

Appendix 2. Canine ADAM9 mRNA and predicted protein.

A. Canine *ADAM9*, normal allele.

A1. *ADAM9* mRNA sequence from normal dogs. Upper case indicates coding sequence, boxed are the first methionine and the stop codon. In bold are exons 15 and 16 that are missing in the affected dog.

A2. Canine ADAM9, predicted protein from a normal dog. The protein is 819 amino-acids long. Features in the protein are as follow: Red sequence: signal peptide- 1-28 aa (translated from exon 1); Grey sequence: 29-211 aa (translated from exon 2- exon 7); Orange sequence: Metalloprotease domain: 212-404 aa (translated from exon 7-exon 12); Blue sequence: Disintegrin domain: 414-501 aa (translated from exon 12-exon 14); Pink sequence: Cystein rich domain: 505-634 aa (translated from exon 14-exon 17); Brown sequence: EGF-like domain: 644-698 aa (translated from exon 17-exon 19); Green sequence: Transmembrane domain: 698-718 aa (translated from exon 19). Amino acids 29-697: extracellular, amino acids 698-718: transmembrane; amino acids 719-819: cytoplasmic.

B. Canine *ADAM9*, *crd3*-mutant allele.

B1. Sequence of *crd3*-mutant canine *ADAM9* mRNA. Boxed are the first methionine and the premature stop codon. \diamond indicates the location of exons 15 and 16 missing in the affecteds. Underlined is the stop codon in a normal dog.

B2. Canine ADAM9 predicted mutant protein product. Colored are the domains. The last two amino acids are not present in the normal protein. The predicted protein is 532 amino-acid long.

A1.

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gccgcg[ATG]GGATCGGGCGCGGGCTCGCCCTTTGGGGTCTTCCGGCTCCAGTGGCTGCTG
TTGTTTGGCACGGTGGGCCCCGGTCCTCGGTGGGGCTCGGCCAGGCTTTC AACAGACCTCA
CATCTCTCTTCTTATGAAATTATAACTCCTTGGAGATTAAGTAGAGAACGAAGAGAAGCC
CCTAGGCCCTATTTCAGAACAGGTGTCTTATATCATTCAAGCTGAAGGAAAAGAGCATATT
ATTCACTTGGAAAGGAACAATGACTTTTTTACCCCGAGATTTTGTAGTTTATACCTACAAC
AAGGAAGGGGCTTTGATCTCAGACCATCCCAGATGTACAGAATCATTGTCATTATCGGGGC
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CAGCTACTTTCGAAGAAGAAGAGCTGTCCCTGCCACAGACCCGATATGTGGAGCTGTTTCATT
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AATAAATTGGTGGATCCTGGGGAAGAGTGTGACTGTGGTACTCCAAAGGAGTGTGAATCG
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GACTGCTGTAAAGACTGTTGGTTCCTTCCAGGAGGTA CTTTGTGCCGAGGAAAAACCAAC
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CAAGACATGCCTGTATTTGGAATCGTGCCTGCTATTATTAGACTCCAGTAAAGGCACC
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TCTCAGGGAAATTTAATTCCTGCTCGTCTGCACCTGCACCTCCTTTATATAGTTCCCTC
ACTTGA)atTTTTTTTTTTTTTTTTTtacctttacttttgcagacatcttcagggaa

A2.

MSGAGSPFGV**F**RLQWLL**F**GT**V**GP**V**LGARPGFQQTSHLSSYEIITPWR 50
L**T**RERREAPR**P**YSEQVSYII**Q**AEGKEHI**I**HLERNND**F**LPRDFV**V**TYN**K**E 100
G**A**LISDHPD**V**QNHCHYRGY**V**EGISNSSIALSD**C**FGLRGL**L**HIENVSY**G**IE 150
P**L**QNSSH**F**EHIFYRMDD**V**HKEPL**K**CGVSN**K**DMEK**E**TTNYEEEE**P**LS**V**T**Q**L 200
L**R**RRRA**V**L**P**Q**T**RY**V**EL**F**IV**V**DK**E**RY**D**MMGR**N**Q**T**AV**R**EEM**I**RLAN**Y**L**D**SM**Y** 250
IML**N**IR**I**VL**V**GLE**I**WT**N**GN**L**INI**I**GGAG**D**VL**G**N**F**V**Q**W**R**E**K**FL**I**TRRR**H**DS 300
AQL**V**L**K**K**G**FG**G**T**A**G**M**A**F**V**G**T**V**CS**R**SHAG**G**IN**V**FG**Q**IT**V**ET**F**AS**I**VA**H**EL**G** 350
HN**L**GM**N**HDD**G**RD**C**FC**G**AK**S**CI**M**NS**G**AS**G**SR**N**F**S**SC**S**AED**F**E**K**LT**L**N**K**GG**N** 400
CLL**N**I**P**K**P**DE**A**YS**A**PF**C**GN**K**L**V**DP**G**E**E**CD**C**GT**P**KE**C**ES**D**PC**C**E**G**TT**C**KL**K** 450
SSA**E**C**A**Y**G**DC**C**K**D**C**W**FL**P**GG**T**LC**R**G**K**T**N**E**C**D**V**PE**Y**C**N**G**S**S**Q**FC**Q**PD**V**F**I**Q 500
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GNC**G**FS**G**NE**Y**KK**C**AT**G**NA**L**CG**K**L**Q**CEN**V**Q**D**MP**V**FG**I**VP**A**II**Q**TP**S**KG**T**K**C** 600
WGV**D**F**Q**L**G**SD**V**PD**P**GM**V**NE**G**TR**C**D**N**G**K**I**C**R**N**F**Q**CV**N**AS**V**L**N**Y**D**CD**I**Q**K**K**C** 650
HH**G**V**C**NS**N**KN**C**HCEN**G**W**A**PP**N**C**E**T**K**GY**G**GS**V**DS**G**PT**Y**NE**K**NT**A**LR**D**GL**L** 700
VFF**F**L**I**V**P**L**I**VC**A**F**V**FI**K**RD**Q**L**W**RS**Y**F**Q**KK**R**S**Q**TY**E**SD**G**KN**Q**A**K**AS**R**Q**P** 750
VSV**P**RV**S**SV**T**PP**R**E**A**PI**Y**AN**R**FP**V**PT**Y**AA**K**Q**P**Q**Q**FP**S**R**P**PP**P**Q**P**K**V**SS**Q** 800
GN**L**IP**A**RP**A**P**A**PLY**S**SL**T**

B1.

gcccgcg**A**T**G**GGATCGGGCGCGGGCTCGCCCTTTGGGGTCTTCCGGCTCCAGTGGCTGCTG
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B2.

MSGAGSPFGVFRLLQWLLLFGTVGPVLG GARPGFQQTSHLSSYEIITPWR 50
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 AQLVLKKGFGGTAGMAFVGTVCSRSHAGGINVFGQITVETFASIVAHEL 350
 HNLGMNHDDGRDCFCAKSCIMNSGASGRNFSSCSAEDFEKLTLLNKGN 400
 CLLNIPKPDEAYSAPFCGNKLVDPGEECDGTPKECESDPCEGTTCKLK 450
 SSAECAYGDCCKDCWFLPGGTLCRGKTNECDVPEYCNGSSQFCQPDVFIQ 500
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