

Figure S1. Haplotype comparison between cases and controls in the region of association. Presented on top is the homozygous haplotype in the 7 cases and below the 19 controls Devon Rex, from position 128,192,494 to 131,992,072 on chromosome C2.



Figure S2 *COLQ* CDS and protein sequence. Presented are the feline wild-type and mutated CDS and amino acid *COLQ* sequences. Boldface indicates the base substitution in the CDS (c.1190G>A) and the associated amino acid substitution (p.397C>Y).

CDS wild-type

ATGGTTGTCCTGAATCCAGTGACTTTGGGAATCTATCTGCAGCTTTTCTTCCGCTTTATC

CDS mutated -----

Prot wild-type M V V L N P V T L G I Y L Q L F F R F I

Prot mutated - - - - -

CDS wild-type

GTGTCTCAGCCTACTTTCGTCAACAGCGTCTCCAATTCAGCAGCTTCCCCGGCCTG

CDS mutated -----

Prot wild-type V S Q P T F V N S V L P I S A A L P G L

Prot mutated - - - - -

CDS wild-type

GATCAGAAGAAGCGTGGCAGCCACAGAGCATGCTGCCTCCTGACGCCCCCTCCACCCCCG

CDS mutated -----

Prot wild-type D Q K K R G S H R A C C L L T P P P P P

Prot mutated - - - - -

CDS wild-type

CTGTTCCCACCACCATTCTTCAGAGGAGGCCGAAGCCTGCTTCTCTCCCCAGACATGAAG

CDS mutated -----

Prot wild-type L F P P P F F R G G R S L L L S P D M K

Prot mutated - - - - -

CDS wild-type

AATTCATCCTGGAAGTGGAGACCTCACAGTCCTCATGTGTGCAAGGATCACTCGGCTCC

CDS mutated -----

Prot wild-type N F I L E L E T S Q S S C V Q G S L G S

Prot mutated - - - - -

CDS wild-type

CCTGGGCCCCCTGGCCCCCAGGGTCCACCGGGACTTCCTGGCAAGATAGGACCAAAGGGA

CDS mutated -----

Prot wild-type P G P P G P Q G P P G L P G K I G P K G

Prot mutated - - - - -

CDS wild-type

GAAAAGGGGGAGCTTGGCCTACCAGGAAGAAAGGGTAGACCTGGCCCCCGGGTGTTCCT

CDS mutated -----

Prot wild-type E K G E L G L P G R K G R P G P P G V P

Prot mutated - - - - -

CDS wild-type
GGCATGCCTGGGCCAGTCGGCCCTGAAGGACCCAGGGGTGAAAAAGGTGACCTGGGTGTG
CDS mutated -----
Prot wild-type G M P G P V G P E G P R G E K G D L G V
Prot mutated - - - - -

CDS wild-type
ATGGGCTTGCCAGGGTCAAGAGGACCAATGGGCTTCAAGGGCTACCCTGGATCCAGAGGG
CDS mutated -----
Prot wild-type M G L P G S R G P M G F K G Y P G S R G
Prot mutated - - - - -

CDS wild-type
GAAAAGGGATCCAGAGGTGAAAGGGGTGACTTGGGTCCCAAAGGAGAAAAGGGTTTCCCG
CDS mutated -----
Prot wild-type E K G S R G E R G D L G P K G E K G F P
Prot mutated - - - - -

CDS wild-type
GGATTTCTTGGAAATGTTGGGGCAGAAAGGTGAAATGGGTCCAAAGGGTGAGCCTGGGATA
CDS mutated -----
Prot wild-type G F P G M L G Q K G E M G P K G E P G I
Prot mutated - - - - -

CDS wild-type
GCAGGACACAGGGGACCCAGAGGAAGACCAGGAAAACGAGGCAAGCAGGGGCAGAAGGG
A
CDS mutated -----
Prot wild-type A G H R G P R G R P G K R G K Q G Q K G
Prot mutated - - - - -

CDS wild-type
GATAGTGGAGTAATGGGCCCACCAGGCAAGCCTGGGCCTTCTGGTCAACCTGGCCGTCCA
CDS mutated -----
Prot wild-type D S G V M G P P G K P G P S G Q P G R P
Prot mutated - - - - -

CDS wild-type
GGTCCCCCAGGCCCCCGGGCCCCCGATCCGCAGGACAACCTTGTGATGGGACCCAAAGGG
CDS mutated -----
Prot wild-type G P P G P P G P R S A G Q L V M G P K G
Prot mutated - - - - -

CDS wild-type
GACAGAGGATTTCCCGGGCCTCCAGGAAGTTGTCTTTGTGGAACCCCTACGAATGTGAAT
CDS mutated -----
Prot wild-type D R G F P G P P G S C L C G T P T N V N
Prot mutated - - - - -

CDS wild-type
AACCCTTCCTACAGGGAATCCATGTATGGGTCCAGCTCCCCTCATGTTCTGTGATTTTT
CDS mutated -----
Prot wild-type N P S Y R E S M Y G S S S P H V P V I F
Prot mutated - - - - -

CDS wild-type
GTGGTCAACAACCAGGAGGAGCTCGAGAGGCTGAACACCCAAAACGCCATTGCCTTCCGC
CDS mutated -----
Prot wild-type V V N N Q E E L E R L N T Q N A I A F R
Prot mutated - - - - -

CDS wild-type
AAAGATCAGAGATCTCTGTACTTCAAGGACAGCCTTGGCTGGCTCCCCATCCAGGTGACC
CDS mutated -----
Prot wild-type K D Q R S L Y F K D S L G W L P I Q V T
Prot mutated - - - - -

CDS wild-type
CCTTCCACCCTCTGGACTATACTGTGGACCACCGTGGCTCCTGCGGGGATGGAGTCCTG
CDS mutated -----
Prot wild-type P F H P L D Y T V D H R G S C G D G V L
Prot mutated - - - - -

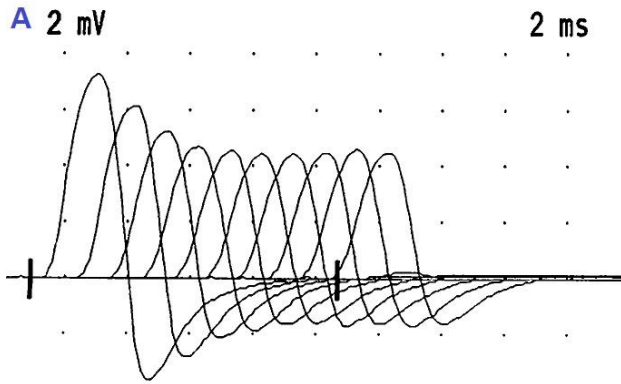
CDS wild-type
CAGCCCGGGGAGGAGTGTGATGACGGAATGATGACGTGGGTGACAGCTGCATCAGCTGT
CDS mutated -----A-----
Prot wild-type Q P G E E C D D G N D D V G D S C I S C
Prot mutated - - - - - Y - - -

CDS wild-type
CACCGGGCCTACTGTGGAGATGGTCACCAGCACAAGGGAGTGGAGGACTGCGACGGCTCT
CDS mutated -----
Prot wild-type H R A Y C G D G H Q H K G V E D C D G S
Prot mutated - - - - -

CDS wild-type
GACTTTGGCCACCTGACCTGCGAGACCTATCTCCCTGGGTTCATATGGGGACCTGCAGTGC
CDS mutated -----
Prot wild-type D F G H L T C E T Y L P G S Y G D L Q C
Prot mutated - - - - -

CDS wild-type ACCCCCTACTGCTACATCGACTCCACGTCCTGCCGCTACTTCACGTGA
CDS mutated -----
Prot wild-type T P Y C Y I D S T S C R Y F T X
Prot mutated - - - - -

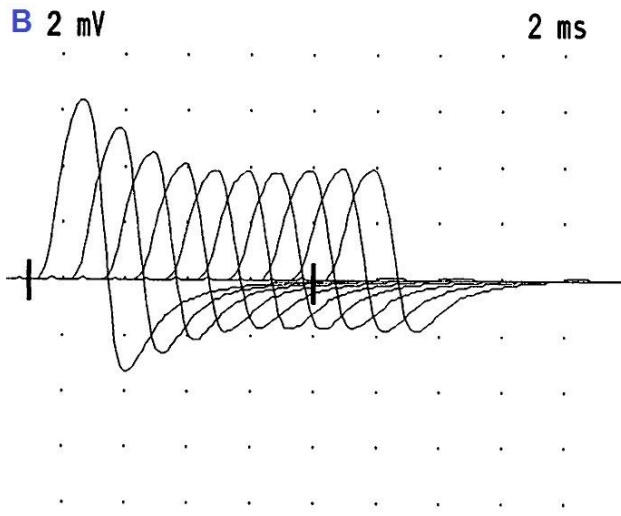
Figure S3. Decremental response to repetitive nerve stimulation at 3 Hz in an affected Sphynx cat. Sequential extensor digitorum brevis lateralis m. CMAP following peroneal n. stimulation at the hock: a) before edrophonium administration, b) after edrophonium administration.



FOOT SWITCH: READY / STIMULATE / STOP
 STIM.MODE: TRAIN / SINGLE

STIM FREQ:	3 Hz	NO. IN TRAIN:	10
STIM DUR:	0.2 ms	STIM RJCT:	0.5 ms
TIME:	11:07:40	STOP WATCH:	0:09
COMMENT:			

POT NO.	P-P AMP mV	AMP. DECR %	AREA mVms	AREA DECR %	STIM. LEVEL
1	10.96	0	18.80	0	1.6mA
2	9.05	17	15.60	17	1.6mA
3	7.46	32	12.90	31	1.6mA
4	6.66	39	11.50	39	1.6mA
5	6.26	43	10.90	42	1.6mA
6	6.14	44	10.60	44	1.6mA
7	6.20	43	10.60	44	1.6mA
8	6.18	44	10.70	43	1.6mA
9	6.39	42	10.90	42	1.6mA
10	6.15	44	10.70	43	1.6mA



FOOT SWITCH: READY / STIMULATE / STOP
 STIM.MODE: TRAIN / SINGLE

STIM FREQ:	3 Hz	NO. IN TRAIN:	10
STIM DUR:	0.2 ms	STIM RJCT:	0.5 ms
TIME:	11:58:09	STOP WATCH:	0:27
COMMENT:			

POT NO.	P-P AMP mV	AMP. DECR %	AREA mVms	AREA DECR %	STIM. LEVEL
1	9.77	0	14.80	0	1.5mA
2	8.07	17	12.10	18	1.5mA
3	6.79	31	10.10	32	1.5mA
4	6.03	38	9.11	38	1.5mA
5	5.68	42	8.61	42	1.5mA
6	5.67	42	8.65	42	1.5mA
7	5.65	42	8.53	42	1.5mA
8	5.69	42	8.60	42	1.5mA
9	5.81	41	8.80	41	1.5mA
10	5.78	41	8.86	40	1.5mA

Table S1. COLQ c.1190G>A genotypes in domestic cat breeds

Type*	Population	Lab	No.	Wildtype (CC)	Carrier (CT)	Affected (TT)
Unbiased	Abyssinian	MU	8	8	0	0
	American Shorthair	MU	8	8	0	0
	Bengal	MU	7	7	0	0
	Birman	MU	7	7	0	0
	British	MU	6	6	0	0
	Burmese	MU	4	4	0	0
	Cornish Rex	MU	8	8	0	0
	Chartreux	MU	6	6	0	0
	Devon Rex	MU	88	82	6	0
	Egyptian Mau	MU	7	7	0	0
	Japanese Bobtail	MU	7	7	0	0
	Khao Manee	MU	1	1	0	0
	Korat	MU	7	7	0	0
	Maine Coon	MU	8	8	0	0
	Manx	MU	5	5	0	0
	Norwegian Forest Cat	MU	7	7	0	0
	Ocicat	MU	7	7	0	0
	Oriental	MU	5	5	0	0
	Persian	MU	7	7	0	0
	Ragdoll	MU	5	5	0	0
	Russian Blue	MU	5	5	0	0
	Siamese	MU	6	6	0	0
	Siberian	MU	7	7	0	0
	Sphynx	MU	98	98	0	0
	Tonkinese	MU	6	6	0	0
	Turkish Angora	MU	6	6	0	0
	Turkish Van	MU	2	2	0	0
	Random Bred	MU	16	16	0	0
Sub-total	28 Breeds	MU	354	348	6	0
	Devon Rex	UM	20	20	0	0
	Sphynx	UM	20	20	0	0
Sub-total	2 Breeds	UM	40	40	0	0
	Devon Rex	VGL	94	92	2	0
	Sphynx	VGL	99	98	1	0
Subtotal	2 Breeds	VGL	193	190	3	0
Biased	Devon Rex	MU	39	17	5	17
	Sphynx	MU	1	0	0	1
Totals	28 breeds		627	595	14	18

*Type implies if the cat samples were ‘biased’ because they were collected as part of the disease study versus ‘unbiased’ because the laboratory conducted a population screen of samples submitted for other genetic testing. Biased affected cats include the cats from all three publications (Malik *et al.* 1993; Shelton *et al.* 2007; Martin *et al.* 2008). Four of five sampled cats from Malik *et al.* (1992) were successfully genotyped from formalin-fixed paraffin-embedded muscle samples. MU – Lyons laboratory, University of Missouri; VGL – Veterinary Genetics Laboratory, UC Davis; UM implies samples tested at the University of Milan.

Table S2. WGS variants identified in 20x coverage of an affected Devon Rex.

Variant		Analysis performed to prioritize variants**		
Impact*	Functional Class	WGS Cat	Segregation	GWAS haplotype
		High	Stop gain	296
	Start / Stop loss	56	4	-
	Splice donor / acceptor	1,350	43	-
	Exon deletion	2	-	-
	Frameshift	3,013	69	-
	Rare amino acid	-	-	-
Moderate	Codon alteration	577	35	-
	Missense	22,905	820	5
	Splice branch	-	-	-
	5' or 3' UTR Deletion	-	-	-
Low		41,926	1,301	8
Modifier		11,646,620	535,250	1,570

*Variant impact as defined by http://snpeff.sourceforge.net/SnpEff_manual.html#eff. **Feline reference genome sequence (V6.2) is included in the analyses. GWAS haplotype indicates the variants within the haplotype that was identified via the GWAS. Effect counts are higher than variant counts because a given variant can potentially affect both the flanking upstream and downstream genes. The full genome sequence of this Devon Rex cat is under submission to the NCBI SRA database (<http://www.ncbi.nlm.nih.gov/sra>) and the variant has been submitted to dbSNP.

Table S3. PCR primers used for genotyping *COLQ* variant in cats.

Assay	5' Primer (5' – 3')	3' Primer (5' – 3')
ASP (VGL) *	agtcagcattggcctgaatg	atgacgtgggtgacagttg
		gatgacgtgggtgacagata
MU sequencing	tgatatgcgtgggcagtaaaaagt	cctagtaactgtcctgtgtttctgtgg

*ASP indicates allele specific PCR (reverse primers specific for wild-type or variant allele). The 5' primer is generally labelled with a fluorescent dye.