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RESEARCH ARTICLE

Sequence Conservation and Variability in Canine Distemper Virus Proteins

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ABSTRACT

Canine distemper virus (CDV), a member of the Paramyxoviridae family, is a highly contagious pathogen with a broad host range, causing considerable morbidity and mortality in domestic and wild carnivores. In this study, a total of 2,882 complete and partial CDV sequences, deposited in GenBank up to 17 August 2025, were analysed. The sequences were aligned and categorized according to their genes (N, P, C, M, F, H, and L), and consensus sequences were generated. Comparative analyses revealed that the M protein was the most conserved (73.35%), followed by the L protein (69.58%). H (2.15%) and N (2.10%) proteins displayed the lowest levels of conservation. The highest variability was observed in the F (3.32%) and H (0.82%) proteins. Critical residues of the H protein, previously associated with viral tropism and antigenicity, were evaluated: position 238 was predominantly Y, position 241 was G, and position 530 was G. Furthermore, position 519 in the N protein, previously linked to virulence, was R in the consensus sequence. Structural modelling of the H protein was performed, highlighting the spatial localization of these key residues. The results underline the genetic diversity and evolutionary dynamics of CDV and provide insights into antigenic drift, host adaptation, and viral persistence. These findings are expected to support future studies focusing on epitope mapping, vaccine development, and antiviral drug design.
Keywords: Canine distemper virus, Consensus sequence, Genetic variability, H protein, N protein

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Köpek Distemper Virusu Proteinlerinde Dizi Korunumu ve Değişkenliği

ÖZ

Canine distemper virus (CDV), *Paramyxoviridae* familyasında yer alan, geniş konak spektrumuna sahip ve yüksek morbidite ile mortaliteye yol açabilen viral bir patojendir. Bu çalışmada, 17 Ağustos 2025 tarihine kadar GenBank'a yüklenen toplam 2,882 parçalı ve tam CDV dizisi indirilerek, analiz edilmiştir. Diziler, gen bölgelerine (N, P, C, M, F, H, L) göre ayrılarak hizalanmış ve her biri için konsensüs dizileri oluşturulmuştur. Analizler sonucunda M proteininin %73,35 oranında, L proteininin ise %69,58 oranında tamamen korunduğu; en az korunmuş proteinlerin ise H (%2,15) ve N (%2,10) olduğu tespit edilmiştir. En değişken amino asitler F (%3,32) ve H (%0,82) proteinlerinde yoğunlaşmıştır. Tropizm ve antijeniteyle ilişkili H proteininin kritik amino asitleri incelendiğinde, 238. pozisyonun çoğunlukla Y, 241. pozisyonun G, 530. pozisyonun ise G olduğu belirlenmiştir. Ayrıca N proteininin patojenite ile ilişkili 519. amino asit pozisyonu konsensüs dizide R olarak saptanmıştır. H proteininin yapısal modellemesi yapılarak kritik amino asitlerin konumları belirlenmiştir. Elde edilen veriler, CDV'nin genetik çeşitliliğini, antijenik sürüklenmesini ve konak adaptasyonunu anlamaya katkı sunmakta olup, gelecekte epitop haritalama, yeni aşı tasarımı ve antiviral ilaç geliştirme çalışmalarına temel oluşturabilecek niteliktedir.
Anahtar Kelimeler: Genetik çeşitlilik, H protein, Konsensüs dizisi, Köpek distemper virusu, N proteini

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INTRODUCTION

Canine distemper virus (CDV) is a member of the genus Morbillivirus within the family Paramyxoviridae (Murphy et al. 2012). CDV particles are pleomorphic, typically spherical, and enveloped virions with an approximate diameter of 150 nm. The virus possesses a non-segmented, single-stranded, negative-sense RNA (ssRNA) genome that is 15,690 nucleotides in length and encodes six structural proteins. These include the nucleocapsid (N) protein, two transcriptase-associated proteins known as the phosphoprotein (P), large protein (L), the envelope-stabilizing matrix protein (M), and two transmembrane glycoproteins embedded in the viral envelope, hemagglutinin (H) and fusion (F), which serve as the major immunogenic components of CDV. Additionally, the P gene encodes two nonstructural proteins, C and V. All of these viral proteins are essential for the replication process (Chen et al. 2023; Martella et al. 2008; Rendon-Marin et al. 2019; da Fontoura Budaszewski et al. 2016). Notably, the 519th amino acid of the CDV N protein has been associated with viral virulence and pathogenicity (Siering et al. 2024).

The hemagglutinin (H) protein of CDV is a critical determinant of viral infectivity due to its role in initiating membrane fusion following receptor engagement (Bi et al. 2023). By binding to signaling lymphocyte activation molecule (SLAM, also known as CD150) on peripheral blood mononuclear cells and to nectin-4 (PVRL4) on epithelial cells, the H protein governs host cell tropism, mediates viral entry, and contributes to CDV pathogenicity (Von Messling et al. 2005; Pratakpiriya et al. 2012). Moreover, it is a principal target of neutralizing antibodies and plays a central role in eliciting protective immune responses (Bi et al. 2015; Feng et al. 2023; Von Messling et al. 2001). Notably, two specific substitutions in the H protein, D238Y and R241G, have been reported to alter its antigenicity (Bi et al. 2023). Given these attributes, H-specific antibodies are a foundational component in the design of CDV vaccines (Hirayama et al. 1991; Bouche et al. 2002; de Swart et al. 2005, de Swart et al. 2009). Importantly, specific amino acid residues of the H protein, namely positions 530, 542, and 549, have been directly associated with viral tropism (McCarthy et al. 2007; Tao et al. 2020).

CDV is characterized by an exceptionally broad host range. To date, infections have been recorded across all terrestrial and several semi-aquatic carnivore families, including Canidae, Felidae, Hyaenidae, Mustelidae, Procyonidae, Ursidae, Viverridae, Ailuridae, Phocidae, and Otariidae. In addition, the virus has been reported in members of other taxonomic groups such as Rodentia, Primates, Cetartiodactyla, Proboscidea, and Pilosa (Deem et al. 2000; Macías-González et al. 2025; Vergara-Wilson et al. 2021). This wide host range is largely attributed to the virus's capacity to overcome species barriers, allowing transmission among distantly related hosts. Previous studies have shown that specific amino acid substitutions in the H protein (e.g., residue 549) and other structural proteins of CDV influence viral host tropism and virulence (Ariyama et al., 2024; Rivera-Martínez et al., 2024; Wilkes et al., 2022). While earlier perspectives considered only certain species as reservoir hosts, current understanding incorporates the broader and more dynamic concept of metareservoirs. This expanded ecological framework reflects CDV's enhanced adaptability and evolutionary potential, which contribute to its persistence in natural ecosystems and present significant challenges to eradication efforts. As a result, the ongoing spread and maintenance of CDV in multiple host populations continue to pose a potential threat to both animal and human health (Macías-González et al. 2025; Wilkes, 2022).

Vaccination represents the most effective strategy in combating viral infections. However, the suboptimal efficacy of currently available CDV vaccines, the lack of formulations specifically developed for wildlife species, and the limited suitability of some vaccines designed for domestic dogs in other susceptible species underscore the necessity and importance of developing new, broadly protective vaccines in this field (Bush et al. 1976; Gilbert et al. 2020; Martella et al. 2008; Anis et al. 2018; Ariyama et al. 2024; Wang et al. 2025; Vergara-Wilson et al. 2021).

In this study, it was aimed to analyze 2,882 CDV sequences shared in the GenBank database until 17 August 2025 in order to generate a consensus sequence. Significant amino acid substitutions within the genes of CDV will be identified. In addition, modelling of important proteins of CDV will be performed based on the consensus sequence. The data obtained from this study are considered to have the potential to support epitope mapping, novel vaccine design studies, and the development of new antiviral drugs.

MATERIALS and METHODS

Ethical Statement

This study is not subject to the permission of HADYEK in accordance with the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees" 8 (k). The data, information and documents presented in this article were obtained within the framework of academic and ethical rules.

Sequence Data and Alignment

In this study, a total of 3,074 complete or partial genome sequences of Canine Distemper Virus submitted to the NCBI GenBank database up to 17 August 2025 were downloaded. Sequences that were

erroneous, derived from vaccines or patents, or potentially belonging to other related viruses such as Phocine distemper virus were excluded. All these steps were carried out using BioEdit 7.7.1 and MEGA X 10.2.6 software. In total, 2,882 partial or complete CDV genome sequences were included in the study.
All datasets were aligned using the MAFFT multiple sequence alignment tool (Katoh et al. 2013).

Detection of Amino Acid Variations

N, P, C, M, F, H, and L genes exported seperately using the AliView 1.30 software. A total of 536 N, 417 P, 406 C, 262 M, 595 F, 1797 H, and 224 L complete and partial gene sequences, were obtained. These genes were translated into amino acid sequences using MEGA X 10.2.6 software.

All nucleotide and amino acid sequences were converted into FASTA format and uploaded into Geneious Prime 2025.2.1 for further analyses. The most variable amino acids were statistically identified using the BLOSUM62 method. Start codons were included and, stop codons were excluded in the calculations. Start codons were not presented in the summary tables of conserved proteins. Amino acid positions with no detected mutations were classified as completely conserved. For the identification of conserved amino acid sequences, the threshold was set at 100%, whereas for the identification of the most variable amino acids, the threshold was set at 65%.

Consensus Sequence Construction

All consensus sequences generated in the study were constructed using Geneious Prime 2025.2.1.

Structural Analysis

The functional roles and structural positions of amino acids were determined using data from the Protein Data Bank and UniProt (Goetschius et al. 2021; UniProt: https://doi.org/10.1093/nar/gkae1010). Structural modeling of the proteins was performed using the Swiss-Model platform (Waterhouse et al. 2018).

RESULTS

A consensus nucleotide and amino acid sequences was presented in Table 1 and Table 2, respectively. The highest similarity to the consensus CDV genome was observed with the sequences KF640687 (98.606%), AF164967 (98.482%), and EU716337 (98.305%), respectively.

Among the 522 amino acids of the N protein, 11 (2.10%) were found to be completely conserved. In the P protein, 195 of 506 amino acids (38.53%); in the C protein, 57 of 173 (32.94%); in the M protein, 245 of 334 (73.35%); in the F protein, 223 of 661 (33.73%); in the H protein, 13 of 603 (2.15%); and in the L protein, 1,519 of 2,183 (69.58%) were completely conserved (Table 3). The most variable amino acids were identified as follows: 2 (0.38%) in the N protein, 4 (0.79%) in the P protein, 3 (1.73%) in the C protein, 22 (3.32%) in the F protein, 5 (0.82%) in the H protein, and 5 (0.22%) in the L protein. No highly variable amino acids were detected in the M protein (Table 4).

In the consensus sequence, residue 238 of the H protein was identified as Y, residue 241 as G, residue 530 as G, residue 542 as I, and residue 549 as Y (McCarthy et al. 2007; Tao et al. 2020; Bi et al. 2023). Residue 519 of the N protein was identified as R (Siering et al. 2024).

Structural modelling of the consensus H protein was performed, and amino acid residues associated with tropism were modelled.

Table 1. Consensus sequences for N, P, C, M, F, H, and L nucleotides.

N (Alignment of 536 Sequences)
ATGGCTAGCCTTCTYAAGAGCCTCACAYTGTTCAAGAGGACTCGGGACCAACCCCCACTTGCCTCGGGCTCC GGAGGAGCAATAAGAGGGATAAAGCATGTCATTATAGTCCTAATCCCGGGTGATTCAAGCATTGTTACAAG ATCTCGACTATTGGATAGACTTGTTAGATTGGTCGGTGATCCGGAAATCAACGGACCTAAATTAACTGGGA TTTTAATCAGTATCCTCTCCTTGTTCGTGGAATCCCCTGGACAGTTGATCCAGAGGATCATAGACGACCCTG ATGTAAGCATCAAGTTAGTAGAGGTAATCCCAAGCATCAACTCTGTTTGYGGTCTTACATTTGCATCCAGAG GAGCAAGTTTGGATTCTGAGGCAGATGAGTTCTTCAAAATTGTAGACGAAGGGTCGAAAGCTCAAGGACA ATTAGGCTGGTTGGAGAATAAGGATATTGTAGACATAGAAGTTGATGATGCTGAGCAATTCAATATATTGC TAGCTTCCATCTTGGCYCAAATTTGGATCCTGCTCGCTAAAGCAGTGACTGCTCCTGATACTGCAGCCGACT CGGAGATGAGAAGGTGGATTAAGTATACCCAACAGAGACGTGTGGTCGGGGAATTTAGAATGAACAAAAT CTGGCTTGATATTGTTAGAAACAGGATTGCTGAGGACTTATCTTTGAGGCGRTTCATGGTGGCACTCATCTT GGAYATCAAACGATCCCCAGGGAACAAGCCTAGAATTGCTGAAATGATTTGTGATATAGATAACTACATTG TGGAAGCTGGATTAGCTAGTTTCATCTTAACTATCAAATTTGGCATTGAAACTATGTATCCGGCTCTTGGGT TGCATGAGTTTTCCGGAGAGTTAACAACTATTGAATCCCTTATGATGCTATATCAACAGATGGGTGAAACAG CACCGTACATGGTTATTCTGGAAAATTCTGTTCAGAACAAATTTAGTGCAGGATCCTACCCATTGCTCTGGA GTTATGCTATGGGAGTTGGTGTTGAACTTGAAAACTCCATGGGAGGGTTAAATTTCGGTAGATCCTACTTT GATCCRGCTTATTTCAGGCTCGGGCAAGAAATGGTKAGAAGATCTGCCGGCAAAGTAAGCTCTGCACTTGC CGCCGAGCTTGGCATCACCAAGGAAGAGGCTCAGCTAGTGTCAGAAATAGCATCCAAGACAACGGAGGAC CGGACGATTCGCRCTGCTGGTCCCAAGCAATCTCAAATCACTTTTCTGCACTCAGAAAGATCCGAAGTCACT AATCAACAACCCCCAACCATCAACAAGAGGTCCGAAAACCAAGGAGGAGACAAATACCCCATCCACTTCART GATGAACGGTTTCCAGGGTAYACCCCWGATGTCAACAGCTCCGAATGGAGTGAATCACGCTATGATACCCA RACTATTCAAGATGATGGAAACGACGATGACCGGAAATCGATGGAAGCAATCGCCAAGATGAGAATGCTTA CTAAGATGCTCAGTCAACCTGGGACCAGTGAAGAGAGTTCTCCTGTCTATAATGATAGAGAGCTACTCAATT AA

P (Alignment of 417 Sequences)

ATGGCTAGCCTTCTYAAGAGCCTCACAYTGTTCAAGAGGACTCGGGACCAACCCCCACTTGCCTCGGGCTCC
GGAGGAGCAATAAGAGGGATAAAGCATGTCATTATAGTCCTAATCCCGGGTGATTCAAGCATTGTTACAAG
ATCTCGACTATTGGATAGACTTGTTAGATTGGTCGGTGATCCGGAAATCAACGGACCTAAATTAACTGGGA
TTTTAATCAGTATCCTCTCCTTGTTCGTGGAATCCCCTGGACAGTTGATCCAGAGGATCATAGACGACCCTG
ATGTAAGCATCAAGTTAGTAGAGGTAATCCCAAGCATCAACTCTGTTTGYGGTCTTACATTTGCATCCAGAG
GAGCAAGTTTGGATTCTGAGGCAGATGAGTTCTTCAAAATTGTAGACGAAGGGTCGAAAGCTCAAGGACA
ATTAGGCTGGTTGGAGAATAAGGATATTGTAGACATAGAAGTTGATGATGCTGAGCAATTCAATATATTGC
TAGCTTCCATCTTGGCYCAAATTTGGATCCTGCTCGCTAAAGCAGTGACTGCTCCTGATACTGCAGCCGACT
CGGAGATGAGAAGGTGGATTAAGTATACCCAACAGAGACGTGTGGTCGGGGAATTTAGAATGAACAAAAT
CTGGCTTGATATTGTTAGAAACAGGATTGCTGAGGACTTATCTTTGAGGCGRTTCATGGTGGCACTCATCTT
GGAYATCAAACGATCCCCAGGGAACAAGCCTAGAATTGCTGAAATGATTTGTGATATAGATAACTACATTG
TGGAAGCTGGATTAGCTAGTTTCATCTTAACTATCAAATTTGGCATTGAAACTATGTATCCGGCTCTTGGGT
TGCATGAGTTTTCCGGAGAGTTAACAACTATTGAATCCCTTATGATGCTATATCAACAGATGGGTGAAACAG
CACCGTACATGGTTATTCTGGAAAATTCTGTTCAGAACAAATTTAGTGCAGGATCCTACCCATTGCTCTGGA
GTTATGCTATGGGAGTTGGTGTTGAACTTGAAAACTCCATGGGAGGGTTAAATTTCGGTAGATCCTACTTT
GATCCRGCTTATTTCAGGCTCGGGCAAGAAATGGTKAGAAGATCTGCCGGCAAAGTAAGCTCTGCACTTGC
CGCCGAGCTTGGCATCACCAAGGAAGAGGCTCAGCTAGTGTCAGAAATAGCATCCAAGACAACGGAGGAC
CGGACGATTCGCRCTGCTGGTCCCAAGCAATCTCAAATCACTTTTCTGCACTCAGAAAGATCCGAAGTCACT
AATCAACAACCCCCAACCATCAACAAGAGGTCCGAAAACCAAGGAGGAGACAAATACCCCATCCACTTCART
GATGAACGGTTTCCAGGGTAYACCCCWGATGTCAACAGCTCCGAATGGAGTGAATCACGCTATGATACCCA
RACTATTCAAGATGATGGAAACGACGATGACCGGAAATCGATGGAAGCAATCGCCAAGATGAGAATGCTTA
CTAAGATGCTCAGTCAACCTGGGACCAGTGAAGAGAGTTCTCCTGTCTATAATGATAGAGAGCTACTCAATT
AA

C (Alignment of 406 Sequences)

ATGTCAGCAAAGGGCTGGAATGCCTCAAAGCCCTCAGAGAGAATCCTCCTGACATTGAGGAGATTCAAGAG
GTCAGCAGCATCAGAGACCAAACCCGCAACCCAGGCCAAGAGAATGGAACCGCAAGCATGCAGGAAGARG
AGGTCTCTCAGGATCTCGATGAATCACACGAGCCAGCAAAAGGATCAAACTATGTCGGCCATGTACTCCAA
AATAATCCGGGATGTGGAGAGAGCAACACTGCGCTTGTGGAGGCAGAGCAGCCCGCTAAAGATGACATCC
AACCAGGACCTGGAATACGATGTTATCATGTTTATGATCACAGCGGTGAAGAGGTTAAGGGAATCGAAGAT
GCTGACAGTCTCGTGGTACCTGCAGGCGCTGTCAGTAATCGAGGATTCGAGAGAGGAGAAGGAAGCCTTG
ATGATAGCACTGAGGATTCTGGCGAAGATTATTCCGARGGAAATGCTTCATCTAACTGGGGATATTCTTTC
GGCCTTAAACCAGACAGAGCAGCTGATGTGA

M (Alignment of 262 Sequences)

ATGACTGAGGTGTACGACTTCGATCAGTCTTCKTGGGACACCAAAGGCTCATTGGCCCCCATTTTGCCCACC
ACYTATCCCGATGGTAGGCTAGTACCCCAAGTCAGAGTGATAGATCCAGGACTCGGCGATCGAAAAGATGA
ATGTTTCATGTATATTTTTYTACTGGGTATAATAGAAGACAAYGATGGCCTCGGACCCCCRATTGGAAGAAC
ATTTGGATCGCTGCCTTTAGGTGTTGGGCGCACTACAGCCAGACCTGAAGAATTATTGAAGGAAGCCACCC
TGTTGGAYATTGTGGTAAGGCGAACTGCAGGTGTCAAGGAACAACTGGTATTTTACAATAACACCCCATTG
CACATCTTAACTCCGTGGAAGAAGGTCCTTACGAGTGGGAGTGTGTTCAGTGCAAATCAAGTCTGTAACGC
AGTCAATTTAATACCATTAGACATAGCACAGAGATTTAGGGTGGTATATATGAGCATCACTCGACTATCAGA
CGATGGAAGTTACAGAATTCCYCGCGGGATGTTTGAATTCCGCTCCAGGAATGCTTTAGCATTTAATATTTT
AGTCACCATTCAAGTTGAGGGAGATGTCTGTTCAAGCCGAGGTAATTTGAGCATGTTCAAAGATCACCAAG
TGACATTCATGGTGCATATCGGCAACTTCAGCCGTAAGAAGAACCAAGCTTACTCTGCTGATTACTGTAAAC
TGAAAATTGAAAAGATGGGATTAGTGTTTGCTCTAGGAGGGATAGGGGGAACCAGTCTTCACATACGATG
TACTGGTAAGATGAGCAAGGCTTTGAATGCCCAGCTAGGRTTCAAGAAAATCCTGTGTTACCCGCTCATGG
AGATCAATGAAGATTTGAATCGATTTCTATGGAGATTAGAGTGCAAAATAGTAAGAATCCAAGCAGTCTTG
CAACCATCAGTCCCACAAGATTTCAGAATTTATAATGATGTTATCATCAGCGATGATCAGGGTCTTTTCAAAA
TTCTCTAA

F (Alignment of 595 Sequences)

ATGACTGAGGTGTACGACTTCGATCAGTCTTCKTGGGACACCAAAGGCTCATTGGCCCCCATTTTGCCCACC
ACYTATCCCGATGGTAGGCTAGTACCCCAAGTCAGAGTGATAGATCCAGGACTCGGCGATCGAAAAGATGA
ATGTTTCATGTATATTTTTYTACTGGGTATAATAGAAGACAAYGATGGCCTCGGACCCCCRATTGGAAGAAC
ATTTGGATCGCTGCCTTTAGGTGTTGGGCGCACTACAGCCAGACCTGAAGAATTATTGAAGGAAGCCACCC
TGTTGGAYATTGTGGTAAGGCGAACTGCAGGTGTCAAGGAACAACTGGTATTTTACAATAACACCCCATTG
CACATCTTAACTCCGTGGAAGAAGGTCCTTACGAGTGGGAGTGTGTTCAGTGCAAATCAAGTCTGTAACGC
AGTCAATTTAATACCATTAGACATAGCACAGAGATTTAGGGTGGTATATATGAGCATCACTCGACTATCAGA
CGATGGAAGTTACAGAATTCCYCGCGGGATGTTTGAATTCCGCTCCAGGAATGCTTTAGCATTTAATATTTT
AGTCACCATTCAAGTTGAGGGAGATGTCTGTTCAAGCCGAGGTAATTTGAGCATGTTCAAAGATCACCAAG
TGACATTCATGGTGCATATCGGCAACTTCAGCCGTAAGAAGAACCAAGCTTACTCTGCTGATTACTGTAAAC
TGAAAATTGAAAAGATGGGATTAGTGTTTGCTCTAGGAGGGATAGGGGGAACCAGTCTTCACATACGATG
TACTGGTAAGATGAGCAAGGCTTTGAATGCCCAGCTAGGRTTCAAGAAAATCCTGTGTTACCCGCTCATGG
AGATCAATGAAGATTTGAATCGATTTCTATGGAGATTAGAGTGCAAAATAGTAAGAATCCAAGCAGTCTTG
CAACCATCAGTCCCACAAGATTTCAGAATTTATAATGATGTTATCATCAGCGATGATCAGGGTCTTTTCAAAA
TTCTCTAA

H (Alignment of 1797 Sequences)
ATGCTCTCCTACCAAGACAAGGTGGGTGCCTTCTATAAGGATAATGCAAGAGCTAATTCATCCAAGCTGTCC TTAGTGACAGAAGAGCAAGGGGGCAGGAGACCACCCTATTTGCTGTTTGTCCTTCTCATCCTACTGGTTGG AATCMTGGCCTTGCTTGCTATCACTGGAGTTCGATTTCACCAAGTATCAACTAGCAATATGGAATTTAGCAG ATTGCTGAAAGAGGATATGGAGAAATCAGAGGCCGTACATCACCAAGTCATAGATGTCTTGACACCGCTCT TCAAAATTATTGGAGATGAGATTGGGTTACGGTTGCCACAAAAACTAAACGAGATCAAACAATTTATCCTTC AAAAGACAAACTTCTTCAATCCGAACAGGGAATTCGACTTCCGCGATCTCCACTGGTGCATTAACCCACCTA GTAAGATCAAGGTGAATTTTACTAATTACTGYGATACAATTGGGATCAGAAAATCTATTGCATCGGCAGCAA ATCCCATCCTTTTATCAGCACTCTCCGGAGGCAGAGGTGACATATTCCCACCATACAGATGCAGTGGAGCTA CTACTTCAGTAGGCAGAGTTTTCCCCCTATCAGTATCATTRTCCATGTCTTTGATMTCAAGAACATCAGAGAT AATCAATATGCTAACCGCTATCTCAGACGGAGTGTATGGTAAAACTTATTTGCTAGTGCCTGATTATATTGA AGGGGAGTTCGACACGCAAAAGATTCGAGTCTTTGAGATAGGGTTCATCAAACGGTGGCTGAATRACATG CCATTACTCCAGACAACCAACTATATGGTCCTCCCGGAGAMTTCCAAAGCCAAGGTATGTACTATAGCAGTG GGCGAGTTGACACTRGCTTCCTTGTGTGTAGATGAGAGCACCGTATTGTTATATCATGACAGCAATGGTTC ACAAGATGGTATTCTAGTAGTGACRCTGGGAATATTTGGGGCAACACCTATGGATCAAGTTGAAGAGGTG ATACCTGTCGCTCACCCATCAGTRGARAAAATACATATAACAAATCACCGTGGGTTCATAAAAGATTCAATA GCAACCTGGATGGTGCCTGCATTGGTCTCTGAGAAACAAGAGGAACAAAAAAATTGTCTGGAGTCGGCTT GTCAAAGAAAAWCCTACCCTATGTGCAACCAAACGTCATGGGAACCCTTTGGAGGAGGACAGTTGCCATCT TATGGGCGGTTGACATTACCTCTAGATCCAAGCATTGACCTTCAACTTAACATATCATTTACATACGGTCCG GTTATACTGAATGGAGACGGTATGGATTATTATGAAAGCCCACTTTTGGACTCCGGATGGCTTACCATTCCT CCCAAGAACGGAACAGTCCTTGGATTGATAAACAAAGCAAGTAGAGGAGACCAGTTCACTGTAATCCCCCA TGTGTTGACATTTGCGCCCAGGGAATCAAGTGGAAATTGTTATTTACCTATTCAAACATCCCAGATTATGGA TAAAGATGTCCTTACTGAGTCCAATTTAGTGGTGTTGCCTACACAGAATTTTAGATATGTCATAGCAACATA TGATATATCCCGGGGCGATCATGCRATTGTTTATTATGTTTATGACCCAATCCGGACGATTTCTTATACRTAC CCATTTAGACTAACTACCAAGGGTAGACCTGATTTCCTAAGGATTGAATGTTTTGTGTGGGATGACGATTT GTGGTGTCACCAATTTTACCGATTCGAGGCTGACATCACCAACTCTACAACCAGTGTTGAGAATTTAGTCCG TATAAGATTCTCATGTAACCGTTCA
L (Alignment of 224 Sequences)
ATGCTCTCCTACCAAGACAAGGTGGGTGCCTTCTATAAGGATAATGCAAGAGCTAATTCATCCAAGCTGTCC TTAGTGACAGAAGAGCAAGGGGGCAGGAGACCACCCTATTTGCTGTTTGTCCTTCTCATCCTACTGGTTGG AATCMTGGCCTTGCTTGCTATCACTGGAGTTCGATTTCACCAAGTATCAACTAGCAATATGGAATTTAGCAG ATTGCTGAAAGAGGATATGGAGAAATCAGAGGCCGTACATCACCAAGTCATAGATGTCTTGACACCGCTCT TCAAAATTATTGGAGATGAGATTGGGTTACGGTTGCCACAAAAACTAAACGAGATCAAACAATTTATCCTTC AAAAGACAAACTTCTTCAATCCGAACAGGGAATTCGACTTCCGCGATCTCCACTGGTGCATTAACCCACCTA GTAAGATCAAGGTGAATTTTACTAATTACTGYGATACAATTGGGATCAGAAAATCTATTGCATCGGCAGCAA ATCCCATCCTTTTATCAGCACTCTCCGGAGGCAGAGGTGACATATTCCCACCATACAGATGCAGTGGAGCTA CTACTTCAGTAGGCAGAGTTTTCCCCCTATCAGTATCATTRTCCATGTCTTTGATMTCAAGAACATCAGAGAT AATCAATATGCTAACCGCTATCTCAGACGGAGTGTATGGTAAAACTTATTTGCTAGTGCCTGATTATATTGA AGGGGAGTTCGACACGCAAAAGATTCGAGTCTTTGAGATAGGGTTCATCAAACGGTGGCTGAATRACATG CCATTACTCCAGACAACCAACTATATGGTCCTCCCGGAGAMTTCCAAAGCCAAGGTATGTACTATAGCAGTG GGCGAGTTGACACTRGCTTCCTTGTGTGTAGATGAGAGCACCGTATTGTTATATCATGACAGCAATGGTTC ACAAGATGGTATTCTAGTAGTGACRCTGGGAATATTTGGGGCAACACCTATGGATCAAGTTGAAGAGGTG ATACCTGTCGCTCACCCATCAGTRGARAAAATACATATAACAAATCACCGTGGGTTCATAAAAGATTCAATA GCAACCTGGATGGTGCCTGCATTGGTCTCTGAGAAACAAGAGGAACAAAAAAATTGTCTGGAGTCGGCTT GTCAAAGAAAAWCCTACCCTATGTGCAACCAAACGTCATGGGAACCCTTTGGAGGAGGACAGTTGCCATCT TATGGGCGGTTGACATTACCTCTAGATCCAAGCATTGACCTTCAACTTAACATATCATTTACATACGGTCCG GTTATACTGAATGGAGACGGTATGGATTATTATGAAAGCCCACTTTTGGACTCCGGATGGCTTACCATTCCT CCCAAGAACGGAACAGTCCTTGGATTGATAAACAAAGCAAGTAGAGGAGACCAGTTCACTGTAATCCCCCA TGTGTTGACATTTGCGCCCAGGGAATCAAGTGGAAATTGTTATTTACCTATTCAAACATCCCAGATTATGGA TAAAGATGTCCTTACTGAGTCCAATTTAGTGGTGTTGCCTACACAGAATTTTAGATATGTCATAGCAACATA TGATATATCCCGGGGCGATCATGCRATTGTTTATTATGTTTATGACCCAATCCGGACGATTTCTTATACRTAC CCATTTAGACTAACTACCAAGGGTAGACCTGATTTCCTAAGGATTGAATGTTTTGTGTGGGATGACGATTT GTGGTGTCACCAATTTTACCGATTCGAGGCTGACATCACCAACTCTACAACCAGTGTTGAGAATTTAGTCCG TATAAGATTCTCATGTAACCGTTCA

Table 2. Consensus sequences for N, P, C, M, F, H, and L amino acids.

N (Alignment of 536 Sequences)
MASLLKSLTLFKRTRDQPPLASGSGGAIRGIKHVIIVLIPGDSSIVTRSRLLDRLVRLVGDPEINGPKLTGILISILSLF VESPGQLIQRIIDDPDVSIKLVEVIPSINSVCGLTFASRGASLDSEADEFFKIVDEGSKAQGQLGWLENKDIVDIEV DDAEQFNILLASILAQIWILLAKAVTAPDTAADSEMRRWIKYTQQRRVVGEFRMNKIWLDIVRNRIAEDLSLRRF MVALILDIKRSPGNKPRIAEMICDIDNYIVEAGLASFILTIKFGIETMYPALGLHEFSGELTTIESLMMLYQQMGET APYMVILENSVQNKFSAGSYPLLWSYAMGVGVELENSMGGLNFGRSYFDPAYFRLGQEMVRRSAGKVSSALAAE LGITKEEAQLVSEIASKTTEDRTIRXAGPKQSQITFLHSERSEVTNQQPPTINKRSENQGGDKYPIHFXDERFPGY TPDVNSSEWSESRYDTQTIQDDGNDDDRKSMEAIAKMRMLTKMLSQPGTSEESSPVYNDRELLN*
P (Alignment of 417 Sequences)

MAEEQAYHVSKGLECLKALRENPPDIEEIQEVSSIRDQTRNPGQENGTASMQEEEVSQDLDESHEPAKGSNYV
GHVLQNNPGCGESNTALVEAEQPAKDDIQPGPGIRCYHVYDHSGEEVKGIEDADSLVVPAGAVSNRGFERGE
GSLDDSTEDSGEDYSEGNASSNWGYSFGLKPDRAADVSMLMEEELSALLXTSRNVGIQKRDGKTLQFPHNPEG
KTXDPECGSIKKGTGERSASHGMGIVAGSTNGATQSAXKSTGGSSGPSVSAENVRQPAMXAKMTQKCKPESGT
QLPPRTSNEAESDSEYDDELFSEIQEIRSAITKLTEDNQAILSKLDTLLLLKGETDSIKKQISKQNIAISTIEGHLSSI
MIAIPGFGKDTGDPTANVDINPELRPIIGRDSGRALAEVLKQPASSRGNRKDSGIALGSKGQLLRDLQLKPIDKES
SSAIGYKPKDTAPSKAVLASLIRSSRVDQSHKHNMLALLKNIKGDDNLNEFYQMIKSITHA*

C (Alignment of 406 Sequences)

MSXKGWNASKPSERILLTLRRFKRSAASETKPATQAKRMEPQACRKXRSLRISMNHTSQQKDQTMSAMYSKIIRD
VERATLRLWRQSSPLKMTSNQDLEYDVIMFMITAVKRLRESKMLTVSWYLQALSVIEDSREEKEALMIALRILAKII
PXEMLHLTGDILSALNQTEQLM*

M (Alignment of 262 Sequences)

MTEVYDFDQSSWDTKGSLAPILPTTYPDGRLVPQVRVIDPGLGDRKDECFMYIFLLGIIEDNDGLGPPIGRTFGS
LPLGVGRTTARPEELLKEATLLDIVVRRTAGVKEQLVFYNNTPLHILTPWKKVLTSGSVFSANQVCNAVNLIPLD
IAQRFRVVYMSITRLSDDGSYRIPRGMFEFRSRNALAFNILVTIQVEGDVCSSRGNLSMFKDHQVTFMVHIGNFSR
KKNQAYSADYCKLKIEKMGLVFALGGIGGTSLHIRCTGKMSKALNAQLGFKKILCYPLMEINEDLNRFLWRLEC
KIVRIQAVLQPSVPQDFRIYNDVIISDDQGLFKIL*

F (Alignment of 595 Sequences)

MHNKIPKXSKXXXHTXQDXXQQHSTXSXETKTSQXRHSITSAQRSTXHGPRTSDRPVHYIMNRTRSCKQXSXRS
DNIPXHXDHEGIIHHTPESVXQGAXSXFKRRQSNATXSGSQCTWLVLWCIGIASLFLCSKAQIHWNNLSTIGIIGT
DSVHYKIMTRPSHQYLVIKLMPNVSLIDNCTKAELGEYEKLLNSVLEPINQALTLMTKNVKPLQSVGSGRRQRRF
AGVVLAGAALGVATAAQITAGIALHQSNLNAQAIQSLRTSLEQSNKAIEEIREATQETVIAVQGVQDYVNNELV
PAMQHMSCELVGQRLGLKLLRYYTELLSIFGPSLRDPISAEISIQALSYALGGEIHKILEKLGYSGNDMIAILESRGI
KTKITHVDLPGKLIILSISYPTLSEVKGVIVHRLEAVSYNIGSQEWYTTVPXYVATNGYLISNFDESSCVFVSESAICS
QNSLYPMSPJLQQCIRGDTSSCARTLVSGTMGNKFILSKGNIVANCASILCKCYSTSTIINQSPDKLLTFIASDTCPLV
EIDGVTIQVGGRQYPDMVYESKVALGPAISLERLDVGTNLGNALKKLDDAKVLIDSSNQILETVRRSSFNFGSLL
SVPILICTALALLLLIYCCKRRYQQTXKXNTKVDPTFKPDLTGTSKSYVRSL*

H (Alignment of 1797 Sequences)

MHNKIPKXSKXXXHTXQDXXQQHSTXSXETKTSQXRHSITSAQRSTXHGPRTSDRPVHYIMNRTRSCKQXSXRS
DNIPXHXDHEGIIHHTPESVXQGAXSXFKRRQSNATXSGSQCTWLVLWCIGIASLFLCSKAQIHWNNLSTIGIIGT
DSVHYKIMTRPSHQYLVIKLMPNVSLIDNCTKAELGEYEKLLNSVLEPINQALTLMTKNVKPLQSVGSGRRQRRF
AGVVLAGAALGVATAAQITAGIALHQSNLNAQAIQSLRTSLEQSNKAIEEIREATQETVIAVQGVQDYVNNELV
PAMQHMSCELVGQRLGLKLLRYYTELLSIFGPSLRDPISAEISIQALSYALGGEIHKILEKLGYSGNDMIAILESRGI
KTKITHVDLPGKLIILSISYPTLSEVKGVIVHRLEAVSYNIGSQEWYTTVPXYVATNGYLISNFDESSCVFVSESAICS
QNSLYPMSPJLQQCIRGDTSSCARTLVSGTMGNKFILSKGNIVANCASILCKCYSTSTIINQSPDKLLTFIASDTCPLV
EIDGVTIQVGGRQYPDMVYESKVALGPAISLERLDVGTNLGNALKKLDDAKVLIDSSNQILETVRRSSFNFGSLL
SVPILICTALALLLLIYCCKRRYQQTXKXNTKVDPTFKPDLTGTSKSYVRSL*

L (Alignment of 224 Sequences)

MDSVSVNQILYPEVHLDSPIVTNKLVAILEYARIRHNYQLLDTTLVRNIKERISEGLSNQMIINCIEIGSIVNQTLLS
YPKHNHVIYPNCNKLLFHAQDRVISLRLRNIFKRGNSIYSKITDGVKXCLNDINLSIGLGXALDKTIGAKIDEAGI
IMQSSQWFEPFLLWFTIKTEMRSVIKSSTHNCRKRRQNPVFVKGESFNVLVSRDLVCIIDLTSHNVYYLTFEMVLM
YCDVIEGRLMTDTAMAIDQRYSTLHVRIRYLWDLIDGFFPDLGNSTYQLVALLEPLSLAYLQLKDITFSLRGAFLS
HCFAEIQEILQDNGFYTEETFQTLTQALDFVFITEDIHITGEIFSFFRSFGHPRLEAITAAENVRKHMNQPKVVSY
ETMMKGHAIFCGIIINGYRDRHGGTWPPMDLPVHASPIIRNAHASGEGITYSQCIENWKSFAGIRFKCFMPLSLDS
DLTMYLKDKALAALKKEWDSVYPKEFLRYNPPRSTESRRLVNVFLEDSQFDPYNMIMYVISGQYLEDPDFNLSY
SLKEKEIKEVGRLFAKMTYKMRACQVIAENLISNGIGKYFKDNGMAKDEHDLTKALHTLAVSGVPKDKKDSH
RGLTNQRKSXKPAPYRGALHSVSSPSSRYIDPNPNFCTSRREDNDIEIYETVSAFITTDLKKYCLNWRYETISIFAQR
LNEIYGLPSFFQWLHRRLEQSILYVSDPHCPPDLDRHVDLNTAPNSQIFIKYPMGGVEGYCQKLWTISTIPYLYLA
AHESGVRIASLVQGDNQTIAVTKRVPSTWSYALKKSEASRVTTEYFIALRQRLHDVGHHLKANETIISSHFFVYSK
GIYYDGMLISQSLKSIARCVFWSETIVDETRAACSNISTTLAKAIEKGFDRYLAYALNILKIIQQVLISLGFTINSAMT
RDVIEPLLQDHCLLTKMAILPAPIGGLNYLNMSRLFVRNIGDPVTSSIADLKRMIRSGLLGVEILHQVMTQYPGDS
SYLDWASDPYSANLPCVQSITRLLKNITARHVLINSPNPMLKGLFHDESQDEDEALAAFLMDRKIIIPRAAHEILD
NTITGAREAIAGMLDTTKGLIRASMKRGGLTPRIINRLSTYDYEQFRAGIRLLSGKGHDPLIDQDSCSVQLARALR
NHMWAKLAKGRPIYGLEVPDILESMKGYMIRRHESCLLCASGSHNYGWFFVPANCQLDSITEGTSALRVPYIGST
TEERTDMKLAFVKSPSRSLKSAVRIATVYSWAYGDDDESWQEAWTLAKQRANISLEELRMITPISTSTNLAHRLR
DKSTQVKYSGTSLIRVARYATISNDNLSFVIADKKVDTNFIYQQGMLLGLGILEHLFRLSSTTGDSNTVLHLHVET
DCCVIPMSDHPRVPGLRKVVIPRNICTNPLIYDSNPIIEKDAVRLYNQSHRKHIVEFVTWTTGQLYHVLAKSTAMS
MVEMITKFEKDHLNEVSALIGDDDINSFITEFLLVEPRLFTVYLGQCAAINWGFEIHYHRPSGKYQMGELLFSFLS
RMSKGVFKILTNALSHPKVYRRFWDSGMIEPVHGPSLDSQNLHITVCNLIYNCYMIYLDLLLNDELDDFSFILCES
DEDVIPERFDNIQARHLCILSDLYCNPRDCPQIRGLTPTQKCAVLSRYLKSKALESHVGLTWNDKPILIDQYSCSL
TYLRRGSIKQIRLRVDPGFITDAVGCLEKRPLRKSPISKASELKSEFDPPKDDLAKLLSQLSTRTHNLPITGLGVRN
YEVHSFRRIGINSTACYKAVEIVSVIKNEFTSEEHGLFLGEGSGAMLTVYKELLRLSRCYYNSGVSVESRTGQREIS
PYPSEVSLVEHQLGLDKLVTVLFNGRPEVTWVGSVDCYKYILSQISASSLGLIHSDIESLPDKDIIEKLEELSAILSM
TLILGKVGSVLVIKIMPASGDWVQGFILYALPHFLRSFIXYPRYSNFVSTEAYLVFTGLRAGRLVNPEGIKQQILRV
GIRTSPGLVGHILSSKQTACVQSLHGPPFQAKSFNPYLQGLTSIEKVLINCGLTINGLKVCKNLLHHDISSGEEGL

KGSITILYRELARFKDNHQXSHGMFHAYPVLIASQERELVSIIARKYCGYILLYSGDLYEITRIVRNLKANHIIFDLH
RNLFMDNLSRSDRSLILTTIPKKNWLFQLETKEIKEWFKLLGYSALIRNH*

Table 3. Fully conserved amino acids of Canine Distemper Virus.

N											P				
8	111	127	137	146	161	168	488	498	503	506	3	4	5	8	9
P	L	Q	H	F	P	D	F	L	A	L	E	E	Q	H	V
11	12	14	15	17	19	20	22	23	25	28	36	42	52	55	62
K	G	E	C	K	L	R	N	P	D	E	R	P	Q	E	E
69	76	92	94	105	108	109	112	113	114	115	116	117	118	119	139
G	V	E	E	P	R	C	V	Y	D	H	S	G	E	E	R
153	155	157	160	163	165	167	169	173	178	181	182	188	189	194	196
E	S	E	S	N	S	N	G	G	R	D	V	E	E	L	T
207	210	213	226	229	230	232	238	246	250	252	253	255	260	267	272
G	L	P	G	K	K	T	S	G	G	T	Q	A	G	V	V
274	275	282	283	285	286	288	290	292	299	300	304	305	306	309	310
Q	P	T	Q	C	K	E	G	Q	N	E	D	S	E	D	E
345	347	348	349	351	352	353	354	355	356	357	359	360	361	362	363
E	D	S	I	K	Q	I	S	K	Q	N	A	I	S	T	I
364	365	366	367	368	369	370	372	373	374	375	376	378	391	392	394
E	G	H	L	S	S	I	I	A	I	P	G	G	N	P	L
395	396	397	398	399	400	401	402	403	404	406	409	410	411	413	414
R	P	I	I	G	R	D	S	G	R	L	V	L	K	P	A
416	417	421	422	427	428	429	430	432	434	436	437	438	439	440	441
S	R	K	D	L	G	S	K	Q	L	D	L	Q	L	K	P
442	446	447	448	449	451	452	453	454	456	457	459	460	461	462	463
I	S	S	S	A	G	Y	K	P	D	T	P	S	K	A	V
464	465	466	467	468	469	470	471	474	475	478	479	480	481	482	484
L	A	S	L	I	R	S	S	D	Q	K	H	N	M	L	L
P														C	
485	486	489	490	492	494	496	497	499	500	503	504	505	506	2	5
L	K	K	G	D	L	E	F	Q	M	S	I	T	H	S	G
8	9	13	15	16	18	21	25	32	40	42	51	52	54	55	56
A	S	E	I	L	T	T	S	P	E	Q	R	I	M	N	H
59	60	62	63	67	68	69	76	77	79	81	83	84	96	98	100
Q	Q	D	Q	A	M	Y	V	E	A	L	L	W	Q	L	Y
101	102	103	104	105	106	108	110	111	112	113	119	122	145	148	153
D	V	I	M	F	M	T	V	K	R	L	L	S	L	L	P
C							M								
155	156	158	159	160	161	162	2	3	5	6	7	8	10	11	12
E	M	H	L	T	G	D	T	E	Y	D	F	D	S	S	W
15	16	18	20	21	22	23	25	26	28	29	30	31	33	34	35
K	G	L	P	I	L	P	T	Y	D	G	R	L	P	Q	V
36	37	38	39	40	41	42	43	44	46	47	48	49	51	52	54
R	V	I	D	P	G	L	G	D	K	D	E	C	M	Y	F
59	61	63	66	67	68	69	70	71	72	73	74	76	77	78	79
I	D	D	G	P	P	I	G	R	T	F	G	L	P	L	G
80	81	83	85	86	87	88	89	90	91	92	93	95	96	97	98
V	G	T	A	R	P	E	E	L	L	K	E	T	L	L	D
99	102	103	104	105	106	108	109	110	111	112	113	114	115	116	117
I	R	R	T	A	G	K	E	Q	L	V	F	Y	N	N	T
118	119	120	121	122	123	124	125	126	127	128	129	130	132	133	134
P	L	H	I	L	T	P	W	K	K	V	L	T	G	S	V
135	136	137	138	139	140	141	142	144	145	146	147	148	149	150	152
F	S	A	N	Q	V	C	N	V	N	L	I	P	L	D	A
153	155	156	158	159	160	161	162	163	165	166	167	169	170	171	174
Q	F	R	V	Y	M	S	I	T	L	S	D	G	S	Y	P
175	176	180	181	182	184	185	186	187	188	190	191	192	193	194	196
R	G	F	R	S	N	A	L	A	F	I	L	V	T	I	V
198	199	204	205	207	209	212	214	216	217	218	221	222	223	224	226
G	D	R	G	L	M	D	Q	T	F	M	I	G	N	F	R
229	230	231	232	233	234	235	236	237	238	240	241	242	245	246	247
N	Q	A	Y	S	A	D	Y	C	K	K	I	E	G	L	V
248	249	250	251	252	253	254	255	258	259	260	262	263	264	265	268
F	A	L	G	G	I	G	G	L	H	I	C	T	G	K	K
270	271	272	273	274	276	278	279	280	281	282	283	284	286	287	288
L	N	A	Q	L	F	K	I	L	C	Y	P	L	E	I	N
289	292	293	295	296	297	299	300	302	305	306	308	309	311	314	317
E	N	R	L	W	R	E	C	I	I	Q	V	L	P	P	F

M												F			
318	320	321	322	323	324	328	330	331	332	333	335	133	135	136	137
R	Y	N	D	V	I	D	G	L	F	K	L	S	A	Q	I
138	141	142	144	145	146	147	148	153	154	155	156	158	160	165	166
H	N	L	T	I	G	I	I	V	H	Y	K	M	R	Y	L
168	169	172	173	175	179	180	181	185	187	188	189	190	191	196	198
I	K	P	N	S	N	C	T	L	E	Y	E	K	L	L	P
203	205	213	218	220	222	224	227	231	232	235	236	238	239	240	242
L	L	L	S	R	Q	R	G	A	G	L	G	A	T	A	Q
245	246	248	249	251	256	257	258	266	267	270	273	276	277	282	286
A	G	A	L	Q	A	Q	A	L	E	N	I	I	R	E	A
287	288	289	294	297	301	304	309	312	316	318	319	321	322	323	324
V	Q	G	V	E	A	H	L	Q	L	L	L	Y	Y	T	E
326	327	329	330	331	332	333	335	336	339	340	342	343	344	345	346
L	S	F	G	P	S	L	D	P	A	E	S	I	Q	A	L
348	350	351	353	357	358	359	361	362	363	365	367	370	371	373	376
Y	L	G	E	I	L	E	L	G	Y	G	D	A	I	E	G
377	381	382	384	385	388	391	393	396	397	398	400	401	403	405	406
I	I	T	V	D	G	I	L	S	Y	P	L	S	V	G	V
411	412	414	415	417	418	420	421	423	424	428	430	432	433	437	442
L	E	V	S	N	I	S	Q	W	Y	P	Y	A	T	L	D
444	446	453	455	461	462	469	472	474	475	479	485	486	488	489	490
S	C	A	C	Y	P	Q	R	D	T	A	G	T	G	N	K
492	495	496	500	502	503	504	505	506	510	511	521	522	523	528	529
I	K	G	A	C	A	S	I	L	Y	S	D	K	L	A	S
530	534	536	537	541	543	549	550	551	553	555	558	559	562	563	564
D	L	E	I	T	Q	Y	P	D	V	E	V	A	P	A	I
565	569	571	572	573	574	575	578	579	581	585	586	588	591	596	601
S	L	V	G	T	N	L	A	L	K	A	K	L	S	L	R

F											H				
606	615	632	648	651	652	653	657	658	659	661	6	10	138	184	319
F	L	R	K	L	T	G	S	Y	V	S	D	A	W	P	T

H								L							
406	431	466	508	533	535	562	579	2	5	7	8	9	10	11	12
Y	I	A	S	A	V	L	Y	D	S	N	Q	I	L	Y	P
16	17	18	19	21	22	23	24	26	28	29	30	31	32	33	34
L	D	S	P	V	T	N	K	V	I	L	E	Y	A	R	I
36	38	40	42	45	48	49	51	52	53	58	59	60	62	63	67
H	Y	L	D	L	N	I	E	R	I	S	N	Q	I	I	E
69	73	74	75	76	77	78	80	84	87	88	89	90	91	94	95
G	N	Q	T	L	L	S	P	H	Y	P	N	C	N	L	F
96	99	103	104	106	107	110	111	113	114	115	116	117	118	119	121
H	D	S	L	L	R	F	K	G	N	S	I	Y	S	K	T
122	123	125	127	128	136	137	138	143	150	151	153	154	156	158	159
D	G	K	C	L	G	L	G	K	D	E	G	I	M	S	S
160	162	163	164	165	166	167	168	169	170	171	172	173	174	175	176
Q	F	E	P	F	L	L	W	F	T	I	K	T	E	M	R
177	178	179	180	181	184	185	186	187	188	189	191	195	196	199	200
S	V	I	K	S	H	N	C	R	K	R	Q	F	V	E	S
203	204	205	207	208	209	210	211	213	214	220	221	222	224	225	226
V	L	V	R	D	L	V	C	I	D	V	Y	Y	T	F	E
227	229	230	231	233	235	236	237	238	239	240	241	242	243	245	246
M	L	M	Y	D	I	E	G	R	L	M	T	D	T	M	A
248	250	251	254	255	260	261	262	264	265	266	267	268	269	271	272
D	R	Y	L	H	Y	L	W	L	I	D	G	F	F	D	L
273	274	276	277	279	280	281	282	283	284	285	286	288	289	290	291
G	N	T	Y	L	V	A	L	L	E	P	L	L	A	Y	L
292	293	295	297	298	300	302	303	304	305	307	308	309	311	312	313
Q	L	D	T	F	L	G	A	F	L	H	C	F	E	I	Q
315	316	320	321	322	323	325	326	327	329	330	331	333	334	336	338
I	L	G	F	Y	T	E	T	F	T	L	T	A	L	F	F
340	341	342	343	344	345	346	347	348	349	381	382	384	386	387	388
T	E	D	I	H	I	T	G	E	I	S	Y	T	M	K	G
389	390	391	392	393	394	396	397	398	399	401	402	403	404	405	406
H	A	I	F	C	G	I	I	N	G	R	D	R	H	G	G
407	408	409	410	413	414	416	418	419	421	422	423	424	427	428	429
T	W	P	P	L	P	H	S	P	I	R	N	A	S	G	E
430	431	432	433	434	435	436	438	439	440	442	443	445	448	450	451
G	I	T	Y	S	Q	C	E	N	W	S	F	G	F	C	F

452	454	456	457	458	459	460	461	462	463	464	465	466	467	468	469
M	L	L	D	S	D	L	T	M	Y	L	K	D	K	A	L
470	471	472	475	476	477	478	479	480	481	484	485	486	487	489	490
A	A	L	E	W	D	S	V	Y	P	F	L	R	Y	P	P
492	493	494	495	496	497	498	499	500	501	502	504	505	508	509	510
S	T	E	S	R	R	L	V	N	V	F	E	D	F	D	P
511	513	514	516	517	520	522	525	526	527	528	529	530	531	532	533
Y	M	I	Y	V	G	Y	D	P	D	F	N	L	S	Y	S
534	535	536	537	538	539	540	541	542	543	544	545	546	547	548	549
L	K	E	K	E	I	K	E	V	G	R	L	F	A	K	M
550	551	552	553	554	555	556	557	558	559	560	561	562	563	564	565
T	Y	K	M	R	A	C	Q	V	I	A	E	N	L	I	S
566	567	569	570	571	572	573	574	575	576	577	578	579	580	581	582
N	G	G	K	Y	F	K	D	N	G	M	A	K	D	E	H
583	584	585	586	588	590	591	592	593	594	595	596	597	598	599	600
D	L	T	K	L	T	L	A	V	S	G	V	P	K	D	K
601	605	606	627	640	642	643	644	652	653	654	655	656	657	659	660
K	R	G	S	F	T	S	R	I	Y	E	T	V	S	F	I
661	662	663	664	665	666	667	668	669	670	671	672	673	674	675	676
T	T	D	L	K	K	Y	C	L	N	W	R	Y	E	T	I
677	679	680	681	682	684	685	686	687	688	689	690	691	692	693	694
S	F	A	Q	R	N	E	I	Y	G	L	P	S	F	F	Q
695	696	697	698	699	700	701	702	703	705	706	707	709	710	711	712
W	L	H	R	R	L	E	Q	S	L	Y	V	D	P	H	C
713	714	715	716	719	722	727	728	729	730	731	732	734	735	736	737
P	P	D	L	H	L	N	S	Q	I	F	I	Y	P	M	G
738	739	740	741	742	743	744	745	746	747	748	749	751	752	753	754
G	V	E	G	Y	C	Q	K	L	W	T	I	T	I	P	Y
755	756	757	758	759	761	762	763	764	765	766	767	768	769	770	771
L	Y	L	A	A	E	S	G	V	R	I	A	S	L	V	Q
772	773	774	775	776	777	778	779	780	781	782	783	784	785	786	787
G	D	N	Q	T	I	A	V	T	K	R	V	P	S	T	W
789	791	792	793	795	796	797	798	799	800	810	811	812	814	815	816
Y	L	K	K	E	A	S	R	V	T	R	L	H	V	G	H
817	818	819	820	821	822	823	824	827	828	829	831	832	833	834	835
H	L	K	A	N	E	T	I	S	H	F	V	Y	S	K	G
836	838	839	840	854	855	856	857	858	859	860	861	862	863	864	865
I	Y	D	G	V	F	W	S	E	T	I	V	D	E	T	R
866	867	868	869	870	871	872	873	874	875	876	877	878	879	880	881
A	A	C	S	N	I	S	T	T	L	A	K	A	I	E	K
882	885	887	888	889	891	892	896	897	898	899	900	901	903	904	905
G	R	L	A	Y	L	N	I	I	Q	Q	V	L	S	L	G
906	907	908	909	910	912	913	915	916	919	920	925	926	927	928	929
F	T	I	N	S	M	T	D	V	P	L	C	L	L	T	K
931	934	935	936	938	939	941	942	943	944	945	946	947	948	949	950
A	P	A	P	G	G	N	Y	L	N	M	S	R	L	F	V
951	952	953	954	955	956	957	958	959	960	962	963	964	965	966	967
R	N	I	G	D	P	V	T	S	S	A	D	L	K	R	M
968	970	973	974	977	978	979	981	982	983	984	986	987	988	989	991
I	S	L	G	I	L	H	V	M	T	Q	P	G	D	S	Y
992	993	994	995	996	997	998	999	1000	1001	1002	1003	1004	1005	1007	1008
L	D	W	A	S	D	P	Y	S	A	N	L	P	C	Q	S
1009	1010	1011	1012	1013	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023	1024
I	T	R	L	L	K	N	I	T	A	R	H	V	L	I	N
1025	1026	1028	1029	1030	1032	1035	1036	1038	1039	1041	1042	1043	1044	1045	1046
S	P	P	M	L	G	H	D	S	Q	E	D	E	A	L	A
1047	1048	1049	1050	1051	1052	1035	1036	1053	1055	1056	1057	1058	1059	1060	1061
A	F	L	M	D	R	H	D	K	I	I	P	R	A	A	H
1062	1063	1064	1065	1067	1069	1070	1071	1072	1073	1074	1075	1077	1078	1079	1080
E	I	L	D	T	T	G	A	R	E	A	I	G	M	L	D
1081	1082	1083	1084	1085	1086	1087	1089	1090	1092	1093	1094	1095	1096	1097	1098
T	T	K	G	L	I	R	S	M	R	G	G	L	T	P	R
1100	1103	1104	1105	1106	1107	1108	1109	1110	1111	1112	1113	1115	1116	1117	1119
I	L	S	T	Y	D	Y	E	Q	F	R	A	I	R	L	S
1120	1121	1124	1126	1127	1128	1130	1131	1132	1133	1134	1135	1136	1137	1138	1139
G	K	D	L	I	D	D	S	C	S	V	Q	L	A	R	A
1140	1141	1142	1143	1144	1145	1146	1149	1150	1151	1154	1155	1156	1157	1158	1159
L	R	N	H	M	W	A	A	K	G	I	Y	G	L	E	V
1160	1161	1163	1164	1165	1166	1168	1171	1172	1173	1175	1176	1177	1180	1183	1184

P	D	L	E	S	M	G	I	R	R	E	S	C	C	G	S
1186	1187	1188	1190	1191	1193	1194	1196	1197	1198	1199	1201	1202	1203	1204	1205
N	Y	G	F	F	P	A	C	Q	L	D	I	T	E	G	T
1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1219	1220	1221
S	A	L	R	V	P	Y	I	G	S	T	T	E	E	R	T
1223	1224	1225	1227	1228	1229	1231	1232	1233	1234	1235	1236	1237	1238	1239	1240
M	K	L	F	V	K	P	S	R	S	L	K	S	A	V	R
1241	1242	1243	1244	1245	1246	1247	1248	1249	1250	1251	1252	1255	1256	1258	1259
I	A	T	V	Y	S	W	A	Y	G	D	D	S	W	E	A
1260	1262	1263	1265	1266	1267	1269	1272	1273	1274	1275	1276	1277	1278	1279	1280
W	L	A	Q	R	A	I	E	E	L	R	M	I	T	P	I
1281	1282	1283	1284	1286	1287	1288	1289	1290	1291	1292	1294	1295	1296	1297	1298
S	T	S	T	L	A	H	R	L	R	D	S	T	Q	V	K
1299	1300	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310	1312	1313	1314	1315
Y	S	G	T	S	L	I	R	V	A	R	Y	T	I	S	N
1316	1317	1318	1319	1320	1322	1324	1325	1326	1327	1328	1329	1330	1331	1332	1333
D	N	L	S	F	I	D	K	K	V	D	T	N	F	I	Y
1334	1335	1336	1337	1338	1339	1340	1341	1342	1344	1345	1346	1348	1349	1350	1351
Q	Q	G	M	L	L	G	L	G	L	E	H	F	R	L	S
1354	1358	1360	1361	1362	1364	1365	1367	1368	1369	1370	1371	1372	1373	1376	1377
T	N	V	L	H	H	V	T	D	C	C	V	I	P	D	H
1378	1380	1384	1387	1393	1394	1396	1397	1398	1399	1400	1403	1404	1405	1407	1408
P	V	R	V	C	T	P	L	I	Y	D	P	I	I	K	D
1409	1411	1412	1413	1414	1415	1418	1419	1420	1421	1423	1424	1426	1427	1429	1431
A	R	L	Y	N	Q	R	K	H	I	E	F	T	W	T	Q
1432	1433	1434	1435	1436	1437	1438	1439	1440	1441	1442	1443	1445	1446	1447	1448
L	Y	H	V	L	A	K	S	T	A	M	S	V	E	M	I
1449	1450	1451	1453	1454	1455	1456	1457	1458	1459	1461	1462	1464	1465	1466	1467
T	K	F	K	D	H	L	N	E	V	A	L	G	D	D	D
1468	1469	1470	1471	1473	1474	1475	1476	1477	1478	1480	1481	1482	1483	1484	1485
I	N	S	F	T	E	F	L	L	V	P	R	L	F	T	V
1487	1488	1489	1490	1491	1492	1493	1494	1495	1496	1497	1498	1500	1501	1502	1503
L	G	Q	C	A	A	I	N	W	G	F	E	H	Y	H	R
1504	1505	1506	1507	1508	1509	1510	1511	1512	1513	1514	1515	1516	1517	1518	1519
P	S	G	K	Y	Q	M	G	E	L	L	F	S	F	L	S
1520	1521	1522	1523	1524	1525	1526	1527	1528	1531	1532	1533	1534	1535	1536	1538
R	M	S	K	G	V	F	K	I	N	A	L	S	H	P	V
1539	1540	1541	1542	1543	1544	1545	1546	1548	1549	1550	1552	1553	1554	1555	1556
Y	R	R	F	W	D	S	G	I	E	P	H	G	P	S	L
1557	1559	1560	1561	1562	1563	1564	1565	1566	1567	1568	1569	1570	1571	1572	1573
D	Q	N	L	H	I	T	V	C	N	L	I	Y	N	C	Y
1574	1575	1576	1577	1578	1579	1580	1581	1582	1583	1586	1588	1592	1594	1596	1597
M	I	Y	L	D	L	L	L	N	D	D	F	L	E	D	E
1598	1600	1601	1602	1603	1604	1605	1606	1607	1608	1609	1610	1611	1612	1613	1614
D	I	P	E	R	F	D	N	I	Q	A	R	H	L	C	I
1615	1617	1618	1619	1625	1626	1628	1629	1630	1631	1632	1633	1634	1635	1636	1637
L	D	L	Y	C	P	I	R	G	L	T	P	T	Q	K	C
1639	1640	1643	1645	1648	1649	1650	1652	1654	1655	1656	1657	1658	1659	1660	1661
V	L	Y	K	A	L	E	H	G	L	T	W	N	D	K	P
1662	1664	1665	1666	1667	1668	1669	1670	1671	1672	1673	1674	1675	1676	1677	1678
I	I	D	Q	Y	S	C	S	L	T	Y	L	R	R	G	S
1679	1680	1681	1682	1683	1684	1685	1686	1687	1688	1689	1690	1691	1693	1720	1722
I	K	Q	I	R	L	R	V	D	P	G	F	I	D	P	K
1723	1725	1728	1730	1733	1736	1737	1738	1740	1742	1743	1745	1746	1747	1748	1749
D	L	L	S	S	T	H	N	P	T	G	G	V	R	N	Y
1750	1752	1756	1758	1760	1761	1762	1763	1764	1765	1766	1767	1768	1769	1772	1777
E	H	R	G	N	S	T	A	C	Y	K	A	V	E	S	E
1778	1782	1784	1786	1787	1788	1789	1791	1792	1793	1794	1795	1797	1798	1799	1801
F	E	G	F	L	G	E	S	G	A	M	L	V	Y	K	L
1802	1804	1806	1807	1808	1809	1810	1811	1812	1813	1818	1819	1820	1821	1822	1823
L	L	R	C	Y	Y	N	S	G	V	R	T	G	Q	R	E
1824	1825	1826	1827	1828	1829	1830	1832	1833	1834	1835	1836	1837	1838	1839	1840
I	S	P	Y	P	S	E	S	L	V	E	H	Q	L	G	L
1841	1846	1847	1848	1849	1850	1851	1852	1853	1854	1855	1856	1857	1858	1859	1860
D	V	L	F	N	G	R	P	E	V	T	W	V	G	S	V
1861	1862	1863	1864	1865	1866	1872	1874	1875	1876	1879	1880	1881	1883	1884	1886
D	C	Y	K	Y	I	A	S	L	G	H	S	D	E	S	P
1888	1889	1892	1893	1894	1895	1896	1898	1899	1900	1901	1902	1904	1905	1907	1908
K	D	E	K	L	E	E	S	A	I	L	S	T	L	L	G

1909	1910	1911	1912	1913	1914	1916	1917	1919	1920	1922	1923	1924	1925	1926	1927
K	V	G	S	V	L	I	K	M	P	S	G	D	W	V	Q
1928	1929	1930	1931	1932	1935	1936	1937	1938	1942	1944	1945	1946	1947	1948	1949
G	F	I	L	Y	P	H	F	L	I	Y	P	R	Y	S	N
1952	1953	1954	1955	1956	1957	1958	1959	1961	1962	1963	1964	1965	1966	1967	1969
S	T	E	A	Y	L	V	F	G	L	R	A	G	R	L	N
1970	1971	1972	1973	1974	1975	1976	1977	1979	1981	1982	1983	1984	1985	1986	1987
P	E	G	I	K	Q	Q	I	R	G	I	R	T	S	P	G
1988	1990	1991	1992	1993	1994	1996	1997	2000	2002	2003	2004	2005	2006	2007	2008
L	G	H	I	L	S	K	Q	C	Q	S	L	H	G	P	P
2009	2013	2015	2016	2018	2021	2022	2025	2028	2029	2030	2031	2032	2033	2035	2037
F	S	N	P	L	L	T	E	L	I	N	C	G	L	I	G
2038	2040	2041	2042	2044	2046	2047	2048	2050	2051	2053	2054	2056	2058	2060	2062
L	V	C	K	L	H	H	D	S	S	E	E	L	G	I	I
2066	2067	2068	2069	2072	2079	2081	2085	2086	2087	2090	2092	2093	2095	2096	2099
E	L	A	R	D	G	F	P	V	L	S	E	R	L	V	I
2100	2102	2105	2106	2109	2111	2113	2116	2121	2122	2124	2125	2128	2129	2131	2133
A	K	G	Y	L	S	D	E	V	R	L	K	H	I	F	L
2134	2136	2143	2147	2148	2150	2153	2154	2155	2159	2160	2161	2164	2165	2166	2167
H	N	S	R	S	I	T	I	P	W	L	F	E	T	K	E
2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	
I	K	E	W	F	K	L	L	G	Y	S	A	L	I	R	

Table 4. Most variable amino acids of Canine Distemper Virus.

N		P				C			F								
409	452	195	221	256	278	3	47	154	8	11	12	13	16	19	20	26	28
A	S	R	G	L	S	A	R	R	R	T	L	T	Q	L	P	K	A
F													H				
35	47	70	72	79	81	95	99	101	111	429	637	639	50	178	277	386	530
A	H	A	H	A	G	S	R	R	N	R	L	Q	L	G	N	S	G
L																	
126	139	614	1943	2076													
K/R	D	I	I	F													

DISCUSSION

The NC_001921 sequence is commonly used as the CDV reference genome, the KF640687, AF164967, and EU716337 sequences appear to provide an even better representation of the existing CDV diversity. Therefore, it is suggested that in future studies, one or all of these sequences, in addition to the reference genome, be incorporated into evolutionary analyses and phylogenetic tree construction.

Amino acid residues that remain conserved throughout evolutionary history are generally indispensable for viral fitness, as mutations at these positions may disrupt protein folding, receptor binding, or other essential functions (Cowton et al. 2018). Conserved residues therefore frequently form the structural or functional cores of critical viral epitopes and represent stable targets for immune recognition (Deng et al. 2025). In this study, the M protein was found to be the most conserved (73.35%), with no highly variable residues detected, followed by the L protein (69.58%). While the P protein (38.53%), F protein (33.73%), C protein (32.94%), H protein (2.15%) and N protein (2.10%) has lower conservation rates, respectively. Comparative analysis revealed different levels of amino acid variability among CDV proteins. The M protein, together with the L and N proteins, appeared to be highly conserved, whereas greater heterogeneity was observed in the surface glycoproteins. Specifically, the F protein displayed the highest variability (3.31%), consistent with its role in membrane fusion and its status as a major target of neutralizing antibodies, which suggests strong immune-driven selective pressure. The H protein, should be considered with caution, since even single amino acid substitutions in this protein can substantially affect viral antigenicity and host tropism (Bi et al. 2023; McCarthy et al. 2007; Tao et al. 2020). Protein structure conservation is crucial in epitope mapping, particularly when using mutagenesis methods such as site-directed mutagenesis or alanine scanning (Nilvebrant and

Rockberg 2018). Therefore, the completely conserved proteins shown in this study may be useful for future epitope mapping studies.

Previous studies have reported that certain residues in the H protein has particular importance (Bi et al. 2023; McCarthy et al. 2007; Tao et al. 2020). Residues at positions 530, 542, and 549 in the H protein have been associated with viral tropism (McCarthy et al. 2007; Tao et al. 2020). Similarly, residues at positions 238 and 241 have been linked to viral antigenicity (Bi et al. 2023). In the consensus sequence, position 238 was identified as Y, position 241 as G, position 530 as G, position 542 as I, and position 549 as Y. Proportional data on other residues detected at these positions are presented in Figure 1. Rare substitutions should be interpreted with caution, as they may represent sequencing errors. Among the residues identified as critical, position 530 was classified as highly variable in this study. A total of nine different variants were observed at this position, and models generated to highlight these variants are expected to support further investigations (Figure 2). The location of position 530 within the H protein is also shown in the model (Figure 3). The other four critical residues localized in the H protein were classified as neither highly variable nor completely conserved. Notable differences were also detected at positions 542 and 549, but they were not variable enough to be classified as highly variable, were marked in the H protein model (Figure 3). The 238Y and 241G amino acids in the H protein, associated with antigenicity, were marked in the H protein model (Figure 3).

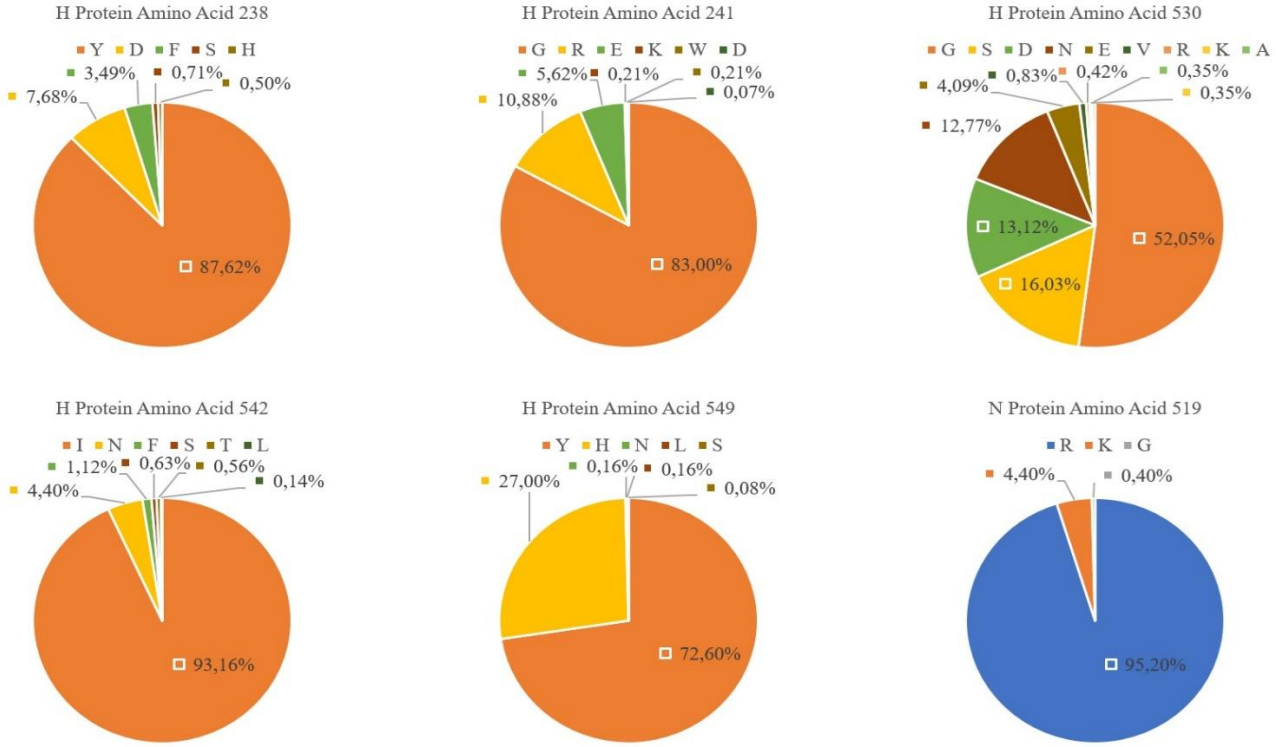

Figure 1: Distributions of variants of critical amino acids

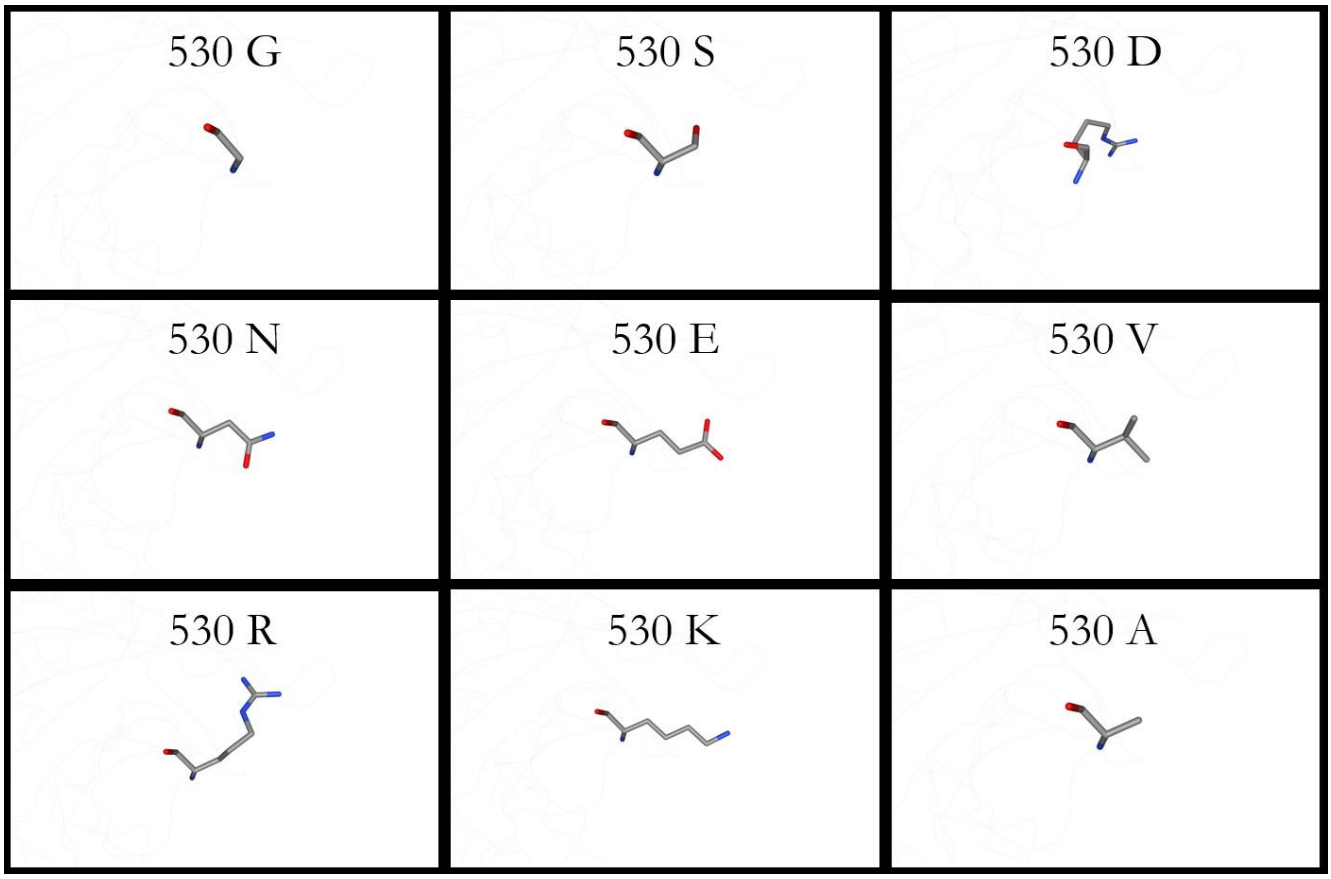

Figure 2: Modeling of variants of the 530th amino acid in the H protein

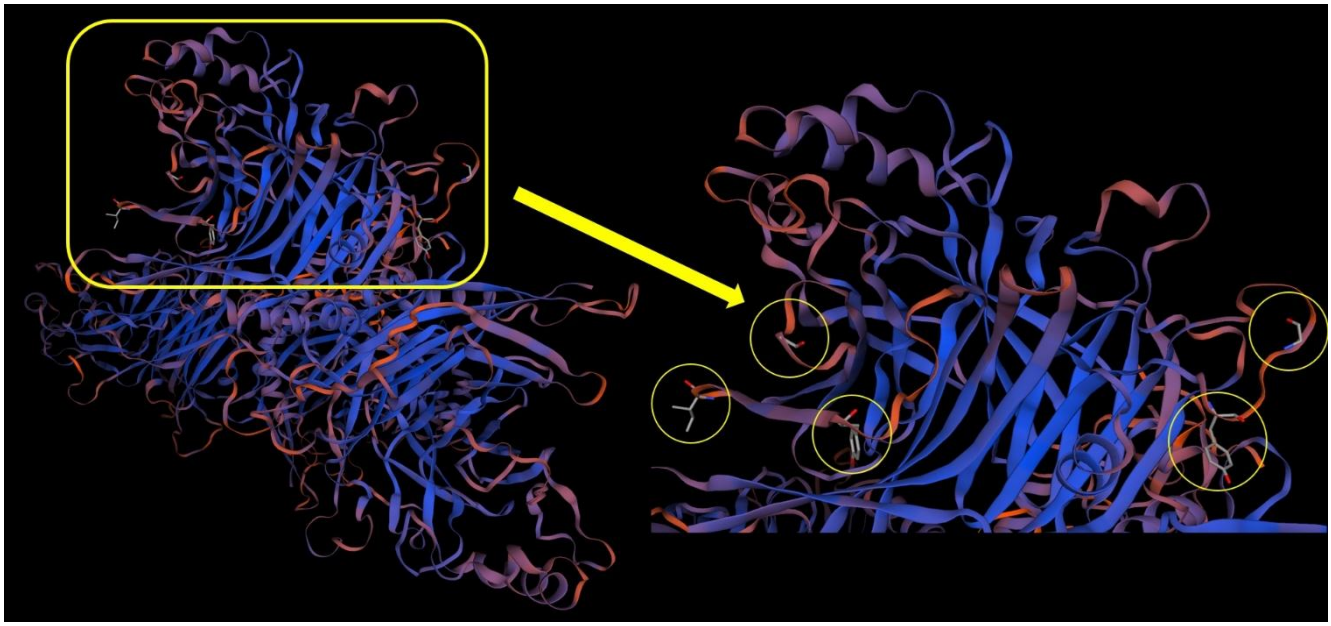

Figure 3: Indication of critical amino acid residues in the H protein model

These findings are expected to contribute to a better understanding of the structure, function, antigenicity, and neutralization mechanisms of the CDV H protein

Residue 519 in the N protein has been reported to be associated with virulence and pathogenicity (Siering et al. 2024). In the consensus sequence, residue 519 was found to be R and was classified as neither highly variable nor completely conserved. The proportional data related to the 519th amino acid are presented in Figure 1. As with the H protein, rare substitutions may represent sequencing errors. Compared to the critical residues in the H protein, residue 519 of the N protein exhibited lower variability. These results are considered valuable for understanding the structure, function, antigenicity, and neutralization mechanisms of the CDV N protein.

CONCLUSION

In conclusion, 2,882 CDV sequences deposited in GenBank up to August 17, 2025 were analysed, and consensus sequences were generated for each gene. The most conserved and the most variable genes were identified, and particular attention was given to residues previously reported to influence viral tropism and antigenicity. Structural models were constructed based on the consensus sequences, with a specific focus on key residues within the H protein. Among these, residue 530 of the H protein, identified as one of the most variable sites and directly associated with viral tropism, was modelled for all observed amino acid variants. The findings of this study are expected to provide valuable insights for vaccine development, epitope mapping, and the monitoring of genetic diversity and antigenic drift in CDV.

Conflict of interest: The authors have no conflicts of interest to report.

Authors' Contributions: SST and MCT contributed to the project idea, design and execution of the study. SST and MCT contributed to the acquisition of data. SST and MCT analysed the data. SST and MCT drafted and wrote the manuscript. SST and MCT reviewed the manuscript critically. All authors have read and approved the finalized manuscript.

Ethical approval: Ethical approval is not required for this study.

Availability of Data and Materials: The data that support the findings of this study are available from the corresponding author on reasonable request.

Declaration of Generative Artificial Intelligence (AI): The authors declare that the article, tables and figures were not written/ created by AI and AI-assisted Technologies.

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