metabolic cages.

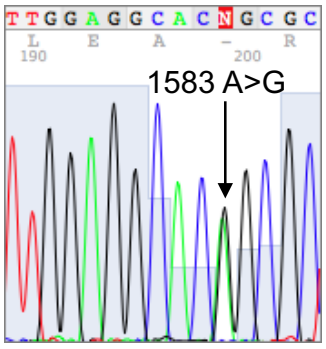
(C) Following a 16-hour fast, small intestine (SI) was excised and contents extruded. *Diet1*$^{-/-}$ mice exhibit increased water content when expressed as absolute amount and when normalized to SI length after 6 weeks on atherogenic diet. N = 4–5 mice per group. Statistical analyses via student's *t*-test. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Supplemental Figure 2

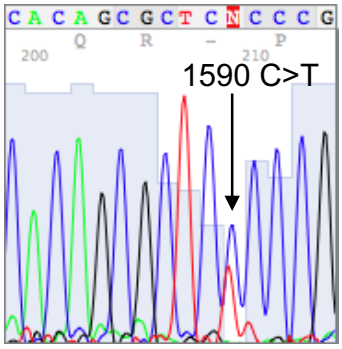
A

	Exon	rs number	Nucleotide	Amino Acid	Class of SNV	n (alleles) out of 88 Cases (44)	n (alleles) out of 88 Controls (44)	Study MAF
B	12	rs539101752	1583 A>G	Q528R	NS	0	1	0.0114
C	12	Unknown	1590 C>T	S530S	S	0	1	0.0114
D	12	rs767131780	1591 C>G	P531A	NS	1	0	0.0114
E	14	rs776910464	1921 T>C	S641P	NS	0	1	0.0114
F	18	Unknown	2678 C>G	T893R	NS	1	0	0.0114
G	21	Unknown	3277 G>A	E1093K	NS	1	0	0.0114
H	22	rs757582955	3534delG	F1179Sfs*4	Del	0	1	0.0114

B



C



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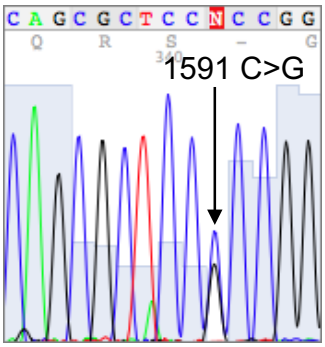

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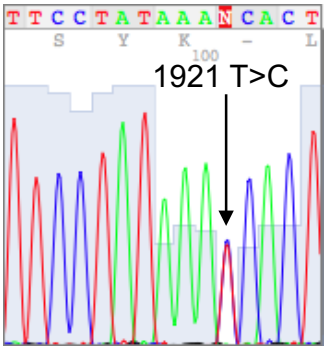

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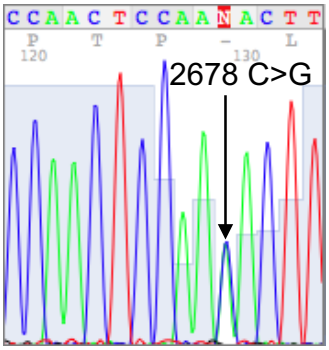

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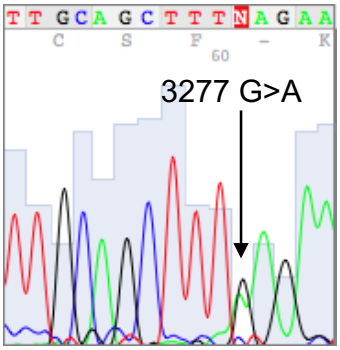
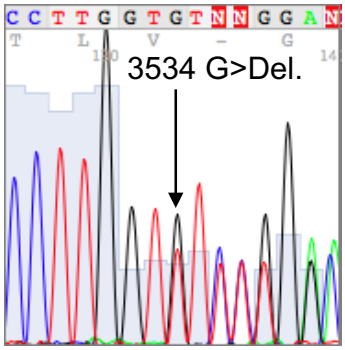


H



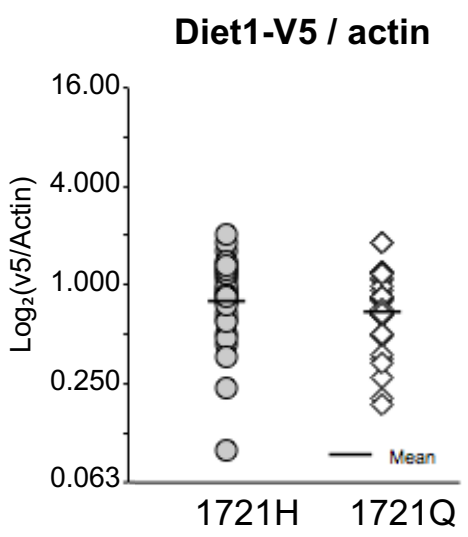
Rare and Novel single nucleotide variants in the coding region of *DIET1*

(A) Each rare or novel single nucleotide variant is listed individually, and sorted by nucleotide position, with the major allele on the left and minor allele on the right. Affected amino acid is listed, as well as the number of minor alleles that appear within the case or control groups. Minor allele frequency (MAF) within the study sample is also listed.

(B-H) Sequence traces for each novel variant listed from (A). Affected nucleotide marked with arrow. Chromatograms imaged with 4peaks (http://nucleobytes.com/index.php/4peaks).

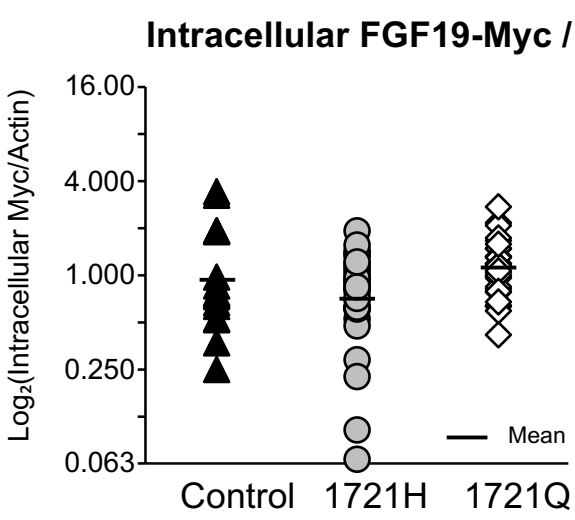
Supplemental Figure 3

A



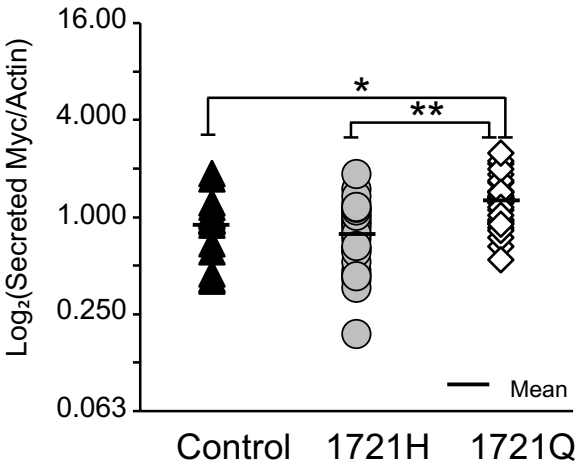
1721H v 1721Q not sig.

B



No sig. differences between groups

C



One-way ANOVA p = 0.000502
Control v 1721H Not Sig.
Control v 1721Q p<0.05
1721H v 1721Q p<0.01

DIET1-1721Q promotes increased extracellular FGF19 compared to DIET1-1721H without influencing intracellular FGF19 levels

Shown are protein levels from Fig. 7 normalized to actin. Statistical analyses performed by one-way ANOVA. *, $p < 0.05$; **, $p < 0.01$.

Supplemental Table I: Sequencing primer sets

Oligonucleotides used in this study to PCR amplify and sequence *DIET1* exons and exon/intron borders.

Exon	Oligonucleotide	strand	Genomic start coordinate	Used for
1-F	gctagataaagaaccagcgta	+	19337636	PCR, seq
1-R	ttcaggctgtacggggaat	-	19338096	PCR, seq
2-F	Gacttatgtcatttgttgcta	+	19355546	PCR
2-R	gaaagggaggtgggaaag	-	19355861	PCR, seq
3 & 4-F1	tcacttggcgccttaaattca	+	19376417	PCR
3 & 4-R1	gtcctgggaaatccctcagt	-	19377219	PCR
3&4-F2	Gtaccctgtctcttctttctg	+	19376744	seq
3&4-R2	acctgaaatctctgtgaactc	-	19377096	seq
5-F	Tgcttcctattgcaggctct	+	19392812	PCR, seq
5-R	ttgcactgaaatctttaaacaca	-	19393037	PCR, seq
6-F	cttgagtctttccagttgcac	+	19412363	PCR, seq
6-R	cacagcctcccaaaaacac	-	19412643	PCR, seq
7-F	gttaagcagccactctagca	+	19413396	PCR, seq
7-R	ccaaggcctcctatgtaatg	-	19413669	PCR, seq
8-F	gtcagacagaaagaagctaatg	+	19417091	PCR, seq
8-R	tcgaaacacaagttgccaaga	-	19417371	PCR, seq
9-F	gtaaatgtgaagattagaatacgg	+	19422728	PCR, seq
9-R	ctttagcagtgcatggtcaattt	-	19422939	PCR, seq
10-F	gccttggttgctttaaacact	+	19425385	PCR, seq

10-R	gacttacctttgccttgatag	-	19425787	PCR, seq
11-F	gcaggcctcctaagatgatt	+	19435034	PCR, seq
11-R	tcattccacaacatgcaagaa	-	19435311	PCR, seq
12-F	gattgtggagcaaagaacagc	+	19443932	PCR, seq
12-R	caagctcagcgatttacaacc	-	19444139	PCR, seq
13-F	ccagagacaggtcaatggaa	+	19454514	PCR, seq
13-R	cctgaaaaggtatgagctatg	-	19454819	PCR, seq
14-F	gattggagaatgggacagatg	+	19464026	PCR, seq
14-R	cacaccctgtattaggtattcg	-	19464342	PCR, seq
14 F2	Gtgatgtgtttttaacagtt	+	19464097	seq
15&16-F1	gctctgccttttcaaagtgtg	+	19492589	PCR
15&16-R1	ctgcaaacacttcaccacca	-	19493387	PCR
15&16-F2	gagcagtttggagagccaac	+	19492611	seq
15&16-R2	cagaaccgtactagctttcc	-	19492876	seq
15&16-F3	cagtgtagggttaagagacag	+	19493154	seq
15&16-R3	Accaccagggtgaactg	-	19493372	seq
17-F	gggaaagaaaagcgtcttatg	+	19493702	PCR, seq
17-R	tatcggtttgattggcaagac	-	19494264	PCR, seq
18-F	gtggttgcatgtatttttgtcc	+	19498138	PCR, seq
18-R	ttgatcaaattccacttgctttt	-	19498693	PCR, seq
19-F	cctcttcatccattccataac	+	19546532	PCR, seq
19-R	ttgatttccttgcaagttttcc	-	19546749	PCR, seq
20-F	gcagtagaaaaccagaaaacc	+	19568920	PCR, seq

20-R	gatgctaggctgtgctactt	-	19569217	PCR, seq
21-F	aagattgtacagatagaaactgc	+	19571884	PCR, seq
21-R	ggcagaaatttgggagatgct	-	19572158	PCR, seq
22-F	Cgtgcccggcctcttattc	+	19612829	PCR, seq
22-R	gcactgtgaacttttagagagaa	-	19613066	PCR, seq
23-F	ctaggggcacaatgctgtag	+	19616313	PCR, seq
23-R	ggggcaagaagactgtgagt	-	19616675	PCR, seq
23-F2	cactggaagaattctacatg	+	19616415	PCR, seq
23-R2	gcaagaagactgtgagtagag	-	19616671	PCR, seq
24-F1	gcccaggttttgaacttcttg	+	19620241	PCR, seq
24-R1	Ccttaccttcccctggtgtt	-	19620612	PCR, seq
24-F2	Gtttaactgtaactggctt	+	19620269	seq
25-F	gcagttttgaattgcatgtttta	+	19636626	PCR, seq
25-R	ccccccttcacatatccaaagt	-	19637070	PCR, seq
26-F1	aagtgcagacagagcaagag	+	19640787	PCR, seq
26-R1	tcacctttcaccatgcaaaaat	-	19641256	PCR, seq
26-F2	Agaagagggcaatgtgatag	+	19640847	PCR, seq
26-R2	Cctttcaccatgcaaaaatacc	-	19641253	PCR, seq
27-F	gctttttgacctcactgaatg	+	19676390	PCR, seq
27-R	Gctccccagttgctatcag	-	19676764	PCR, seq
28-F1	ttggcagctcagatcatacg	+	19678268	PCR, seq
28-R1	agccaagtcaactccctcag	-	19678914	PCR, seq
28-F2	aatcccatcattgttatttcg	+	19678330	PCR, seq

28-R2	Tgcagcctgagtgacaga	-	19678581	seq
29-F	gcatcatcttcttttgtgtttg	+	19739180	PCR, seq
29-R	aaatggctagattaaaaatgtgc	-	19739451	PCR, seq
30-F	acaggaatcttcaagtctaatg	+	19780379	PCR, seq
30-R	tgaaggaaaatatctgctgaac	-	19780606	PCR, seq
31-F	gtagtagcaaatgtgatagaca	+	19787356	PCR, seq
31-R	ttcacacaaattgttaaagcaga	-	19787624	PCR, seq
32-F	cacattccgactcatgcgata	+	19820061	PCR, seq
32-R	ctgccccagaaagaaatgag	-	19820402	PCR, seq
33-F	gagctgttacatagccagag	+	19856327	PCR, seq
33-R	ggcgaagttcataggcagag	-	19856785	PCR, seq
34-F1	ggagggaaactccctaatgc	+	19884073	PCR, seq
34-R1	tcattttatctgtcgagctttc	-	19884446	PCR, seq
34-F2	aatgtcccaacactggatgg	+	19884055	PCR, seq
34-R2	ggacagatgccttgttttgc	-	19884527	PCR, seq
35-F1	tgtgagaattcattgggacaaa	+	19896637	PCR, seq
35-R1	gcaggttaagttgctggttc	-	19896866	PCR, seq
35 F2	Ttttttttttgcagccaac	+	19896692	seq
36-F	atcttcttcttcctcctaatac	+	19904723	PCR, seq
36-R	accacaaactgattgatgctc	-	19904931	PCR, seq
37&38-F	ccatgccagttgtgttcaaa	+	19981140	PCR, seq
37&38-R	ctgcccagaaaaataaatcca	-	19981611	PCR, seq
39-F1	aatgtggttgccttggtgtc	+	20019442	PCR, seq

39-R1	tcaagcaacactggttcagc	-	20019781	PCR, seq
39-F2	Atttttgatggccctgtgtg	+	20019608	PCR, seq
39-R2	Ctggttcagcctgtgtgtgt	-	20019771	PCR, seq
40-F1	caagcagtgtgggctgtag	+	20022921	PCR, seq
40-R1	atacggcaaagaaagagcattt	-	20023488	PCR, seq
40-F2	Caacatcaggaagcctggaga	+	20023123	PCR, seq
40-F3	Gaagtctccacaatctgatag	+	20023215	PCR, seq
40-R2	Tctccaggcttcctgatgtt	-	20023124	PCR, seq
40-R3	actggcatttacaatcctttct	-	20023263	PCR, seq
40-R4	tgaagataaggtactgattctg	-	20023345	PCR, seq

Supplemental Table II. Nucleotide variants identified by sequencing *DIET1* coding region.

Unique nucleotide variants identified in the 44 individuals of the case-control study. The novel variants represent a subset of the total variants.

	All Single Nucleotide Variants			Novel Variants	
	Cases	Controls	Both	Cases	Controls
Synonymous	1	1	7	0	1
Nonsynonymous	3	6	16	3	2

Supplemental Table III. Catalog of *DIET1* coding region variants and their frequencies.

Variants are sorted by nucleotide position, with major and minor alleles and corresponding amino acid identities indicated. The minor allele frequency within the study sample and within the 1000 Genomes project are shown **(1)**. The final column lists the *p*-value of association between a particular variant and case-control status, as calculated by Fisher's Exact Test. The corrected α-level for multiple testing is $p < 0.00143$. Shading highlights *rs12256835*, which meets the significance threshold. S, synonymous; NS, nonsynonymous.

					n (allele) out of 88				
Exon	rs number	Nucleotide	Amino Acid	Class of SNV	Cases (44)	Controls (44)	Study MAF	1000 Genomes MAF	Fisher's Test *p* value
5	rs57243552	615 A>G	Q205Q	S	4	2	0.0682	0.1227	0.6763
8	rs11008573	975 T>C	G325G	S	10	7	0.1932	0.1259	0.5902
8	rs78076387	1002 G>A	R334R	S	3	0	0.0341	0.0714	0.2414
10	rs12779623	1232 A>G	Q411R	NS	9	7	0.1818	0.1516	0.7830
10	rs10826986	1405 A>G	T469A	NS	2	4	0.0682	0.0810	0.6763
12	Unknown	1583 A>G	Q528R	NS	0	1	0.0114	0	1
12	Unknown	1590 C>T	S530S	S	0	1	0.0114	0	1
12	Unknown	1591 C>G	P531A	NS	1	0	0.0114	0	1
13	rs78786296	1806 G>A	A602A	S	5	5	0.1136	0.0453	1
14	Unknown	1921 T>C	S641P	NS	0	1	0.0114	0	1
15	rs16918344	1997 C>T	A666V	NS	8	5	0.1477	0.0907	0.5494
16	rs10508578	2177 G>A	S726N	NS	3	2	0.0568	0.0389	1
17	rs4601653	2377 G>C	D793H	NS	10	6	0.1818	0.0916	0.4077
18	rs2358355	2660 A>G	N887S	NS	8	7	0.1705	0.1330	1
18	Unknown	2678 C>G	T893R	NS	1	0	0.0114	0	1
21	Unknown	3277 G>A	E1093K	NS	1	0	0.0114	0	1

21	rs72796460	3369 C>T	I1123I	S	1	2	0.0341	0.0481	1
22	Unknown	3534delG	F1179Sfs*4	Del.	0	1	0.0114	0	1
24	rs7100382	3797 C>A	A1266D	NS	15	20	0.3977	0.3942	0.3838
24	rs7100403	3829 G>A	V1277I	NS	15	21	0.4091	0.4643	0.2783
25	rs76551926	3981 C>T	N1327N	S	1	2	0.0341	0.0250	1
25	rs1609746	4071 T>G	N1357K	NS	15	21	0.4091	0.4661	0.2783
26	rs10827306	4250 C>T	A1417V	NS	16	21	0.4205	0.4501	0.3879
27	rs12773592	4538 A>G	D1513G	NS	9	9	0.2045	0.1190	1
27	rs12271333	4546 G>A	E1516K	NS	9	9	0.2045	0.1190	1
28	rs78832888	4756 A>G	M1586V	NS	4	4	0.0909	0.1035	1
28	rs10763975	4804 A>G	I1602V	NS	1	4	0.0568	0.1364	0.3604
30	rs16918863	5047 C>A	L1683I	NS	1	7	0.0909	0.1919	0.0580
30	rs10827499	5127 C>T	D1709D	S	8	11	0.2159	0.2550	0.3052
30	rs35934077	5135 A>G	D1712G	NS	0	1	0.0114	0.0055	1
31	rs12256835	5163 T>G	H1721Q	NS	0	11	0.1250	0.2816	0.0005
32	rs7100661	5420 T>C	M1807T	NS	0	3	0.0641	0.0916	0.2412
32	rs41276112	5453 A>T	D1818V	NS	0	3	0.0341	0.0192	0.2412
34	rs10827628	5822 A>G	S1941N	NS	21	23	0.5000	0.4766	0.8313
35	rs7909976	6069 A>C	S2023S	S	4	5	0.1023	0.1685	1

Supplemental Reference

1. 1000 Genomes Project Consortium, G. R. Abecasis, A. Auton, L. D. Brooks, M. A. DePristo, R. M. Durbin, R. E. Handsaker, H. M. Kang, G. T. Marth, and G. A. McVean. 2012. An integrated map of genetic variation from 1,092 human genomes. *Nature*. **491**: 56–65.