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Review

Feline Calicivirus: An Emerging Companion Animal RNA Virus and Its Implications for Genomic Surveillance, Outbreak Preparedness, and One Health

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Abstract

Feline calicivirus (FCV) is a genetically diverse and rapidly evolving positive-sense RNA virus that remains a major cause of infectious disease in domestic cats worldwide. FCV is classically associated with upper respiratory tract disease and oral ulceration; however, the emergence of highly virulent systemic FCV (VS-FCV) strains has expanded its clinical significance owing to severe multisystemic disease, increased mortality, and frequent outbreaks in shelters, breeding colonies, and veterinary healthcare facilities. Continuous viral evolution driven by mutation, recombination, and immune selection promotes antigenic diversity, prolonged asymptomatic shedding, vaccine escape, and the emergence of novel variants, thereby complicating diagnosis, prevention, and disease control. This review summarizes recent advances in FCV molecular biology, viral evolution, host–virus interactions, pathogenesis, epidemiology, clinical manifestations, diagnostics, vaccination, and emerging antiviral and immunomodulatory therapies. The review also examines the available epidemiological evidence on FCV in India, highlighting reported regional findings, limitations in geographic and genomic coverage, and the need for coordinated surveillance. Within a One Health framework, FCV is considered primarily as an important companion-animal pathogen and a model for strengthening veterinary surveillance, biosecurity, genomic monitoring, and outbreak preparedness, rather than as a confirmed zoonotic threat. By integrating current scientific evidence with identified surveillance and research gaps, this review outlines priorities for improving FCV surveillance, prevention, and control and for strengthening preparedness for emerging companion-animal viral diseases.

Keywords: feline calicivirus; genomic surveillance; molecular epidemiology; vaccine escape; molecular diagnostics

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1. Introduction

Emerging and re-emerging RNA viruses continue to represent a major challenge to global animal and public health because of their rapid evolutionary rates, extensive genetic diversity, and remarkable ability to adapt to changing host and environmental conditions. Although many RNA viruses of public-health concern are zoonotic, companion-animal pathogens such as feline calicivirus (FCV) are primarily important because of their effects on animal health, welfare, and veterinary healthcare systems. A One Health perspective recognizes the interconnectedness of companion animal health, environmental management, veterinary practice, and human activities. The growing companion animal population, increasing international movement of pets, expansion of animal shelters and breeding facilities, and changing patterns of urbanization can facilitate the persistence and dissemination of infectious pathogens within animal populations. Accordingly, strengthening surveillance, biosecurity, and outbreak preparedness for companion-animal diseases can improve veterinary disease control and laboratory capacity, while also providing infrastructure that may be applicable to the surveillance of other emerging pathogens [1].

Among viral pathogens affecting domestic cats, feline calicivirus (FCV) remains one of the most widespread, genetically diverse, and evolutionarily dynamic RNA viruses worldwide. FCV is a non-enveloped, positive-sense single-stranded RNA virus belonging to the genus *Vesivirus* within the family *Caliciviridae*. Similar to many RNA viruses, the lack of proofreading activity in its RNA-dependent RNA polymerase results in a high mutation rate that continuously generates genetically heterogeneous viral populations. Together with homologous recombination and immune-mediated selection, these evolutionary processes facilitate viral persistence, antigenic diversification, vaccine escape, and the emergence of novel variants capable of adapting to changing host populations [2–4].

FCV exhibits substantial genetic and antigenic diversity, and infection may result in prolonged viral shedding, allowing continued transmission within multi-cat populations. Although vaccination reduces clinical disease, protection against infection and shedding is incomplete, contributing to continued circulation of genetically diverse field viruses [3,5]. Molecular epidemiological studies have demonstrated extensive strain diversity within and between feline populations, emphasizing the importance of continued genomic surveillance and characterization of circulating variants [6,7].

Clinically, FCV is recognized as a major cause of feline upper respiratory tract disease, oral ulceration, conjunctivitis, polyarthritis, and chronic gingivostomatitis. However, the emergence of virulent systemic feline calicivirus (VS-FCV) has significantly altered the perception of FCV from a relatively mild respiratory pathogen to one capable of causing severe multisystemic disease characterised by vasculitis, facial oedema, cutaneous ulceration, pneumonia, hepatic dysfunction, and mortality exceeding 50% during outbreaks. Such outbreaks have been reported in veterinary hospitals, shelters, rescue centres, breeding colonies, and multi-cat households, where high animal density, environmental contamination, and prolonged viral shedding facilitate rapid transmission and continuous viral evolution [3,4,8,9].

One of the greatest challenges in FCV control is its remarkable genetic and antigenic diversity. Unlike genetically stable viruses, FCV circulates as heterogeneous quasi-species that continually evolve under host immune pressure. Consequently, naturally acquired and vaccine-induced immunity often provide incomplete cross-protection, allowing vaccinated animals to become infected and shed virus despite reduced clinical severity. Persistent carrier cats further contribute to viral maintenance and act as evolutionary reservoirs in which genetically distinct variants may emerge over time. These characteristics closely resemble evolutionary processes observed in several medically important RNA viruses and

highlight FCV as an informative model for understanding viral adaptation, persistence, and outbreak dynamics in companion animal populations [10,11].

Recent advances in molecular diagnostics and whole-genome sequencing have improved the understanding of FCV epidemiology and viral evolution. Molecular epidemiological studies have demonstrated substantial genetic diversity among circulating FCV strains, while sequence-based investigations have identified geographically distributed lineages and recombination events. These findings highlight the limitations of relying solely on conventional epidemiological investigations and underscore the growing importance of genomic epidemiology for monitoring viral evolution, characterizing circulating variants, and evaluating vaccine–field strain relationships [2,6–8,12–15].

These challenges are particularly relevant in developing countries such as India, where the rapidly expanding companion animal population, increasing establishment of shelters and breeding facilities, and limited molecular surveillance provide favourable conditions for sustained viral circulation and evolution. Although sporadic molecular studies have reported genetically distinct Indian FCV isolates, comprehensive nationwide epidemiological data, whole-genome surveillance, and systematic evaluation of circulating strains remain limited. Addressing these knowledge gaps is essential for strengthening veterinary preparedness and developing evidence-based prevention and control strategies.

This review provides a comprehensive and updated overview of FCV biology, with emphasis on viral evolution, molecular epidemiology, host–virus interactions, clinical manifestations, diagnostics, vaccination, and emerging antiviral approaches. Particular attention is given to recent advances in genomic surveillance, outbreak preparedness, and One Health strategies, together with the current status of FCV in India and future research priorities. By integrating contemporary advances in virology with modern surveillance and preparedness concepts, this review aims to provide a practical framework for improving the prevention and control of FCV while illustrating the broader significance of companion animal RNA viruses in global infectious disease preparedness.

2. Global Importance of Feline Calicivirus as an Emerging Companion Animal RNA Virus

Feline calicivirus (FCV) is one of the most prevalent and evolutionarily dynamic viral pathogens affecting domestic cats worldwide. Although traditionally recognized as an important cause of feline upper respiratory tract disease, increasing evidence indicates that FCV should be regarded as an emerging companion animal RNA virus because of its remarkable genetic plasticity, broad clinical spectrum, capacity for persistent infection, and ability to generate highly virulent outbreak-associated variants. Similar to many medically important RNA viruses, FCV evolves continuously through mutation, recombination, and immune-mediated selection, enabling rapid adaptation to changing host populations and facilitating long-term persistence despite widespread vaccination [2,3,11].

The global expansion of companion animal ownership has substantially altered the epidemiology of infectious diseases affecting domestic cats. Urbanization, international movement of pets, commercial breeding, rescue organizations, and increasing numbers of multicat households have created favourable conditions for the introduction, maintenance, and dissemination of contagious pathogens. In these environments, FCV is efficiently transmitted through direct contact with oral and respiratory secretions as well as indirect exposure to contaminated fomites. Furthermore, prolonged viral shedding by clinically recovered or asymptomatic carrier cats enables continuous circulation within feline populations, making eradication virtually impossible [10,16,17].

Unlike many respiratory viruses that cause self-limiting infections, FCV exhibits considerable clinical and genetic heterogeneity. While most infections result in mild respiratory

disease and oral ulceration, the emergence of virulent systemic feline calicivirus (VS-FCV) has demonstrated the virus's capacity to cause severe multisystemic disease characterised by vasculitis, cutaneous ulceration, facial oedema, pneumonia, hepatic dysfunction, and mortality rates exceeding 50% during outbreaks. Such outbreaks have been reported in veterinary hospitals, animal shelters, breeding colonies, and rescue centres across North America, Europe, Asia, and Australia, emphasising the global significance of FCV and the importance of rapid outbreak recognition and containment [4,8,9].

A defining feature of FCV is its extraordinary antigenic diversity. The error-prone RNA-dependent RNA polymerase continuously generates genetically heterogeneous viral populations, while selective pressure imposed by host immunity promotes the emergence of variants capable of escaping neutralizing antibodies. Consequently, currently available vaccines generally reduce disease severity but do not consistently prevent infection, viral shedding, or transmission. Persistent infection further accelerates viral evolution by providing opportunities for within-host diversification, allowing chronically infected cats to serve both as reservoirs of infection and as sources of novel viral variants [2,3]. These evolutionary characteristics closely resemble those observed in several rapidly evolving RNA viruses of human and veterinary importance, making FCV an informative model for studying viral adaptation, antigenic drift, and outbreak emergence.

Recent advances in molecular diagnostics and whole-genome sequencing have transformed the understanding of FCV epidemiology. High-resolution genomic surveillance has demonstrated that genetically distinct FCV variants frequently circulate simultaneously within individual shelters or veterinary hospitals, whereas closely related viruses may be detected across geographically distant regions owing to international movement of companion animals. These findings highlight the limitations of relying solely on traditional epidemiological investigations and underscore the growing importance of genomic epidemiology for identifying transmission pathways, monitoring viral evolution, and evaluating vaccine relevance [11].

Although FCV has no confirmed zoonotic potential, its importance extends beyond feline medicine. The virus exemplifies many of the evolutionary and epidemiological principles that govern emerging RNA viruses, including rapid mutation, recombination, immune escape, persistent infection, and outbreak-associated evolution. Within the One Health framework, surveillance of FCV contributes to strengthening veterinary diagnostic capacity, improving infection-control practices, supporting antimicrobial stewardship, and enhancing preparedness for future emerging companion animal pathogens [1]. Consequently, FCV should be viewed not only as a significant feline pathogen but also as a valuable model for understanding the emergence, surveillance, and control of rapidly evolving RNA viruses in companion animal populations.

FCV continues to circulate worldwide in household, shelter, breeding and free-roaming cat populations, posing substantial challenges to companion animal health through its extensive genetic diversity, efficient transmission and persistent carrier states (Figure 1).

Epidemiological Status of Feline Calicivirus in India

Information on the epidemiology of feline calicivirus (FCV) in India remains relatively limited and geographically fragmented, with available studies differing in sampling populations, clinical presentation, diagnostic approaches, and molecular characterization. Recent Indian investigations nevertheless provide evidence of ongoing FCV circulation among domestic cats. A retrospective cross-sectional study conducted at the ICAR–Indian Veterinary Research Institute, Bareilly, Uttar Pradesh, evaluated 675 feline clinical samples collected between November 2023 and November 2025. FCV was detected by PCR in 1 of 675 samples (0.14%), whereas feline panleukopenia virus and feline herpesvirus-1

were detected at higher frequencies. The authors emphasized the continued circulation of feline viral pathogens despite vaccination and highlighted the need for sustained molecular surveillance and optimization of vaccination strategies [18].



Figure 1. Worldwide distribution of feline calicivirus (FCV) infection. The map illustrates the reported geographical occurrence of FCV in domestic cats across different continents, highlighting the widespread distribution of the virus globally. Created in BioRender. Publication License Details: https://BioRender.com/r9vygl1.

Recent molecular evidence from Northeast India further indicates regional circulation and genetic variation of FCV. In a 2025 study from Assam, 56 vaccinated cats presenting with upper respiratory tract disease were investigated using RT-PCR targeting the FCV VP1 gene. FCV was detected in 5 of 56 cats (8.93%) when FCV-positive animals, including co-infections, were considered, while three animals showed FCV as a standalone infection (5.36%). The study also identified FCV/FHV-1 co-infections and examined the partial VP1 sequence of an FCV-positive sample.

Importantly, phylogenetic analysis of the Assam FCV isolate (PZ727510) showed clustering within an Asian lineage, with the isolate grouping closely with Chinese and South Korean field strains and occupying a branch distinct from the commercial vaccine strains F9 and 2024 included in the analysis. These findings provide preliminary evidence that FCV circulating in Indian cats may be genetically related to regional Asian field viruses, although the interpretation is limited by the analysis of a single partial VP1 sequence [18].

The marked difference between the detection frequencies reported in Bareilly (0.14%) and Assam (8.93% overall FCV positivity; 5.36% standalone FCV detection) should not be interpreted as a direct estimate of regional prevalence. The studies examined different populations and clinical settings: the Bareilly investigation used a broader retrospective collection of feline clinical samples, whereas the Assam investigation specifically enrolled cats presenting with upper respiratory tract disease. Differences in sampling strategy, disease status, geographic location, diagnostic methodology, and population structure may therefore contribute to the observed variation.

Despite these emerging observations, India currently lacks a coordinated nationwide FCV surveillance framework integrating standardized molecular diagnostics, systematic sampling across geographic regions, sequence-based epidemiology, and longitudinal monitoring of circulating strains. Available evidence is concentrated in individual institutions or regions, limiting assessment of the national distribution, genetic diversity, evolutionary dynamics, and relationship between field strains and vaccine strains. Future studies should therefore incorporate multicentric sampling from owned, free-roaming, shelter, breeding,

and clinically affected cat populations; standardized RT-PCR/RT-qPCR-based detection; capsid gene sequencing and, where feasible, whole-genome sequencing; and phylogenetic and recombination analyses. Such coordinated surveillance would help establish an evidence-based epidemiological baseline for FCV in India and support evaluation of vaccine cross-protection, outbreak investigation, and development of regionally relevant prevention and control strategies.

3. Molecular Evolution and Genomic Epidemiology of Feline Calicivirus

Feline calicivirus (FCV) is a non-enveloped, positive-sense single-stranded RNA virus belonging to the genus *Vesivirus* within the family *Caliciviridae*. Its approximately 7.5–7.7 kb genome comprises three open reading frames (ORF1–ORF3), encoding non-structural proteins involved in viral replication and two structural proteins, VP1 and VP2, responsible for virion assembly and infectivity [3,19]. Although structurally compact, the FCV genome exhibits remarkable functional plasticity, enabling efficient replication, rapid adaptation, and continuous genetic diversification. These characteristics underpin the virus's persistence in feline populations and its ability to generate antigenically distinct variants capable of causing endemic disease and sporadic outbreaks.

The viral capsid is primarily composed of the major structural protein VP1, which contains conserved shell (S) and variable protruding (P) domains. The hypervariable P2 subdomain is exposed on the virion surface and mediates receptor binding and antibody recognition. Consequently, this region accumulates mutations more rapidly than other genomic regions and represents the principal determinant of antigenic diversity and vaccine escape. In contrast, the minor structural protein VP2, although present in small quantities, plays an essential role in virion stability and genome delivery during viral entry [20,21].

FCV initiates infection by binding to feline junctional adhesion molecule-A (fJAM-A) expressed on epithelial cells of the oral and upper respiratory tract. Receptor engagement induces conformational rearrangements within the viral capsid, facilitating clathrin-mediated endocytosis and release of the viral RNA genome into the cytoplasm. Following entry, the genomic RNA functions directly as messenger RNA for translation of the ORF1 polyprotein, which is subsequently cleaved into functional non-structural proteins, including the viral protease, VPg, helicase, and RNA-dependent RNA polymerase (RdRp). These proteins coordinate viral RNA synthesis, intracellular membrane remodeling, and assembly of replication complexes within the cytoplasm [3,19]. The genome organization and intracellular replication strategy of FCV are summarized in Figure 2.

A defining molecular characteristic of FCV is the absence of proofreading activity in the viral RNA-dependent RNA polymerase, resulting in a high mutation rate during replication. Continuous accumulation of nucleotide substitutions generates genetically heterogeneous viral populations, commonly referred to as quasispecies, which provide a substrate for natural selection [22]. Under host immune pressure, variants possessing enhanced replication efficiency, altered receptor affinity, or reduced susceptibility to neutralizing antibodies are preferentially maintained. This dynamic evolutionary process promotes antigenic drift, persistent infection, and adaptation to vaccinated populations, thereby complicating long-term disease control [11].

In addition to point mutations, homologous recombination contributes significantly to FCV evolution. Recombination occurs when genetically distinct viruses co-infect the same host cell, allowing exchange of genomic segments and generation of novel viral lineages with altered biological characteristics. Most recombination events have been reported near the ORF1–ORF2 junction, although recombination within capsid-associated regions has also been described. Together with mutation, recombination accelerates viral diversification and contributes to the emergence of epidemiologically distinct strains [10,11].

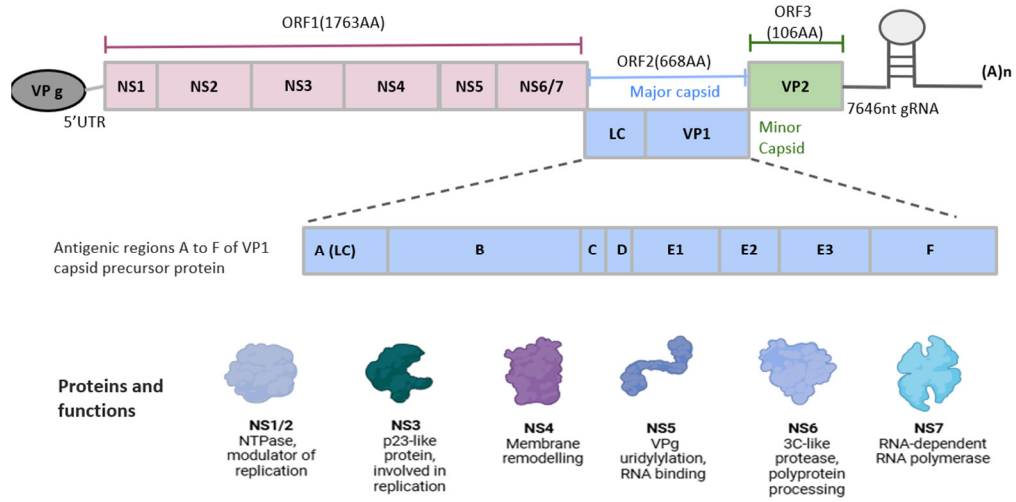


Figure 2. Genome organization of feline calicivirus (FCV). Schematic representation of the FCV genome organization. The figure also illustrates the structural and non-structural proteins involved in viral replication, assembly, and release following receptor-mediated cell entry. Created in BioRender. Publication License Details: https://BioRender.com/2xzxj8t.

The major viral, host, and environmental determinants responsible for FCV evolution, persistence, epidemiological spread and outbreak amplification are summarized in Table 1.

Table 1. Determinants of Feline Calicivirus Evolution, Persistence, Transmission and Outbreak Amplification.

Determinant	Underlying Mechanism	Effect on Viral Evolution or Transmission	Epidemiological Significance	Implication for Prevention and Control
Error-prone RNA replication [3,23]	Lack of proofreading by viral RdRp generates frequent mutations.	Produces genetically diverse quasispeciesand continuous sequence variation.	Facilitates adaptation to host immunity and transmission conditions.	Use conserved diagnostic targets and monitor circulating sequence variation.
Recombination [3,24–26]	Template switching occurs during co-infection with related viruses.	Generates novel genomic combinations and phenotypes.	Promotes lineage diversification and emergence of distinct variants.	Use whole-genome sequencing to detect and characterize recombination.
Immune selection [27,28]	Infection or vaccine-induced antibodies exert pressure on exposed capsid epitopes.	Favors variants with reduced susceptibility to existing antibodies.	May contribute to breakthrough infection and variable cross-protection.	Monitor antigenic and genetic relatedness of vaccine and field strains.
Persistent infection and carrier state [3,25,29]	Prolonged replication and intermittent shedding allow within-host diversification.	Maintains viral circulation and provides opportunities for viral evolution.	Recovered cats may act as reservoirs for recurrent transmission.	Apply isolation and appropriate carrier management in high-risk settings.
Host susceptibility and concurrent disease [30–32]	Young age, stress, poor nutrition, immunosuppression and co-infections impair antiviral defence	Increases viral replication, shedding and disease severity.	Sustains transmission and severe disease in vulnerable populations.	Reduce stress, manage co-infections and maintain vaccination.

Table 1. *Cont.*

Determinant	Underlying Mechanism	Effect on Viral Evolution or Transmission	Epidemiological Significance	Implication for Prevention and Control
High-density multicat environments [28,30]	Close contact, shared facilities and contaminated equipment increase exposure.	Enhances direct and indirect transmission and strain co-circulation.	Shelters, breeding colonies and veterinary hospitals favour outbreak amplification.	Implement cohorting, ventilation, disinfection and rapid isolation.
Environmental persistence and fomites [33–35]	Non-enveloped virions can persist on contaminated surfaces and equipment.	Extends transmission beyond direct cat-to-cat contact.	Facilitates shelter-associated and nosocomial spread.	Use effective disinfectants, adequate contact times and environmental decontamination.
Animal movement and population connectivity [6,25]	Movement between households, shelters, breeding facilities and veterinary settings spreads infection.	Disseminates established and newly evolved variants across populations.	Connects outbreaks and increases opportunities for strain mixing.	Apply health screening, quarantine and movement records.
Incomplete population immunity [3,36]	Uneven vaccination, waning immunity and antigenic mismatch create susceptible populations.	Permits infection and shedding despite reduced clinical disease.	Supports endemic circulation and outbreaks in partially protected populations.	Maintain vaccination alongside surveillance, biosecurity and rapid diagnostics.

Abbreviations: RdRp, RNA-dependent RNA polymerase.

Persistent infection further amplifies viral evolution. Approximately 10–20% of infected cats continue to shed infectious virus for prolonged periods despite apparent clinical recovery. Continuous replication within these carrier animals provides opportunities for accumulation of adaptive mutations under immune selection, allowing chronically infected cats to function as both reservoirs of transmission and evolutionary incubators for novel variants [10]. This characteristic distinguishes FCV from many acute respiratory viruses and contributes substantially to its global persistence.

Despite extensive genomic diversity, no universally conserved molecular marker has been identified that reliably differentiates virulent systemic FCV (VS-FCV) from classical field strains. Comparative genomic studies indicate that highly virulent viruses emerge independently through multiple evolutionary pathways rather than from dissemination of a single hypervirulent lineage. Disease severity therefore appears to result from complex interactions among viral genotype, host immune responses, tissue tropism, and environmental factors rather than specific nucleotide substitutions alone [4,8]. Consequently, diagnosis of VS-FCV requires integration of clinical findings, epidemiological investigation, and genomic analysis rather than reliance on molecular detection alone.

Advances in structural biology and next-generation sequencing have substantially improved understanding of FCV molecular evolution. Whole-genome sequencing has demonstrated that genetically distinct variants frequently coexist within individual shelters and veterinary hospitals, while closely related viruses may circulate across geographically distant regions through movement of companion animals. Such observations highlight the limitations of partial capsid sequencing and emphasise the importance of comprehensive genomic surveillance for outbreak investigation, transmission tracking, and evaluation of vaccine–field strain relationships [11].

Collectively, the compact genome, error-prone replication machinery, capacity for recombination, and prolonged persistence make FCV one of the most evolutionarily dynamic RNA viruses affecting companion animals. These molecular characteristics not only explain the remarkable diversity observed among circulating field strains but also provide the biological basis for viral persistence, diagnostic challenges, vaccine escape, and the continuing emergence of novel variants. A detailed understanding of these mechanisms is therefore fundamental for the development of improved molecular diagnostics, broadly protective vaccines, and effective surveillance strategies.

4. Host–Virus Interactions and Pathogenesis

The pathogenesis of feline calicivirus (FCV) is determined by the interaction between viral genetic characteristics, cellular receptor usage, innate and adaptive immune responses, tissue tropism, and host susceptibility. This complex relationship explains the broad spectrum of outcomes ranging from asymptomatic infection and localized oral or respiratory disease to persistent infection and fatal virulent systemic feline calicivirus (VS-FCV). Importantly, disease severity cannot be attributed to a single viral mutation; rather, it reflects the combined effects of viral replication, immune evasion, inflammatory injury, and host-related factors [2,3].

4.1. Cellular Attachment, Entry, and Replication

FCV infection begins with attachment of the VP1 capsid protein to feline junctional adhesion molecule-A (fJAM-A), an immunoglobulin-superfamily receptor expressed at epithelial tight junctions. Receptor binding is mediated predominantly by the protruding P2 domain of VP1 and induces conformational rearrangements within the viral capsid. These structural changes expose the minor capsid protein VP2, which assembles into a portal-like structure that facilitates transfer of the viral genome across the endosomal membrane into the cytoplasm [20,21]. The functions of the major viral proteins, their interactions with host cellular pathways, and their potential exploitation as therapeutic targets are summarized in Table 2.

Table 2. Viral Proteins, Host–Virus Interactions and Therapeutic Targets. Integrated summary of the major FCV proteins involved in host entry, replication, immune evasion and their potential exploitation for antiviral intervention.

Viral Protein/Host Component	Principal Function	Host Molecule or Pathway	Biological Consequence	Therapeutic Opportunity/ Research Direction
VP1 (major capsid) [37–39]	Attachment and receptor binding	fJAM-A	Initiates cell entry; contains major neutralizing epitopes and varies antigenically.	Neutralizing monoclonal antibodies; vaccine antigen optimization; entry inhibitors
VP2 (minor capsid) [21]	Portal formation and genome delivery	Endosomal membrane	Facilitates genome release after receptor engagement	Portal/entry inhibitors; structure-guided antivirals
VPg [40–42]	Translation initiation	eIF4E/eIF4G translation complex	Promotes viral protein synthesis	Host translation modulators
NS1/2 [43]	Replication complex formation	Intracellular membranes	Supports replication organelles	Replication complex inhibitors

Table 2. *Cont.*

Viral Protein/Host Component	Principal Function	Host Molecule or Pathway	Biological Consequence	Therapeutic Opportunity/ Research Direction
NS3 [19,44]	NTPase/helicase	ATP-dependent RNA metabolism	RNA unwinding and replication	Helicase inhibitors (experimental)
NS4 [42]	Membrane remodeling	ER-derived membranes	Formation of replication vesicles	Host-directed membrane trafficking inhibitors
NS5 (VPg precursor) [19,45]	Genome-linked protein processing	Replication machinery	Efficient RNA synthesis	Replication inhibitors
NS6 [46,47]	3C-like protease	Viral polyprotein	Proteolytic processing essential for maturation	Protease inhibitors; broad-spectrum 3CL inhibitor development
NS7 [45,48]	RNA-dependent RNA polymerase	Viral RNA synthesis	Genome replication and mutation generation	Nucleoside analogues; RdRp inhibitors
p39 [49,50]	Innate immune antagonism	RIG-I signaling; autophagy	Reduced interferon response and enhanced viral persistence	Host-directed immunomodulators; autophagy-targeted therapy
Host interferon pathway [51–53]	Antiviral defense	Type I interferon signaling	Restricts viral replication	Recombinant feline IFN-ω; innate immune stimulation
Inflammatory cytokine network [54]	Immunopathology	IL-6, TNF-α, chemokines	Tissue injury during severe disease	Selective immunomodulation in VS-FCV

Abbreviations: FCV, feline calicivirus; fJAM-A, feline junctional adhesion molecule A; ER, endoplasmic reticulum; RdRp, RNA-dependent RNA polymerase; RIG-I, retinoic acid-inducible gene I; eIF4E, eukaryotic translation initiation factor 4E; eIF4G, eukaryotic translation initiation factor 4 gamma; IL-6, interleukin-6; TNF-α, tumor necrosis factor alpha; fIFN-ω, feline interferon omega; VS-FCV, virulent systemic feline calicivirus.

Following predominantly clathrin-mediated endocytosis and endosomal acidification, the positive-sense RNA genome is released into the cytoplasm and translated directly. Viral non-structural proteins reorganize intracellular membranes to form replication complexes in which genomic and subgenomic RNAs are synthesized. Viral protease-mediated polyprotein processing and RNA-dependent RNA polymerase activity support rapid viral amplification, whereas suppression of cellular protein synthesis redirects host resources toward viral replication. Productive infection culminates in marked cytopathic effects and cell lysis, particularly within oral and respiratory epithelia [3,19].

4.2. Innate Immune Modulation and Inflammatory Injury

Early recognition of FCV RNA by intracellular pattern-recognition receptors would normally activate type I interferon and other antiviral pathways. However, FCV has evolved mechanisms that suppress these responses, thereby permitting efficient replication before effective adaptive immunity develops. Viral non-structural proteins interfere with interferon-associated signalling, host translation, autophagy, and cellular stress responses. In particular, the FCV p39 protein has been reported to promote autophagy-dependent degradation of retinoic acid-inducible gene I, thereby reducing antiviral signalling and favouring viral replication [51].

Although immune evasion facilitates replication, excessive host inflammation is an equally important determinant of tissue injury. FCV infection induces inflammatory mediators, including interleukin-1β, interleukin-6, tumour necrosis factor-α, chemokines, and interferons, which recruit neutrophils and macrophages to affected tissues. Controlled inflammation may contribute to viral clearance, whereas dysregulated responses can intensify epithelial necrosis, ulceration, vascular leakage, oedema, and secondary tissue damage. Thus, FCV pathogenesis reflects both direct virus-mediated cytolysis and immune-mediated injury.

4.3. Tissue Tropism and Clinical Correlates

The oral cavity and upper respiratory tract are the principal sites of FCV replication. Infection and destruction of lingual, palatal, and oropharyngeal epithelial cells produce the characteristic oral ulcers associated with acute disease. Replication in nasal and respiratory epithelia contributes to fever, sneezing, nasal discharge, conjunctivitis, and upper respiratory inflammation. Disruption of mucosal barriers may also predispose affected cats to secondary bacterial infection.

Certain strains exhibit broader tissue tropism and may involve the lungs, synovial tissues, skin, liver, pancreas, and vascular endothelium. Pulmonary infection may cause bronchointerstitial pneumonia, alveolar injury, and respiratory distress, particularly in young or immunocompromised cats. Transient polyarthritis and limping syndrome are thought to involve immune-complex deposition and inflammatory synovitis rather than extensive direct viral destruction of joints. Persistent viral antigen stimulation has also been associated with feline chronic gingivostomatitis, although FCV is unlikely to act as the sole cause of this multifactorial inflammatory disorder [2].

4.4. Persistence and Immune Escape

A proportion of infected cats continue to shed FCV after clinical recovery. Persistent shedding is supported by incomplete immune clearance, ongoing viral replication, antigenic variation, and selection of escape variants. Within-host viral populations may progressively diverge under antibody pressure, allowing FCV to remain detectable for months and, in some animals, considerably longer [10].

Carrier cats are epidemiologically important because they maintain infection within multicat populations and may introduce virus into shelters, breeding colonies, or households without displaying clinical signs. Persistent infection also provides an extended evolutionary environment in which mutations can accumulate, potentially generating variants with altered antigenicity, transmission efficiency, or tissue tropism. Vaccination generally reduces clinical severity but does not consistently prevent infection or shedding, further permitting circulation of FCV in vaccinated populations. The sequential events involved in FCV pathogenesis and the principal mechanisms of immune evasion are summarized in Figure 3.

4.5. Pathogenesis of Virulent Systemic FCV

VS-FCV represents the most severe clinical outcome of infection and is characterised by fever, facial and limb oedema, ulcerative skin lesions, pneumonia, jaundice, hepatic dysfunction, coagulopathy, and multiorgan failure. Pathological findings commonly include epithelial necrosis, vasculitis, endothelial injury, oedema, and widespread inflammatory lesions. These features indicate that systemic disease is driven by expanded tissue tropism together with severe vascular and inflammatory dysfunction [9,55].

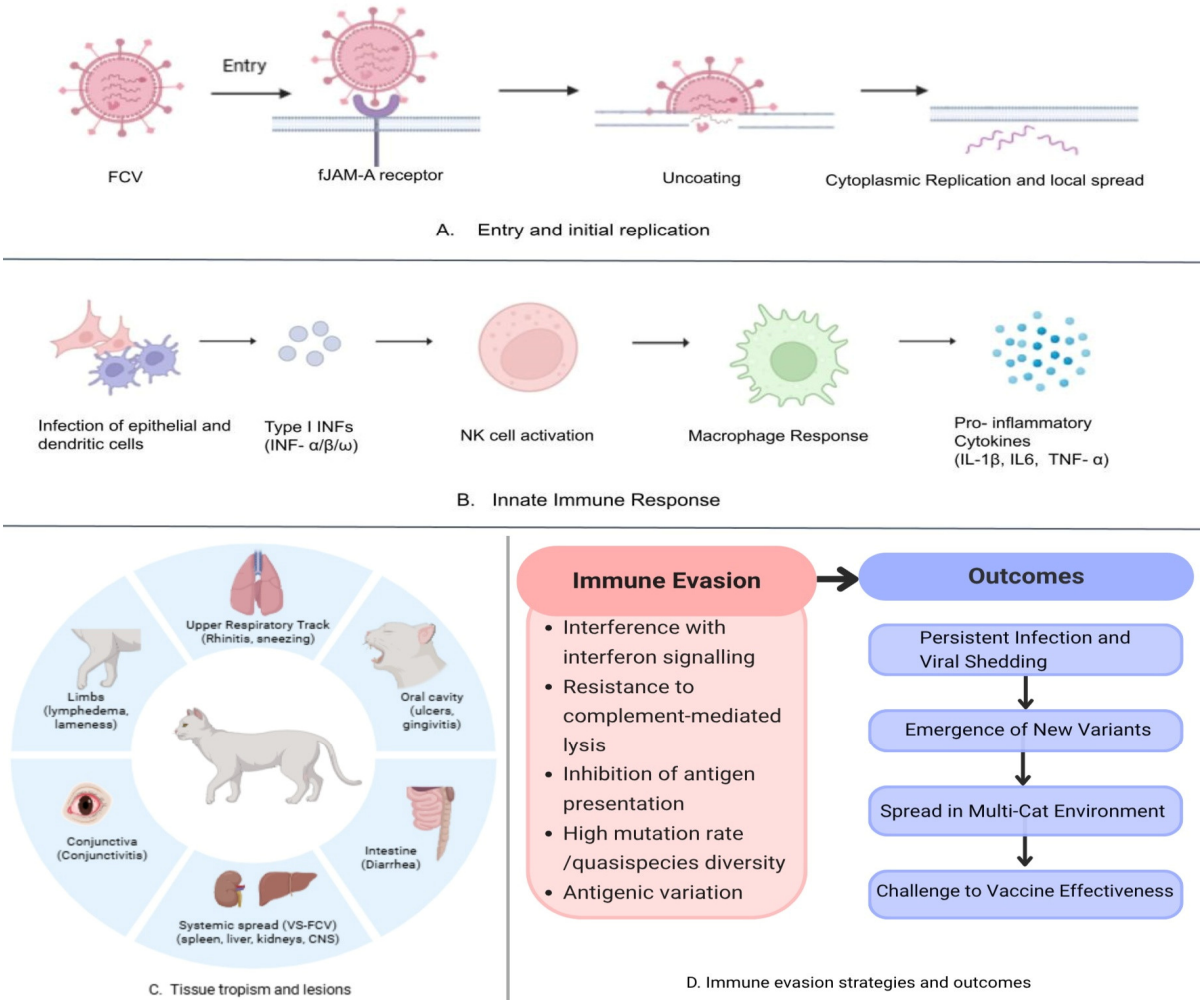


Figure 3. Pathogenesis and immune evasion of feline calicivirus (FCV). Sequential overview of FCV pathogenesis from viral entry and tissue tropism to host immune responses and immune evasion mechanisms. The figure summarizes the key events leading to persistent infection, systemic dissemination, and disease progression. Created in BioRender. Publication License Details: https://BioRender.com/4jdabmh.

Recent experimental evidence suggests that functional divergence among FCV genotypes may contribute to differences in pathogenicity. Two major FCV genotypes, GI and GII, have been identified, with the GII isolate WX9 exhibiting higher mortality and broader tissue tropism than the GI isolate WH0531 in experimental infection. GII was also associated with distinct codon usage patterns and VP1 structural evolution, suggesting that genotype-associated capsid variation may influence viral fitness and disease severity. Nevertheless, GII cannot be considered a universal molecular marker of VS-FCV, as pathogenicity is influenced by complex interactions among viral genetic variation, host responses, and tissue tropism [56]. Recent clinical and pathological evidence further supports the complex relationship between FCV genetic variation and disease phenotype. A fatal FCV-VSD infection in a young kitten was associated with severe pneumonia and footpad oedema, with FCV RNA detected in multiple organs and the highest viral RNA load observed in the lungs. Immunohistochemical analysis confirmed viral antigen in pulmonary tissue, with alveolar macrophages identified as the principal target cells and potential site of viral replication. Notably, phylogenetic analysis of the ORF2 gene showed that the highly virulent virus was not genetically distinguishable from FCV strains associated with upper respiratory tract disease. These findings indicate that severe systemic disease may

arise from genetically diverse FCV populations and further support the view that VS-FCV pathogenicity is influenced by the interaction of viral genetic variation, tissue tropism, host factors, and environmental conditions rather than by a single molecular signature [57].

Comparative sequencing has not identified a single mutation or conserved genomic signature that reliably distinguishes all VS-FCV isolates from classical strains. Most systemic outbreaks appear to arise independently and involve genetically distinct viruses, suggesting that virulence can emerge through multiple evolutionary pathways. Alterations in capsid structure may influence receptor engagement or tissue tropism, whereas changes in non-structural proteins may affect replication kinetics and immune evasion. Nevertheless, these viral properties interact with host immunity, age, vaccination status, concurrent infection, and environmental stress to determine clinical outcome [4,8].

5. Clinical Spectrum and Diagnostic Approaches

5.1. Clinical Manifestations and Disease Spectrum

Feline calicivirus (FCV) infection exhibits remarkable clinical diversity, ranging from inapparent infection and mild upper respiratory disease to chronic inflammatory disorders and highly fatal systemic illness. Disease outcomes are influenced by viral strain, host age, immune status, vaccination history, concurrent infections, and environmental stress. Consequently, FCV should be regarded as a disease continuum rather than a single clinical entity. Because asymptomatic viral shedding is common and clinical signs frequently overlap with other pathogens of the feline upper respiratory disease complex (FURDC), clinical examination alone is insufficient for definitive diagnosis [2,3].

The majority of naturally infected cats develop acute upper respiratory disease, particularly kittens, shelter cats, and animals housed in multi-cat environments. Following an incubation period of approximately 2–5 days, affected cats typically present with pyrexia, lethargy, anorexia, sneezing, serous to mucopurulent nasal discharge, conjunctivitis, hypersalivation, and oral ulceration. Ulcerative lesions involving the tongue, hard palate, lips, and gingiva are considered among the most characteristic manifestations of FCV infection and often contribute to dysphagia, reduced food intake, and dehydration. While uncomplicated infections are generally self-limiting, secondary bacterial infections may prolong recovery, particularly in young or immunocompromised animals [3,16].

Although the respiratory tract represents the principal site of viral replication, FCV demonstrates considerable tissue tropism. Infection of pulmonary epithelial cells may result in bronchointerstitial pneumonia, especially in neonatal kittens, geriatric cats, or animals with compromised immunity. Some strains are also associated with limping syndrome, a transient febrile polyarthritis characterised by acute lameness, joint pain, and reluctance to move. These musculoskeletal manifestations are believed to result primarily from immune-mediated inflammation rather than extensive viral destruction of synovial tissues and generally resolve without permanent joint damage [3,58].

Persistent infection represents a distinctive biological feature of FCV. A proportion of clinically recovered cats continue to shed infectious virus for months or even years despite the absence of overt disease. These carrier animals play a critical epidemiological role by maintaining viral circulation within households, breeding colonies, shelters, and veterinary hospitals. Continuous viral replication under host immune pressure also facilitates antigenic diversification, allowing emergence of variants capable of evading pre-existing immunity [2,10]. Persistent FCV infection has additionally been implicated as one of several contributing factors in feline chronic gingivostomatitis, a severe immune-mediated inflammatory disorder characterised by painful proliferative oral lesions and chronic oral discomfort. Although FCV is unlikely to represent the sole etiological agent, viral persistence may amplify local immune dysregulation and perpetuate chronic inflammation [59].

The most severe manifestation of FCV infection is virulent systemic feline calicivirus (VS-FCV), an uncommon but devastating syndrome associated with high morbidity and mortality. Unlike classical respiratory disease, VS-FCV is characterised by widespread viral dissemination and systemic inflammatory injury. Affected cats commonly develop high fever, facial and limb oedema, ulcerative dermatitis, jaundice, dyspnoea, pneumonia, hepatic dysfunction, pancreatitis, coagulopathy, and multiorgan failure. Mortality frequently exceeds 50% during institutional outbreaks, particularly in veterinary hospitals and animal shelters where close animal contact facilitates rapid transmission [4,9,55]. Importantly, genomic studies have demonstrated that VS-FCV strains do not share a single conserved virulence marker, indicating that systemic disease results from complex interactions between viral evolution and host responses rather than a unique genetic lineage [8,11].

From a clinical perspective, recognition of disease severity is essential for early intervention and outbreak control. Mild respiratory disease generally requires supportive care, whereas the occurrence of rapidly progressive oedema, cutaneous ulceration, jaundice, unexplained pneumonia, or increased mortality within multicat populations should immediately raise suspicion of VS-FCV and prompt laboratory confirmation and implementation of strict infection-control measures. Thus, appreciation of the full clinical spectrum of FCV not only facilitates appropriate case management but also provides the foundation for selecting suitable diagnostic tests and guiding epidemiological investigations. The distinguishing clinical features of classical and virulent systemic FCV are summarized in Table 3.

Table 3. Clinical spectrum of classical feline calicivirus (FCV) and virulent systemic FCV (VS-FCV).

Clinical Feature	Classical FCV	Virulent Systemic FCV	Diagnostic Significance
Oral cavity [2,3]	Oral ulcers; mild gingivitis	Severe ulceration; necrotizing stomatitis	Highly characteristic of FCV infection
Respiratory tract [48]	Rhinitis, sneezing, nasal discharge	Severe pneumonia and respiratory distress	Common presenting syndrome
Eyes [60]	Conjunctivitis	Conjunctivitis with periocular edema	Supports respiratory diagnosis
Musculoskeletal [61,62]	Occasional transient lameness	Polyarthritis may occur	May support diagnosis in young cats
Skin [9]	Usually absent	Facial edema, cutaneous ulcers, crusting	Strong indicator of VS-FCV
Systemic signs [54]	Mild fever; self-limiting	High persistent fever, jaundice, vasculitis, multiorgan involvement	Suggests virulent systemic disease
Mortality [54,60]	Low	Often exceeds 40–60% during outbreaks	Important prognostic marker
Hospital transmission [63–65]	Occasional	Frequent nosocomial outbreaks	Immediate infection-control measures required

5.2. Laboratory Diagnosis and Emerging Diagnostic Technologies

Accurate laboratory diagnosis is essential for confirming feline calicivirus (FCV) infection, differentiating it from other pathogens within the feline upper respiratory disease complex (FURDC), identifying persistent carriers, and rapidly detecting outbreaks of virulent systemic feline calicivirus (VS-FCV). Because clinical manifestations vary considerably and asymptomatic viral shedding is common, diagnosis should integrate clinical findings, epidemiological information, and laboratory testing. No single diagnostic assay is univer-

sally applicable, and selection of appropriate methods depends on the clinical presentation, stage of infection, specimen quality, and intended diagnostic objective [2,3].

The key features of conventional and emerging diagnostic technologies for feline calicivirus (FCV), including their turnaround time, major advantages, limitations, and primary applications, are compared in Table 4.

Table 4. Comparison of current and emerging diagnostic technologies.

Method	Turnaround	Major Advantages	Limitations	Primary Application
Virus isolation [66,67]	3–7 days	Confirms infectious virus	Slow; specialized laboratory facilities required	Virus characterization
RT-qPCR [68]	1.5–3 h	Highly sensitive and quantitative	Primer mismatch with divergent strains	Routine diagnosis
Multiplex RT-qPCR [69]	2–4 h	Simultaneous pathogen detection	Optimization required	Respiratory disease panels
HRM analysis [70]	2–4 h	Rapid strain discrimination	Sequencing confirmation desirable	Screening variants
RT-LAMP [67]	30–60 min	Rapid; minimal instrumentation	Complex primer design	Point-of-care testing
CRISPR-Cas assays [71]	30–60 min	Very high specificity	Usually requires pre-amplification	Rapid confirmatory testing
Digital PCR [72]	3–5 h	Absolute quantification	High cost	Reference laboratories
Whole-genome sequencing [73]	1–3 days	Variant identification and outbreak tracing	Bioinformatics intensive	Genomic surveillance
Metagenomic sequencing [74]	2–5 days	Detects unexpected pathogens	Lower sensitivity; expensive	Unexplained outbreaks

Abbreviations: FCV, feline calicivirus; HRM, high-resolution melting; RT-qPCR, reverse transcription quantitative PCR. Emerging molecular methods should complement—not replace—clinical assessment, virus isolation and genomic surveillance.

Appropriate sample selection is fundamental for reliable diagnosis. Oropharyngeal, oral, conjunctival, and nasal swabs collected during the acute phase generally contain the highest viral loads and are therefore preferred for molecular detection. In cats with lower respiratory involvement, bronchoalveolar lavage fluid may improve diagnostic sensitivity, whereas tissue samples from the liver, lungs, spleen, or skin collected during necropsy are valuable for investigating suspected VS-FCV outbreaks. Because viral shedding may continue long after clinical recovery, positive molecular results should always be interpreted in conjunction with clinical signs and epidemiological evidence rather than being regarded as definitive proof of active disease [3,10].

Historically, virus isolation in feline cell cultures was considered a diagnostic reference method because it confirmed the presence of infectious virus and enabled antigenic characterisation. However, isolation is labor-intensive, requires specialized laboratory facilities, and may fail when viral titres are low or specimens have been improperly transported. Consequently, virus isolation is now primarily reserved for epidemiological investigations, vaccine studies, and characterisation of emerging strains rather than routine clinical diagnosis [3].

Molecular techniques have become the cornerstone of FCV diagnosis. Conventional reverse transcription polymerase chain reaction (RT-PCR) and real-time quantitative RT-PCR (RT-qPCR) provide rapid, sensitive, and highly specific detection of viral RNA directly from clinical specimens. Real-time assays additionally permit quantification of viral load and reduce contamination risk associated with post-amplification processing. Nevertheless, the extensive genetic diversity of FCV presents an important diagnostic challenge because mutations within primer- and probe-binding regions may reduce assay sensitivity. Accordingly, diagnostic laboratories should periodically evaluate and update primer sets using contemporary sequence data to maintain analytical performance [11,66].

Multiplex molecular assays capable of simultaneously detecting FCV together with feline herpesvirus type 1, *Chlamydia felis*, *Mycoplasma felis*, and other respiratory pathogens have substantially improved the diagnosis of feline respiratory disease. These assays reduce turnaround time, conserve clinical specimens, and facilitate recognition of mixed infections, which are common in shelters and multi-cat environments. Interpretation, however, should remain cautious because molecular detection of FCV does not necessarily distinguish active infection from asymptomatic viral carriage [75].

Growing demand for rapid point-of-care diagnosis has stimulated development of several isothermal nucleic acid amplification technologies, including loop-mediated isothermal amplification (RT-LAMP), recombinase polymerase amplification (RPA), and recombinase-aided amplification (RAA). These methods eliminate the need for thermal cycling, substantially reduce assay time, and can be performed using portable equipment, making them attractive for field investigations and resource-limited veterinary settings. When combined with colorimetric detection or lateral-flow readouts, isothermal assays offer practical alternatives to conventional PCR, although broader multi-centre validation and standardization remain necessary before routine implementation [67,76].

Recent advances in molecular biosensing have introduced CRISPR-Cas-based diagnostics for FCV detection. CRISPR-Cas12 and Cas13 systems combine isothermal amplification with sequence-specific recognition, enabling rapid detection with high analytical sensitivity while minimizing false-positive results. Although these assays remain largely experimental, they represent promising next-generation diagnostic platforms capable of supporting decentralized testing during disease outbreaks [77]. Similarly, integration of microfluidics, nanotechnology, smartphone-assisted image analysis, and biosensor-based detection is expected to accelerate the development of affordable point-of-care devices suitable for veterinary practice and shelter surveillance.

Whole-genome sequencing (WGS) has become increasingly important for understanding FCV epidemiology. Unlike routine diagnostic PCR, WGS enables comprehensive analysis of viral evolution, recombination, transmission pathways, and vaccine–field strain relationships. Genomic surveillance has demonstrated that genetically distinct FCV variants often circulate simultaneously within individual shelters and veterinary hospitals, whereas closely related viruses may spread across geographically distant regions through movement of companion animals. During suspected VS-FCV outbreaks, sequencing therefore provides valuable information for outbreak reconstruction and monitoring viral evolution, although no conserved molecular marker currently distinguishes all systemic strains from classical FCV isolates [4,11].

Despite substantial technological progress, several diagnostic challenges remain unresolved. Persistent viral shedding, extensive antigenic diversity, intermittent virus excretion, and absence of genotype-specific virulence markers complicate interpretation of laboratory findings. Consequently, laboratory diagnosis should not rely solely on detection of viral RNA but should incorporate clinical assessment, vaccination history, epidemiological context, and, when appropriate, genomic investigation. Future diagnostic strategies will likely

combine multiplex molecular detection, portable isothermal amplification, CRISPR-based biosensing, whole-genome sequencing, and artificial intelligence-assisted interpretation to enable rapid identification of emerging variants and strengthen outbreak preparedness.

Collectively, advances in molecular diagnostics have transformed FCV detection from conventional laboratory confirmation to comprehensive genomic surveillance. Continued development of rapid, affordable, and field-deployable diagnostic platforms, together with coordinated international surveillance, will be essential for improving disease control, monitoring viral evolution, and supporting evidence-based prevention strategies for this continuously evolving companion animal pathogen.

6. Vaccination, Vaccine Escape, and Future Vaccination Strategies

Vaccination remains the cornerstone of feline calicivirus (FCV) prevention and has substantially reduced the severity of clinical disease worldwide. Nevertheless, complete control of FCV remains challenging because of extensive genetic and antigenic diversity, persistent viral shedding, incomplete sterilizing immunity, and the continual emergence of novel variants. Unlike many viral diseases where vaccination effectively prevents infection, current FCV vaccines primarily reduce disease severity, viral shedding, and mortality rather than completely preventing infection or transmission. Consequently, vaccinated cats may still become infected and contribute to viral circulation, particularly in multicat environments such as shelters, breeding colonies, and veterinary hospitals [3,16].

Current commercial vaccines consist predominantly of modified-live virus (MLV) and inactivated (killed) vaccines, either as monovalent formulations or combined with other core feline vaccines against feline herpesvirus-1 (FHV-1) and feline panleukopenia virus (FPV). Modified-live vaccines generally induce rapid mucosal, humoral, and cell-mediated immune responses and often provide broader cross-protection than inactivated vaccines because limited viral replication better mimics natural infection. However, MLV vaccines should be used cautiously in severely immunocompromised animals and are generally avoided in situations where vaccine virus shedding could present theoretical concerns. Inactivated vaccines exhibit excellent safety profiles but usually require booster immunizations and adjuvants to achieve comparable immune protection [16,78].

Protective immunity against FCV depends on both virus-neutralizing antibodies and cellular immune responses. Neutralizing antibodies directed primarily against the hypervariable P2 domain of the VP1 capsid protein reduce viral attachment and spread, whereas T-cell responses contribute to clearance of infected cells and may provide broader protection against antigenically distinct strains. Although vaccination induces durable immunological memory, antibody titres do not always correlate with protection because antigenically divergent field isolates may partially escape neutralization despite previous vaccination [2,3].

One of the greatest challenges facing FCV vaccination is the extraordinary genetic plasticity of the virus. The error-prone RNA-dependent RNA polymerase continuously generates mutations during viral replication, producing highly diverse quasi-species that accumulate under immune selection pressure. The capsid VP1 P2 domain, which contains the principal neutralizing epitopes and receptor-binding regions, exhibits particularly high mutation rates. Amino acid substitutions within these epitopes can reduce antibody recognition and diminish cross-neutralization by vaccine-induced antibodies without necessarily altering viral fitness. Consequently, field strains frequently demonstrate variable susceptibility to vaccine-induced immunity, contributing to sporadic vaccine breakthrough infections [10,11].

Unlike influenza viruses, however, FCV does not evolve through globally synchronized antigenic drift involving dominant seasonal lineages. Instead, multiple genetically

distinct strains circulate simultaneously within local cat populations, creating a complex antigenic landscape. This extensive diversity complicates vaccine design because no single vaccine strain adequately represents the global FCV population. Although most commercially available vaccines are based on historical isolates such as F9 or FCV-255, these strains remain capable of providing substantial clinical protection against many contemporary viruses despite relatively limited sequence similarity. This apparent paradox reflects the contribution of conserved neutralizing epitopes and cellular immunity in addition to strain-specific antibodies [3,79].

The emergence of virulent systemic feline calicivirus (VS-FCV) has further highlighted the limitations of existing vaccination strategies. Numerous outbreaks have occurred in well-vaccinated cat populations, demonstrating that current vaccines cannot always prevent systemic disease caused by highly divergent strains. Importantly, vaccination generally reduces mortality and disease severity even during VS-FCV outbreaks, emphasising that vaccine failure often represents incomplete cross-protection rather than complete absence of immunity. Since no unique molecular signature consistently predicts systemic virulence, routine vaccine updates based solely on genetic sequence remain difficult to implement [4,9]. The characteristics of currently available and emerging vaccine platforms, together with the principal mechanisms responsible for vaccine escape and future vaccine development strategies, are summarized in Table 5.

Table 5. Vaccination Strategies and Mechanisms of Vaccine Escape in Feline Calicivirus. Integrated overview of currently available and emerging FCV vaccines together with the major biological mechanisms responsible for reduced vaccine efficacy and future vaccination strategies.

Vaccine Platform	Immune Characteristics/ Advantages	Principal Limitations	Mechanisms Contributing to Vaccine Escape	Future Directions
Modified-live (MLV) vaccines [80,81]	Induce strong humoral and cellular immunity; rapid onset; broad clinical protection.	Transient vaccine virus shedding; not ideal for severely immunocompromised cats.	Antigenic drift, quasispecies evolution and emergence of genetically divergent field strains may reduce cross-neutralization.	Updated multistrain formulations; genomic surveillance-guided strain selection.
Inactivated (killed) vaccines [82,83]	Excellent safety profile; suitable where live vaccines are contraindicated.	Require adjuvants and booster vaccinations; lower mucosal immunity.	Antigenic mismatch between vaccine and circulating variants can reduce protection.	Improved adjuvants and optimized antigen composition.
Multivalent FVRCP vaccines [84–86]	Protect against FCV, FHV-1 and FPV; cornerstone of routine preventive medicine.	Protection against infection is incomplete despite reduction in disease severity.	Genetic and regional viral variation permits circulation of heterologous strains.	Periodic vaccine updating and region-specific surveillance.
Recombinant vaccines (experimental) [87–89]	Targeted antigen presentation with improved safety and design flexibility.	Limited commercial availability and clinical evaluation.	Escape mutations affecting dominant neutralizing epitopes remain possible.	Structure-guided immunogen design targeting conserved epitopes.
mRNA vaccines (experimental) [89,90]	Rapid vaccine redesign; scalable manufacturing; variant adaptability.	Currently under experimental development in companion animals.	Future variants may require continual sequence updating.	Rapid-response vaccination following genomic surveillance.

Table 5. *Cont.*

Vaccine Platform	Immune Characteristics/ Advantages	Principal Limitations	Mechanisms Contributing to Vaccine Escape	Future Directions
Nanoparticle-based vaccines (experimental) [91]	Enhanced antigen stability and delivery; broader epitope presentation.	Manufacturing complexity and limited veterinary validation.	Escape less likely when conserved multi-epitope antigens are incorporated.	Broadly protective FCV vaccine development.
Universal FCV vaccine (future concept) [11,89]	Targets highly conserved epitopes to provide broad cross-lineage protection.	Not yet available; conserved protective epitopes require validation.	Designed specifically to overcome antigenic drift, recombination and quasispecies diversity.	Integration of structural biology, reverse vaccinology and AI-assisted antigen prediction.

Abbreviations: FCV, feline calicivirus; FVRCP, feline viral rhinotracheitis-calicivirus-panleukopenia vaccine. Current vaccines substantially reduce clinical disease and mortality but do not completely prevent infection or viral shedding. Continual genomic surveillance, antigenic monitoring and next-generation vaccine platforms are expected to improve long-term control of FCV.

Future vaccine development is therefore shifting toward broader and more durable protective immunity rather than strain-specific protection. One promising strategy involves multivalent vaccines containing antigenically diverse FCV isolates to expand neutralizing antibody breadth. Another approach focuses on identifying conserved structural epitopes capable of inducing broadly neutralizing antibodies that remain effective across genetically divergent viruses. Advances in structural biology, particularly cryo-electron microscopy studies of the VP1–fJAM-A interaction, provide valuable insights into conserved receptor-binding interfaces that may serve as rational vaccine targets [21].

Next-generation vaccine platforms are also being actively explored. Recombinant viral-vectored vaccines, virus-like particles (VLPs), DNA vaccines, messenger RNA (mRNA) vaccines, nanoparticle-based delivery systems, and mucosal immunization strategies have demonstrated encouraging results in experimental studies. Among these, mRNA technology offers particular promise because vaccine sequences can be rapidly updated to match emerging variants, as demonstrated during the COVID-19 pandemic. Likewise, nanoparticle formulations and intranasal vaccines may enhance local mucosal immunity, potentially reducing viral shedding and transmission more effectively than conventional injectable vaccines. Although these approaches remain largely experimental for FCV, they represent important directions for future vaccine innovation [11].

Increasingly, genomic surveillance is becoming an essential component of vaccine development. Continuous monitoring of circulating FCV strains through whole-genome sequencing enables identification of emerging variants, characterisation of antigenic evolution, and evaluation of vaccine–field strain relationships. Integration of genomic epidemiology with structural modelling, antigenic cartography, and artificial intelligence-based prediction of epitope evolution may facilitate periodic optimization of vaccine formulations and improve preparedness for future outbreaks. Similar surveillance-driven approaches have transformed influenza and SARS-CoV-2 vaccine strategies and are likely to become increasingly relevant for rapidly evolving companion animal RNA viruses [8,11].

Ultimately, vaccination should be regarded as one component of an integrated disease-control strategy rather than a standalone intervention. Optimal prevention requires appropriate vaccination schedules, strict hygiene, quarantine of newly introduced animals, environmental disinfection, early molecular diagnosis, genomic surveillance, and rapid

outbreak response. Continued advances in immunology, structural virology, and vaccine engineering are expected to generate broader, longer-lasting, and more adaptable vaccines capable of addressing the remarkable evolutionary capacity of FCV while strengthening preparedness against future emergence of highly virulent variants.

7. Emerging Antiviral and Immunomodulatory Therapies

Despite the widespread availability of vaccines, therapeutic options for feline calicivirus (FCV) infection remain largely supportive. Current management focuses on maintaining hydration, nutritional support, analgesia, antimicrobial therapy for secondary bacterial infections, and intensive care for severely affected cats. While these interventions improve clinical outcomes in uncomplicated infections, they do not directly inhibit viral replication or prevent persistent infection. Consequently, the development of targeted antiviral and host-directed therapies has become an important research priority, particularly in view of the continuing emergence of highly virulent systemic feline calicivirus (VS-FCV) strains [2,3].

Several experimental antiviral compounds have demonstrated activity against FCV by interfering with different stages of the viral replication cycle. Small-molecule inhibitors targeting the viral RNA-dependent RNA polymerase (RdRp), viral protease, and capsid assembly have shown encouraging in vitro efficacy. Structural characterisation of the VP1–fJAM-A interaction has additionally identified receptor binding as a potential antiviral target. Therapeutic agents capable of blocking viral attachment or preventing VP2-mediated genome release may offer broad activity against genetically diverse FCV strains because these early stages of infection are relatively conserved [21].

Host-directed antiviral strategies are receiving increasing attention because they are less susceptible to viral escape mutations. FCV replication depends extensively on host translational machinery, membrane remodeling, autophagy pathways, and intracellular metabolic processes. Pharmacological modulation of these cellular pathways has demonstrated partial inhibition of viral replication in experimental systems. Recent studies have shown that FCV manipulates autophagy and suppresses innate antiviral signalling through degradation of retinoic acid-inducible gene I (RIG-I), suggesting that restoration of host antiviral responses may represent a promising therapeutic approach [49].

Because excessive inflammation contributes significantly to tissue injury, immunomodulatory therapy may also improve clinical outcomes. Dysregulated production of inflammatory cytokines, neutrophil recruitment, endothelial injury, and vascular leakage are particularly evident during VS-FCV infection. Future therapies may therefore combine direct antiviral agents with selective modulation of inflammatory pathways to reduce tissue damage while preserving protective antiviral immunity. Similar host-directed therapeutic strategies have successfully improved outcomes in several human viral diseases and warrant further investigation in feline medicine.

Monoclonal antibodies represent another promising therapeutic platform. Neutralizing antibodies directed against conserved regions of the VP1 capsid protein may provide immediate passive protection during outbreaks, particularly for high-risk animals housed in shelters or veterinary hospitals. Likewise, recombinant antibody engineering may enable development of broadly neutralizing antibodies capable of overcoming the remarkable antigenic diversity of FCV.

Novel drug delivery technologies are also likely to accelerate antiviral development. Nanoparticle formulations, liposomal drug delivery, inhalational therapeutics, and sustained-release intranasal preparations may enhance local antiviral concentrations within the upper respiratory tract while minimizing systemic adverse effects. Artificial intelligence-

assisted virtual drug screening and structure-guided drug design are increasingly facilitating identification of candidate antiviral molecules targeting conserved viral proteins.

Although no licensed FCV-specific antiviral currently exists, continued integration of structural biology, medicinal chemistry, immunology, and computational drug discovery provides an encouraging framework for developing effective therapeutics. Future treatment strategies will likely combine antiviral agents, host-directed immunomodulators, and supportive care to reduce viral replication, limit inflammatory injury, and improve survival during severe outbreaks. Current therapeutic approaches and the major translational priorities for future FCV research and control are summarized in Table 6.

Table 6. Emerging Therapeutic Strategies and Future Research Priorities for Feline Calicivirus. Translational overview linking current therapeutic approaches with host-directed interventions and priority research areas required for next-generation prevention and control of feline calicivirus.

Therapeutic Strategy/Priority Research Area	Target	Current Status	Potential Advantages	Current Limitations	Future Research Priorities
Supportive care [3,92]	Clinical stabilization	Standard of care	Improves survival and welfare	No direct antiviral activity	Evidence-based treatment protocols and severity scoring
RdRp inhibitors (e.g., favipiravir analogues) [93]	Viral RNA polymerase	Experimental	Inhibits viral RNA synthesis	Limited feline efficacy/safety data	Pharmacokinetics studies and clinical trials
3C-like protease inhibitors [46,93]	NS6 protease	Preclinical	Blocks polyprotein processing	No FCV-specific drug available	Structure-guided optimization
Entry inhibitors [39,94]	VP1–fJAM-A interaction	Experimental	Blocks virus attachment and entry	Receptor-binding diversity	Broad-spectrum entry blockade targeting conserved interfaces
Monoclonal antibodies [89,94]	VP1 neutralizing epitopes	Experimental	Specific antiviral activity	Cost and antigenic variation	Broadly neutralizing antibodies
Recombinant feline IFN-ω [51,95]	Innate immune response	Limited clinical use	Enhances antiviral defenses	Variable efficacy	Combination therapy with direct antivirals
Host-directed therapy [49,51]	Autophagy, interferon and inflammatory pathways	Experimental	Potentially reduced resistance	Host toxicity requires evaluation	Precision immunomodulation and biomarker-guided therapy
RNA-targeting therapeutics [95–97]	Viral RNA (siRNA/CRISPR-Cas13)	Experimental	Sequence-specific inhibition	Delivery challenges	Nanocarrier-mediated respiratory delivery
Nanoparticle drug delivery	Respiratory mucosa	Experimental	Improved drug stability and local bioavailability	Manufacturing complexity	Targeted pulmonary delivery systems

Table 6. *Cont.*

Therapeutic Strategy/Priority Research Area	Target	Current Status	Potential Advantages	Current Limitations	Future Research Priorities
Artificial intelligence-assisted drug discovery	Multiple viral and host targets	Emerging	Rapid candidate identification	Requires experimental validation	Integration with structural biology and high-throughput screening
Integrated genomic surveillance [73]	Whole-genome sequencing	Increasing adoption	Early detection of variants and outbreak tracing	Resource intensive	Global databases and real-time molecular epidemiology

Abbreviations: FCV, feline calicivirus; RdRp, RNA-dependent RNA polymerase; fJAM-A, feline junctional adhesion molecule A; IFN-ω, interferon omega. Future control of FCV will likely depend on combining next-generation antivirals, host-directed immunomodulation, genomic surveillance, AI-assisted therapeutic discovery and updated vaccination strategies within a One Health framework.

8. One Health, Outbreak Preparedness and Future Perspectives

Although FCV is not considered zoonotic, its rapid evolution, persistence, and outbreak dynamics provide a useful veterinary model for understanding evolutionary processes relevant to emerging RNA virusesHigh mutation rates, extensive quasispecies diversity, persistent infection, recombination, and rapid adaptation under immune selection mirror evolutionary processes observed in several medically important RNA viruses, including influenza virus, norovirus, and SARS-CoV-2. Consequently, FCV serves as a valuable model for investigating viral emergence, immune escape, and outbreak dynamics within densely populated animal communities [3,11].

The increasing global population of companion animals has substantially altered the epidemiology of infectious diseases. International movement of pets, expanding shelter populations, intensive breeding facilities, and frequent animal movement through veterinary hospitals provide ideal conditions for sustained viral transmission and emergence of novel FCV variants. These interconnected animal populations resemble complex transmission networks capable of supporting rapid viral evolution. Consequently, surveillance strategies should increasingly extend beyond individual clinical cases toward population-level genomic monitoring.

A One Health perspective recognizes the interconnectedness of companion animal health, environmental management, and human activities. Although FCV has no confirmed zoonotic potential, FCV outbreaks can generate important animal welfare concerns, economic costs, and demands on veterinary healthcare systems. Surveillance of FCV can also strengthen veterinary laboratory capacity, molecular diagnostic infrastructure, genomic sequencing capability, and outbreak response systems. These capacities may provide broader preparedness benefits by strengthening surveillance infrastructure applicable to other emerging animal pathogens, including those with zoonotic potential.

Rapid outbreak recognition remains fundamental for disease control. Veterinary hospitals, shelters, rescue organizations, and breeding colonies should implement standardized biosecurity protocols including vaccination, quarantine of newly admitted animals, isolation of clinically affected cats, rigorous environmental disinfection, and appropriate personal protective equipment for personnel. Early molecular diagnosis combined with rapid epidemiological investigation can substantially reduce transmission during institutional outbreaks, particularly when supported by whole-genome sequencing to identify transmission pathways.

Advances in genomic epidemiology are increasingly useful for FCV outbreak investigation. Portable sequencing technologies can enable real-time characterisation of viral genomes, facilitating identification of transmission clusters, monitoring of viral evolution, and differentiation between persistent circulation and repeated viral introduction. Integration of genomic data with geographical information systems, digital epidemiology, and mathematical transmission models will further improve understanding of FCV dissemination across local, national, and international animal populations. The transmission ecology of FCV, together with the major epidemiological drivers and integrated control strategies, is illustrated in Figure 4.

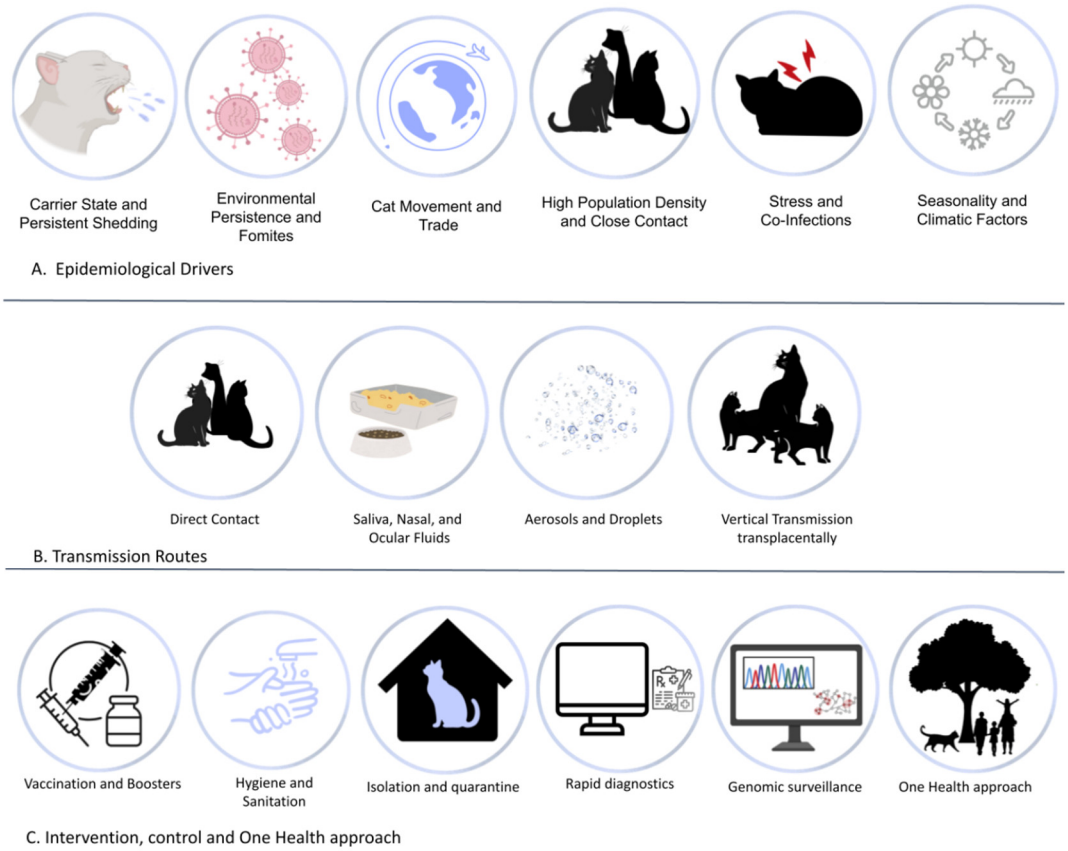


Figure 4. Transmission ecology and epidemiological drivers of feline calicivirus (FCV). Major transmission routes, epidemiological drivers and intervention strategies involved in FCV circulation. The figure highlights the role of surveillance, vaccination, biosecurity, and coordinated veterinary disease-control measures in FCV prevention and outbreak management. Created in BioRender. Publication License Details: https://BioRender.com/t37ngns.

Artificial intelligence (AI) is expected to play an increasingly important role in companion animal infectious disease surveillance. Machine learning algorithms may assist prediction of viral evolution, identification of conserved vaccine targets, optimization of diagnostic primers, automated interpretation of sequencing data, and early recognition of outbreak clusters from electronic veterinary health records. Coupled with cloud-based genomic databases, AI-supported surveillance platforms could provide near real-time monitoring of emerging FCV variants and facilitate evidence-based public health decision-making.

Several important research gaps remain. The molecular determinants responsible for systemic virulence are still incompletely understood, and reliable biomarkers capable of predicting disease severity have not been identified. Likewise, improved understanding of mucosal immunity, long-term viral persistence, and host genetic susceptibility is required for development of broadly protective vaccines and targeted therapeutics. Future studies in-

tegrating comparative genomics, transcriptomics, proteomics, metabolomics, and structural biology will provide a more comprehensive understanding of FCV-host interactions.

International collaboration will be essential for addressing these challenges. Standardized genomic surveillance, harmonized diagnostic protocols, open-access sequence databases, and coordinated vaccine evaluation studies will substantially enhance preparedness against future FCV emergence. Because companion animal infectious diseases increasingly reflect global patterns of pathogen evolution, collaborative surveillance networks should become integral components of veterinary public health infrastructure.

Overall, FCV exemplifies how rapidly evolving RNA viruses continue to challenge conventional disease-control strategies despite decades of vaccination. Continued investment in molecular surveillance, innovative diagnostics, next-generation vaccines, antiviral development, and interdisciplinary One Health collaboration will be critical for reducing disease burden and strengthening preparedness against future companion animal viral outbreaks.

9. Conclusions

Feline calicivirus remains one of the most important viral pathogens of companion cats because of its exceptional genetic diversity, capacity for persistent infection, and continual emergence of antigenically distinct variants. Advances in structural virology, molecular epidemiology, and genomic surveillance have substantially improved understanding of viral evolution, host–pathogen interactions, and mechanisms underlying vaccine escape. Nevertheless, significant challenges remain, including the absence of reliable molecular markers of virulence, incomplete sterilizing immunity following vaccination, persistent viral shedding, and limited availability of virus-specific therapeutics.

Recent progress in whole-genome sequencing, isothermal molecular diagnostics, CRISPR-based detection platforms, artificial intelligence-assisted genomic analysis, and rational vaccine design is transforming the approach to FCV prevention and control. Future strategies should emphasise integrated surveillance systems capable of rapidly identifying emerging variants, supporting outbreak investigation, and informing evidence-based vaccine updates. Simultaneously, advances in antiviral drug discovery and host-directed immunomodulation offer promising opportunities to improve management of severe and systemic disease. In India, the currently available molecular evidence remains geographically limited, with recent reports from northern and northeastern regions demonstrating FCV detection and highlighting the need for broader, standardized surveillance across diverse feline populations.

Beyond its importance in feline medicine, FCV represents a valuable comparative model for understanding the evolution of rapidly mutating RNA viruses. Its capacity for immune escape, adaptation, and persistence illustrates fundamental biological principles shared by many emerging viral pathogens. Continued interdisciplinary collaboration among veterinarians, virologists, immunologists, molecular epidemiologists, and computational scientists will therefore be essential for translating fundamental discoveries into improved diagnostics, therapeutics, and vaccines. Sustained genomic surveillance, technological innovation, and international cooperation can strengthen veterinary capacity to monitor and respond to future companion-animal viral diseases.

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Abbreviations

The following abbreviations are used in this manuscript:

CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
FCV	Feline Calicivirus
fJAM-A	Feline Junctional Adhesion Molecule-A
FURDC	Feline Upper Respiratory Disease Complex
HRM	High-Resolution Melting
IFN	Interferon
IL	Interleukin
NTPase	Nucleoside Triphosphatase
ORF	Open Reading Frame
PCR	Polymerase Chain Reaction
RdRp	RNA-Dependent RNA Polymerase
RIG-I	Retinoic Acid-Inducible Gene I
RNA	Ribonucleic Acid
RT-LAMP	Reverse Transcription Loop-Mediated Isothermal Amplification
RT-qPCR	Reverse Transcription Quantitative Polymerase Chain Reaction
TNF-α	Tumor Necrosis Factor Alpha
VP1	Viral Capsid Protein 1
VP2	Viral Capsid Protein 2
VPg	Virus Protein, Genome-Linked
VS-FCV	Virulent Systemic Feline Calicivirus

References

1. Destoumieux-Garzón, D.; Mavingui, P.; Boetsch, G.; Boissier, J.; Darriet, F.; Duboz, P.; Fritsch, C.; Giraudoux, P.; Le Roux, F.; Morand, S.; et al. The One Health Concept: 10 Years Old and a Long Road Ahead. *Front. Vet. Sci.* **2018**, *5*, 14. [CrossRef] [PubMed]
2. Hofmann-Lehmann, R.; Hosie, M.J.; Hartmann, K.; Egberink, H.; Truyen, U.; Tasker, S.; Belák, S.; Boucraut-Baralon, C.; Frymus, T.; Lloret, A.; et al. Calicivirus Infection in Cats. *Viruses* **2022**, *14*, 937. [CrossRef] [PubMed]
3. Radford, A.D.; Addie, D.; Belák, S.; Boucraut-Baralon, C.; Egberink, H.; Frymus, T.; Gruffydd-Jones, T.; Hartmann, K.; Hosie, M.J.; Lloret, A.; et al. Feline Calicivirus Infection. ABCD Guidelines on Prevention and Management. *J. Feline Med. Surg.* **2009**, *11*, 556–564. [CrossRef] [PubMed]
4. Willi, B.; Spiri, A.M.; Meli, M.L.; Samman, A.; Hoffmann, K.; Sydler, T.; Cattori, V.; Graf, F.; Diserens, K.A.; Padrutt, I.; et al. Molecular Characterization and Virus Neutralization Patterns of Severe, Non-Epizootic Forms of Feline Calicivirus Infections Resembling Virulent Systemic Disease in Cats in Switzerland and in Liechtenstein. *Vet. Microbiol.* **2016**, *182*, 202–212. [CrossRef] [PubMed]
5. Feline Calicivirus-PubMed. Available online: https://pubmed.ncbi.nlm.nih.gov/17296159/ (accessed on 27 July 2026).

6. Hou, J.; Sánchez-Vizcaíno, F.; McGahie, D.; Lesbros, C.; Almeras, T.; Howarth, D.; O'Hara, V.; Dawson, S.; Radford, A.D. European Molecular Epidemiology and Strain Diversity of Feline Calicivirus. *Vet. Rec.* **2016**, *178*, 114–115. [CrossRef] [PubMed]
7. Afonso, M.M.; Pinchbeck, G.L.; Smith, S.L.; Daly, J.M.; Gaskell, R.M.; Dawson, S.; Radford, A.D. A Multi-National European Cross-Sectional Study of Feline Calicivirus Epidemiology, Diversity and Vaccine Cross-Reactivity. *Vaccine* **2017**, *35*, 2753–2760. [CrossRef] [PubMed]
8. Duclos, A.A.; Guzmán Ramos, P.J.; Mooney, C.T. Virulent Systemic Feline Calicivirus Infection: A Case Report and First Description in Ireland. *Ir. Vet. J.* **2024**, *77*, 1. [CrossRef] [PubMed]
9. Pedersen, N.C.; Elliott, J.B.; Glasgow, A.; Poland, A.; Keel, K. An Isolated Epizootic of Hemorrhagic-like Fever in Cats Caused by a Novel and Highly Virulent Strain of Feline Calicivirus. *Vet. Microbiol.* **2000**, *73*, 281–300. [CrossRef] [PubMed]
10. Coyne, K.P.; Jones, B.R.D.; Kipar, A.; Chantrey, J.; Porter, C.J.; Barber, P.J.; Dawson, S.; Gaskell, R.M.; Radford, A.D. Lethal Outbreak of Disease Associated with Feline Calicivirus Infection in Cats. *Vet. Rec.* **2006**, *158*, 544–550. [CrossRef] [PubMed]
11. Wei, Y.; Zeng, Q.; Gou, H.; Bao, S. Update on Feline Calicivirus: Viral Evolution, Pathogenesis, Epidemiology, Prevention and Control. *Front. Microbiol.* **2024**, *15*, 1388420. [CrossRef] [PubMed]
12. Radford, A.D.; Bennett, M.; McArdle, F.; Dawson, S.; Turner, P.C.; Glenn, M.A.; Gaskell, R.M. The Use of Sequence Analysis of a Feline Calicivirus (FCV) Hypervariable Region in the Epidemiological Investigation of FCV Related Disease and Vaccine Failures. *Vaccine* **1997**, *15*, 1451–1458. [CrossRef] [PubMed]
13. Lee, S.-Y.; Kim, Y.-K.; Kim, Y.-S.; Na, E.-J.; Kim, Y.-J.; Oem, J.-K. Intergenic Recombination in Feline Calicivirus Associated with a Hemorrhagic-like Disease in the Republic of Korea. *Acta Virol.* **2021**, *65*, 232–236. [CrossRef] [PubMed]
14. Kim, S.; Cheng, Y.; Fang, Z.; Liu, X.; Zhongqi, Q.; Weidong, Y.; Yilmaz, A.; Yilmaz, H.; Umar, S. Molecular Epidemiology and Phylogenetic Analysis of Feline Calicivirus in Kunshan, China. *Virol. J.* **2024**, *21*, 50. [CrossRef] [PubMed]
15. Frontiers | Classification of Genotypes Based on the VP1 Gene of Feline Calicivirus and Study of Cross-Protection between Different Genotypes. Available online: https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2023.1226877/full (accessed on 19 September 2026).
16. Coyne, K.P.; Gaskell, R.M.; Dawson, S.; Porter, C.J.; Radford, A.D. Evolutionary Mechanisms of Persistence and Diversification of a Calicivirus within Endemically Infected Natural Host Populations. *J. Virol.* **2007**, *81*, 1961–1971. [CrossRef] [PubMed]
17. Day, M.J.; Horzinek, M.C.; Schultz, R.D.; Squires, R.A. Vaccination Guidelines Group (VGG) of the World Small Animal Veterinary Association (WSAVA) WSAVA Guidelines for the Vaccination of Dogs and Cats. *J. Small Anim. Pract.* **2016**, *57*, E1–E45. [CrossRef] [PubMed]
18. Khandelwal, S.; Ranjeet, P.; Kumar, P.M.; Singh, K.; Dixit, S.; Gopinathan, A.; De, U.K.; Parveen, H.; Mahajan, S. A Retrospective Cross-Sectional Study on the Molecular Prevalence of Viral Infections in Domestic Canines and Felines in Bareilly, India. *Indian J. Comp. Microbiol. Immunol. Infect. Dis.* **2025**, *46*, 180–188. [CrossRef]
19. Incidence and Characterization of Feline Alphaherpesvirus 1 and Feline Calicivirus from Domestic Cats in Assam, India | Request PDF. Available online: https://www.researchgate.net/publication/413600139_Incidence_and_Characterization_of_Feline_Alphaherpesvirus_1_and_Feline_Calicivirus_from_Domestic_Cats_in_Assam_India (accessed on 19 September 2026).
20. Sosnovtsev, S.V.; Belliot, G.; Chang, K.-O.; Onwudiwe, O.; Green, K.Y. Feline Calicivirus VP2 Is Essential for the Production of Infectious Virions. *J. Virol.* **2005**, *79*, 4012–4024. [CrossRef] [PubMed]
21. Bhella, D.; Gatherer, D.; Chaudhry, Y.; Pink, R.; Goodfellow, I.G. Structural Insights into Calicivirus Attachment and Uncoating. *J. Virol.* **2008**, *82*, 8051–8058. [CrossRef] [PubMed]
22. Conley, M.J.; McElwee, M.; Azmi, L.; Gabrielsen, M.; Byron, O.; Goodfellow, I.G.; Bhella, D. Calicivirus VP2 Forms a Portal-like Assembly Following Receptor Engagement. *Nature* **2019**, *565*, 377–381. [CrossRef] [PubMed]
23. Quasispecies Evolution of a Hypervariable Region of the Feline Calicivirus Capsid Gene in Cell Culture and in Persistently Infected Cats-PubMed. Available online: https://pubmed.ncbi.nlm.nih.gov/9460915/ (accessed on 28 July 2026).
24. Wang, Z. Feline Calicivirus (FCV): From Molecular Characteristics to Vaccine Development Prospects. *Int. J. Mol. Vet. Res.* **2023**, *13*, 1–10.
25. Coyne, K.P.; Christley, R.M.; Pybus, O.G.; Dawson, S.; Gaskell, R.M.; Radford, A.D. Large-Scale Spatial and Temporal Genetic Diversity of Feline Calicivirus. *J. Virol.* **2012**, *86*, 11356–11367. [CrossRef] [PubMed]
26. Coyne, K.P.; Dawson, S.; Radford, A.D.; Cripps, P.J.; Porter, C.J.; McCracken, C.M.; Gaskell, R.M. Long-Term Analysis of Feline Calicivirus Prevalence and Viral Shedding Patterns in Naturally Infected Colonies of Domestic Cats. *Vet. Microbiol.* **2006**, *118*, 12–25. [CrossRef] [PubMed]
27. Porter, C.J.; Radford, A.D.; Gaskell, R.M.; Ryvar, R.; Coyne, K.P.; Pinchbeck, G.L.; Dawson, S. Comparison of the Ability of Feline Calicivirus (FCV) Vaccines to Neutralise a Panel of Current UK FCV Isolates. *J. Feline Med. Surg.* **2008**, *10*, 32–40. [CrossRef] [PubMed]

28. Localized Adaptive Evolution in VP1 Drives Antigenic Divergence of Feline Calicivirus despite High Sequence Conservation | Veterinary Research | Springer Nature Link. Available online: https://link.springer.com/article/10.1186/s13567-026-01778-y (accessed on 19 September 2026).
29. Zhang, Y.; Cheng, Z.; Guo, C.; Yang, T.; Zhao, W.; Qian, J.; Xia, X.; Bi, J.; Zhou, D.; Xu, S.; et al. Discovery of a Novel Genogroup Feline Calicivirus through Molecular Evolution in Group-Housed Cats in China. *Sci. Rep.* **2025**, *15*, 19059. [CrossRef] [PubMed]
30. Wardley, R.C. Feline Calicivirus Carrier State. A Study of the Host/Virus Relationship. *Arch. Virol.* **1976**, *52*, 243–249. [CrossRef] [PubMed]
31. Bannasch, M.J.; Foley, J.E. Epidemiologic Evaluation of Multiple Respiratory Pathogens in Cats in Animal Shelters. *J. Feline Med. Surg.* **2005**, *7*, 109–119. [CrossRef] [PubMed]
32. Zicola, A.; Saegerman, C.; Quatpers, D.; Viandier, J.; Thiry, E. Feline Herpesvirus 1 and Feline Calicivirus Infections in a Heterogeneous Cat Population of a Rescue Shelter. *J. Feline Med. Surg.* **2009**, *11*, 1023–1027. [CrossRef] [PubMed]
33. Binns, S.H.; Dawson, S.; Speakman, A.J.; Cuevas, L.E.; Hart, C.A.; Gaskell, C.J.; Morgan, K.L.; Gaskell, R.M. A Study of Feline Upper Respiratory Tract Disease with Reference to Prevalence and Risk Factors for Infection with Feline Calicivirus and Feline Herpesvirus. *J. Feline Med. Surg.* **2000**, *2*, 123–133. [CrossRef] [PubMed]
34. Doultree, J.C.; Druce, J.D.; Birch, C.J.; Bowden, D.S.; Marshall, J.A. Inactivation of Feline Calicivirus, a Norwalk Virus Surrogate. *J. Hosp. Infect.* **1999**, *41*, 51–57. [CrossRef] [PubMed]
35. Duizer, E.; Bijkerk, P.; Rockx, B.; De Groot, A.; Twisk, F.; Koopmans, M. Inactivation of Caliciviruses. *Appl. Environ. Microbiol.* **2004**, *70*, 4538–4543. [CrossRef] [PubMed]
36. Clay, S.; Maherchandani, S.; Malik, Y.S.; Goyal, S.M. Survival on Uncommon Fomites of Feline Calicivirus, a Surrogate of Noroviruses. *Am. J. Infect. Control* **2006**, *34*, 41–43. [CrossRef] [PubMed]
37. A Feline Calicivirus Strain Confers Broad Immunity | Animal Diseases | Springer Nature Link. Available online: https://link.springer.com/article/10.1186/s44149-026-00268-0 (accessed on 19 September 2026).
38. Lu, Z.; Ledgerwood, E.D.; Hinchman, M.M.; Dick, R.; Parker, J.S.L. Conserved Surface Residues on the Feline Calicivirus Capsid Are Essential for Interaction with Its Receptor Feline Junctional Adhesion Molecule A (fJAM-A). *J. Virol.* **2018**, *92*, e00035-18. [CrossRef] [PubMed]
39. Makino, A.; Shimojima, M.; Miyazawa, T.; Kato, K.; Tohya, Y.; Akashi, H. Junctional Adhesion Molecule 1 Is a Functional Receptor for Feline Calicivirus. *J. Virol.* **2006**, *80*, 4482–4490. [CrossRef] [PubMed]
40. Bhella, D.; Goodfellow, I.G. The Cryo-Electron Microscopy Structure of Feline Calicivirus Bound to Junctional Adhesion Molecule A at 9-Angstrom Resolution Reveals Receptor-Induced Flexibility and Two Distinct Conformational Changes in the Capsid Protein VP1. *J. Virol.* **2011**, *85*, 11381–11390. [CrossRef] [PubMed]
41. Goodfellow, I.; Chaudhry, Y.; Gioldasi, I.; Gerondopoulos, A.; Natoni, A.; Labrie, L.; Laliberté, J.-F.; Roberts, L. Calicivirus Translation Initiation Requires an Interaction between VPg and eIF 4 E. *EMBO Rep.* **2005**, *6*, 968–972. [CrossRef] [PubMed]
42. Chaudhry, Y.; Nayak, A.; Bordeleau, M.-E.; Tanaka, J.; Pelletier, J.; Belsham, G.J.; Roberts, L.O.; Goodfellow, I.G. Caliciviruses Differ in Their Functional Requirements for eIF4F Components. *J. Biol. Chem.* **2006**, *281*, 25315–25325. [CrossRef] [PubMed]
43. Willcocks, M.M.; Carter, M.J.; Roberts, L.O. Cleavage of Eukaryotic Initiation Factor eIF4G and Inhibition of Host-Cell Protein Synthesis during Feline Calicivirus Infection. *J. Gen. Virol.* **2004**, *85*, 1125–1130. [CrossRef] [PubMed]
44. Bailey, D.; Kaiser, W.J.; Hollinshead, M.; Moffat, K.; Chaudhry, Y.; Wileman, T.; Sosnovtsev, S.V.; Goodfellow, I.G. Feline Calicivirus P32, P39 and P30 Proteins Localize to the Endoplasmic Reticulum to Initiate Replication Complex Formation. *J. Gen. Virol.* **2010**, *91*, 739–749. [CrossRef] [PubMed]
45. Frontiers | Calicivirus Non-Structural Proteins: Potential Functions in Replication and Host Cell Manipulation. Available online: https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2021.712710/full (accessed on 19 September 2026).
46. Wei, L.; Huhn, J.S.; Mory, A.; Pathak, H.B.; Sosnovtsev, S.V.; Green, K.Y.; Cameron, C.E. Proteinase-Polymerase Precursor as the Active Form of Feline Calicivirus RNA-Dependent RNA Polymerase. *J. Virol.* **2001**, *75*, 1211–1219. [CrossRef] [PubMed]
47. Humoud, M.N.; Doyle, N.; Royall, E.; Willcocks, M.M.; Sorgeloos, F.; van Kuppeveld, F.; Roberts, L.O.; Goodfellow, I.G.; Langereis, M.A.; Locker, N. Feline Calicivirus Infection Disrupts Assembly of Cytoplasmic Stress Granules and Induces G3BP1 Cleavage. *J. Virol.* **2016**, *90*, 6489–6501. [CrossRef] [PubMed]
48. Sosnovtseva, S.A.; Sosnovtsev, S.V.; Green, K.Y. Mapping of the Feline Calicivirus Proteinase Responsible for Autocatalytic Processing of the Nonstructural Polyprotein and Identification of a Stable Proteinase-Polymerase Precursor Protein. *J. Virol.* **1999**, *73*, 6626–6633. [CrossRef] [PubMed]
49. Di Profio, F.; Carnevale, M.; Marsilio, F.; Pellegrini, F.; Martella, V.; Di Martino, B.; Sarchese, V. Feline Calicivirus Infection: Current Understanding and Implications for Control Strategies. *Animals* **2025**, *15*, 2009. [CrossRef] [PubMed]
50. Mao, J.; Ye, S.; Deng, J.; Song, J.; Wang, Z.; Chen, A.; Zhou, P.; Li, S. Feline Calicivirus P39 Inhibits Innate Immune Responses by Autophagic Degradation of Retinoic Acid Inducible Gene I. *Int. J. Mol. Sci.* **2023**, *24*, 5254. [CrossRef] [PubMed]

51. Yumiketa, Y.; Narita, T.; Inoue, Y.; Sato, G.; Kamitani, W.; Oka, T.; Katayama, K.; Sakaguchi, T.; Tohya, Y. Nonstructural Protein P39 of Feline Calicivirus Suppresses Host Innate Immune Response by Preventing IRF-3 Activation. *Vet. Microbiol.* **2016**, *185*, 62–67. [CrossRef] [PubMed]
52. Liu, Y.; Liu, X.; Kang, H.; Hu, X.; Liu, J.; Tian, J.; Qu, L. Identification of Feline Interferon Regulatory Factor 1 as an Efficient Antiviral Factor against the Replication of Feline Calicivirus and Other Feline Viruses. *Biomed. Res. Int.* **2018**, *2018*, 2739830. [CrossRef] [PubMed]
53. Tian, J.; Kang, H.; Huang, J.; Li, Z.; Pan, Y.; Li, Y.; Chen, S.; Zhang, J.; Yin, H.; Qu, L. Feline Calicivirus Strain 2280 P30 Antagonizes Type I Interferon-Mediated Antiviral Innate Immunity through Directly Degrading IFNAR1 mRNA. *PLoS Pathog.* **2020**, *16*, e1008944. [CrossRef] [PubMed]
54. DGIST Scholar: Evaluation of Antiviral Efficacy of Recombinant Feline Interferon Lambda-1 Against Calicivirus. Available online: https://scholar.dgist.ac.kr/handle/20.500.11750/57802 (accessed on 19 September 2026).
55. Foley, J.; Hurley, K.; Pesavento, P.A.; Poland, A.; Pedersen, N.C. Virulent Systemic Feline Calicivirus Infection: Local Cytokine Modulation and Contribution of Viral Mutants. *J. Feline Med. Surg.* **2006**, *8*, 55–61. [CrossRef] [PubMed]
56. Pesavento, P.A.; Chang, K.-O.; Parker, J.S.L. Molecular Virology of Feline Calicivirus. *Vet. Clin. N. Am. Small Anim. Pract.* **2008**, *38*, 775–786. [CrossRef] [PubMed]
57. Yan, Q.; Ye, M.; Zhao, Z.; Li, W.; Ye, Z.; Li, L.; Zhang, Y.; Xiong, J.; Lei, Z.; Cao, S. Functional Divergence of Feline Calicivirus Genotypes Shapes Virulence and Antigenic Diversity. *Vet. Microbiol.* **2026**, *321*, 111183. [CrossRef] [PubMed]
58. Magliocca, M.; Mandrioli, L.; Battilani, M.; Bacci, B.; Ballotta, G.; Anjomanibenisi, M.; Urbani, L.; Martella, L.; Facile, V.; Scarpellini, R.; et al. Description of a Virulent Systemic Feline Calicivirus Infection in a Kitten with Footpads Oedema and Fatal Pneumonia. *Pathogens* **2025**, *14*, 1183. [CrossRef] [PubMed]
59. Hurley, K.F.; Sykes, J.E. Update on Feline Calicivirus: New Trends. *Vet. Clin. N. Am. Small Anim. Pract.* **2003**, *33*, 759–772. [CrossRef] [PubMed]
60. Dowers, K.L.; Hawley, J.R.; Brewer, M.M.; Morris, A.K.; Radecki, S.V.; Lappin, M.R. Association of Bartonella Species, Feline Calicivirus, and Feline Herpesvirus 1 Infection with Gingivostomatitis in Cats. *J. Feline Med. Surg.* **2010**, *12*, 314–321. [CrossRef] [PubMed]
61. Hurley, K.E.; Pesavento, P.A.; Pedersen, N.C.; Poland, A.M.; Wilson, E.; Foley, J.E. An Outbreak of Virulent Systemic Feline Calicivirus Disease. *J. Am. Vet. Med. Assoc.* **2004**, *224*, 241–249. [CrossRef] [PubMed]
62. Balboni, A.; Verin, R.; Buldrini, I.; Zamagni, S.; Morini, M.; Terrusi, A.; Gallina, L.; Urbani, L.; Dondi, F.; Battilani, M. Natural Cases of Polyarthritis Associated with Feline Calicivirus Infection in Cats. *Vet. Res. Commun.* **2022**, *46*, 613–619. [CrossRef] [PubMed]
63. Lanave, G.; Buonavoglia, A.; Pellegrini, F.; Di Martino, B.; Di Profio, F.; Diakoudi, G.; Catella, C.; Omar, A.H.; Vasinioti, V.I.; Cardone, R.; et al. An Outbreak of Limping Syndrome Associated with Feline Calicivirus. *Animals* **2023**, *13*, 1778. [CrossRef] [PubMed]
64. Schorr-Evans, E.M.; Poland, A.; Johnson, W.E.; Pedersen, N.C. An Epizootic of Highly Virulent Feline Calicivirus Disease in a Hospital Setting in New England. *J. Feline Med. Surg.* **2003**, *5*, 217–226. [CrossRef] [PubMed]
65. Reynolds, B.S.; Poulet, H.; Pingret, J.-L.; Jas, D.; Brunet, S.; Lemeter, C.; Etievant, M.; Boucraut-Baralon, C. A Nosocomial Outbreak of Feline Calicivirus Associated Virulent Systemic Disease in France. *J. Feline Med. Surg.* **2009**, *11*, 633–644. [CrossRef] [PubMed]
66. Deschamps, J.-Y.; Topie, E.; Roux, F. Nosocomial Feline Calicivirus-Associated Virulent Systemic Disease in a Veterinary Emergency and Critical Care Unit in France. *JFMS Open Rep.* **2015**, *1*, 2055116915621581. [CrossRef] [PubMed]
67. Abd-Eldaim, M.; Potgieter, L.; Kennedy, M. Genetic Analysis of Feline Caliciviruses Associated with a Hemorrhagic-Like Disease. *J. Vet. Diagn. Investig.* **2005**, *17*, 420–429. [CrossRef] [PubMed]
68. Khamsingnok, P.; Rapichai, W.; Rattanasrisomporn, A.; Rungsuriyawiboon, O.; Choowongkomon, K.; Rattanasrisomporn, J. Comparison of PCR, Nested PCR, and RT-LAMP for Rapid Detection of Feline Calicivirus Infection in Clinical Samples. *Animals* **2024**, *14*, 2432. [CrossRef] [PubMed]
69. Mu, H.Y.; Zhou, H.L.; Jing, Z.; Lu, W.; Zhang, J.W. An Exo Probe-Based Reverse Transcription and Recombinase Polymerase Amplification for Rapid Detection of Feline Calicivirus in Cats. *Biomed. Environ. Sci.* **2024**, *37*, 325–330. [CrossRef] [PubMed]
70. Thieulent, C.J.; Carossino, M.; Peak, L.; Wolfson, W.; Balasuriya, U.B.R. Development and Validation of Multiplex One-Step qPCR/RT-qPCR Assays for Simultaneous Detection of SARS-CoV-2 and Pathogens Associated with Feline Respiratory Disease Complex. *PLoS ONE* **2024**, *19*, e0297796. [CrossRef] [PubMed]
71. Phongroop, K.; Rattanasrisomporn, J.; Tangtrongsup, S.; Rungsipipat, A.; Piewbang, C.; Techangamsuwan, S. High-Resolution Melting Analysis for Simultaneous Detection and Discrimination between Wild-Type and Vaccine Strains of Feline Calicivirus. *Vet. Q.* **2023**, *43*, 2272188. [CrossRef] [PubMed]
72. Zhang, Z.; Li, J.; Zhang, C.; Bai, X.; Zhang, T. Rapid Detection of Feline Calicivirus Using Lateral Flow Dipsticks Based on CRISPR/Cas13a System. *Animals* **2024**, *14*, 3663. [CrossRef] [PubMed]

73. Zhou, Y.; Wu, D.; Tang, M.; Ye, Z.; Feng, E.; Zhang, H.; Luo, G.; Wang, Z.; Wang, C.; Liu, L.; et al. Development and Validation of a Droplet Digital PCR Assay for Detection of Feline Herpesvirus Type-1. *Vet. Sci.* **2025**, *12*, 1107. [CrossRef] [PubMed]
74. Frontiers | Whole-Genome Sequencing of Feline Calicivirus in Domestic Cats, South Korea, 2023. Available online: https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2025.1570761/full (accessed on 19 September 2026).
75. Zhang, W.; Li, L.; Deng, X.; Kapusinszky, B.; Pesavento, P.A.; Delwart, E. Faecal Virome of Cats in an Animal Shelter. *J. Gen. Virol.* **2014**, *95*, 2553–2564. [CrossRef] [PubMed]
76. Isolation and Phylogenetic Analysis of Feline Calicivirus Strains from Various Region of China | Animal Diseases | Springer Nature Link. Available online: https://link.springer.com/article/10.1186/s44149-022-00047-7 (accessed on 28 July 2026).
77. Complete Genome Sequence of Feline Calicivirus Strain HRB-SS from a Cat in Heilongjiang Province, Northeastern China-PubMed. Available online: https://pubmed.ncbi.nlm.nih.gov/25189577/ (accessed on 28 July 2026).
78. Huang, J.; Liu, Y.; He, Y.; Yang, X.; Li, Y. CRISPR-Cas13a Based Visual Detection Assays for Feline Calicivirus Circulating in Southwest China. *Front. Vet. Sci.* **2022**, *9*, 913780. [CrossRef] [PubMed]
79. Schultz, R.D.; Thiel, B.; Mukhtar, E.; Sharp, P.; Larson, L.J. Age and Long-Term Protective Immunity in Dogs and Cats. *J. Comp. Pathol.* **2010**, *142*, S102–S108. [CrossRef] [PubMed]
80. Poulet, H.; Jas, D.; Lemeter, C.; Coupier, C.; Brunet, S. Efficacy of a Bivalent Inactivated Non-Adjuvanted Feline Calicivirus Vaccine: Relation between in Vitro Cross-Neutralization and Heterologous Protection in Vivo. *Vaccine* **2008**, *26*, 3647–3654. [CrossRef] [PubMed]
81. Spiri, A.M.; Novacco, M.; Meli, M.L.; Stirn, M.; Riond, B.; Fogle, J.E.; Boretti, F.S.; Herbert, I.; Hosie, M.J.; Hofmann-Lehmann, R. Modified-Live Feline Calicivirus Vaccination Elicits Cellular Immunity against a Current Feline Calicivirus Field Strain in an Experimental Feline Challenge Study. *Viruses* **2021**, *13*, 1736. [CrossRef] [PubMed]
82. Spiri, A.M.; Meli, M.L.; Riond, B.; Herbert, I.; Hosie, M.J.; Hofmann-Lehmann, R. Environmental Contamination and Hygienic Measures After Feline Calicivirus Field Strain Infections of Cats in a Research Facility. *Viruses* **2019**, *11*, 958. [CrossRef] [PubMed]
83. Cao, L.; Liu, J.; Li, Y.; Xie, D.; Yan, Q.; Li, Q.; Cao, Y.; Du, W.; Li, J.; Ye, Z.; et al. Biological Characteristics of Feline Calicivirus Epidemic Strains in China and Screening of Broad-Spectrum Protective Vaccine Strains. *Vaccines* **2023**, *11*, 1858. [CrossRef] [PubMed]
84. Addie, D.; Poulet, H.; Golder, M.C.; McDonald, M.; Brunet, S.; Thibault, J.-C.; Hosie, M.J. Ability of Antibodies to Two New Caliciviral Vaccine Strains to Neutralise Feline Calicivirus Isolates from the UK. *Vet. Rec.* **2008**, *163*, 355–357. [CrossRef] [PubMed]
85. DACVIM, M.R.L. PhD Feline Vaccination: Guidelines, Indications, and Risks (Proceedings) | Dvm360. Available online: https://www.dvm360.com/view/feline-vaccination-guidelines-indications-and-risks-proceedings (accessed on 19 September 2026).
86. Phongroop, K.; Rattanasrisomporn, J.; Piewbang, C.; Tangtrongsup, S.; Rungsipipat, A.; Techangamsuwan, S. Molecular Epidemiology and Strain Diversity of Circulating Feline Calicivirus in Thai Cats. *Front. Vet. Sci.* **2024**, *11*, 1377327. [CrossRef] [PubMed]
87. Poulet, H.; Brunet, S.; Leroy, V.; Chappuis, G. Immunisation with a Combination of Two Complementary Feline Calicivirus Strains Induces a Broad Cross-Protection against Heterologous Challenges. *Vet. Microbiol.* **2005**, *106*, 17–31. [CrossRef] [PubMed]
88. Yang, Y.; Liu, Z.; Chen, M.; Feng, K.; Qi, R.; Kang, H.; Jiang, Q.; Qu, L.; Liu, J. An Effectively Protective VLP Vaccine Candidate for Both Genotypes of Feline Calicivirus. *Front. Immunol.* **2024**, *15*, 1515342. [CrossRef] [PubMed]
89. Tang, A.; Zhu, M.; Zhu, J.; Zhang, D.; Zhu, S.; Meng, C.; Li, C.; Liu, G. The Recombinant Feline Herpesvirus 1 Expressing Feline Calicivirus VP1 Protein Is Safe and Effective in Cats. *Vaccine* **2024**, *42*, 126468. [CrossRef] [PubMed]
90. Cubillos-Zapata, C.; Angulo, I.; Almanza, H.; Borrego, B.; Zamora-Ceballos, M.; Castón, J.R.; Mena, I.; Blanco, E.; Bárcena, J. Precise Location of Linear Epitopes on the Capsid Surface of Feline Calicivirus Recognized by Neutralizing and Non-Neutralizing Monoclonal Antibodies. *Vet. Res.* **2020**, *51*, 59. [CrossRef] [PubMed]
91. Zhang, M.-D.; Xie, Z.-F.; Li, X.-H.; Huang, W.; Qian, Q.-Y.; Cao, H.-T.; Liu, J.-W.; Zhang, Y.-Q.; Wang, B.; Qin, Y.; et al. Engineered VP1 mRNA Vaccine Induces Immunity and Complete Protection Against Feline Calicivirus in Cats. *Transbound. Emerg. Dis.* **2026**, *2026*, 9499266. [CrossRef] [PubMed]
92. Li, P.; Jiang, Z.; Shi, J.; Sha, H.; Yu, Z.; Zhao, Y.; Han, S.; Ma, L. A Self-Assembled Nanoparticle Vaccine Elicits Effective Neutralizing Antibody Response against EBV Infection. *Front. Immunol.* **2025**, *15*, 1530364. [CrossRef] [PubMed]
93. Marif, H.; Raoof, H.; Ali, K.; Muhamad, S.; Ali, B.; Sulaiman, R.; Nasrullah, O. Feline Calicivirus: A Comprehensive Review. *Basrah J. Vet. Res.* **2025**, *24*, 141–165. [CrossRef]
94. Fumian, T.M.; Tuipulotu, D.E.; Netzler, N.E.; Lun, J.H.; Russo, A.G.; Yan, G.J.H.; White, P.A. Potential Therapeutic Agents for Feline Calicivirus Infection. *Viruses* **2018**, *10*, 433. [CrossRef] [PubMed]
95. Fujita, S.; Koba, R.; Tohya, Y. Identification of Amino Acid Substitutions Escaping from a Broadly Neutralizing Monoclonal Antibody of Feline Calicivirus. *Virus Res.* **2022**, *318*, 198848. [CrossRef] [PubMed]

96. McDonagh, P.; Sheehy, P.A.; Fawcett, A.; Norris, J.M. Antiviral Effect of Mefloquine on Feline Calicivirus in Vitro. *Vet. Microbiol.* **2015**, *176*, 370–377. [CrossRef] [PubMed]
97. Suppression of Feline Calicivirus Replication Using Small Interfering RNA Targeted to Its Polymerase Gene. Available online: https://www.jstage.jst.go.jp/article/bio/17/2/17_87/_article/-char/en (accessed on 19 September 2026).

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