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Genomics and outbreaks: foot and mouth disease

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Summary

Foot and mouth disease virus (FMDV) is an animal pathogen of global economic significance. Identifying the sources of outbreaks plays an important role in disease control; however, this can be confounded by the ease with which FMDV can spread via movement of infected livestock and animal products, aerosols or fomites, e.g. contaminated persons and objects. As sequencing technologies have advanced, this review highlights the uses of viral genomic data in helping to understand the global distribution and transboundary movements of FMDV, and the role that these approaches have played in control and surveillance programmes. The recent application of next-generation sequencing platforms to address important epidemiological and evolutionary challenges is discussed with particular reference to the advent of 'omics' technologies.

Keywords

Foot and mouth disease virus – Genomics – Molecular epidemiology – Next-generation sequencing – Outbreak tracing – Sanger sequencing – Sequencing – Viral diversity – Virus.

Introduction

Foot and mouth disease (FMD) is one of the most highly contagious diseases that affect cloven-hoofed domesticated livestock (e.g. cattle, sheep, pigs and goats) and wildlife species. The causative agent is a virus (FMDV) which is the prototype member of the genus *Aphthovirus*, family *Picornaviridae*. This virus exists as seven genetically distinct serotypes (A, O, C, Asia 1, Southern African Territories [SAT] 1, SAT 2 and SAT 3), distributed on three continents: Asia, Africa and South America (Fig. 1). Genetic and antigenic analyses of the virus have led to further subdivision of FMDV distribution into seven endemic pools of infection in which particular virus strains circulate (1), reflecting trade and animal movement patterns in addition to the presence and spatial distribution of susceptible wildlife. Ongoing vaccination programmes continue to reduce the geographical extent of FMD at the margins of the disease's geographical range, although campaigns tailored to specific regions are still required.

Although FMD does not typically cause high mortality among susceptible animals, its highly contagious nature and the associated productivity losses make it a major economic concern for livestock farming in many developing countries (2). Outbreaks can also be closely associated with social factors such as migration, conflict or social breakdown (3). In order to maintain commercial trade links, effective vaccination campaigns and stringent control measures have been used to eradicate FMD in Europe and much of South America where the disease was previously endemic. Despite this, the disease continues to circulate on several continents as a consequence of complex epidemiological dynamics and maintenance patterns within both wildlife and livestock (4, 5). Sporadic incursions of FMD from these endemic pools continue to threaten countries with disease-free status (6). The FMD epidemic in the United Kingdom (UK) in 2001, which resulted in approximately 7 million animals slaughtered and £8 billion of losses, is a well-documented example of the severe impacts of the disease in a previously FMD-free country (7, 8).

Conventional field-based investigations employing forward- and back-tracing are important approaches that are widely used to identify the sources of outbreaks and risks for onward transmission within disease clusters. Laboratory testing also plays an essential role in the generation of supporting data (7, 9), with both virological diagnostic assays and analyses of nucleotide sequence data being employed in FMD Reference Laboratories. In particular,

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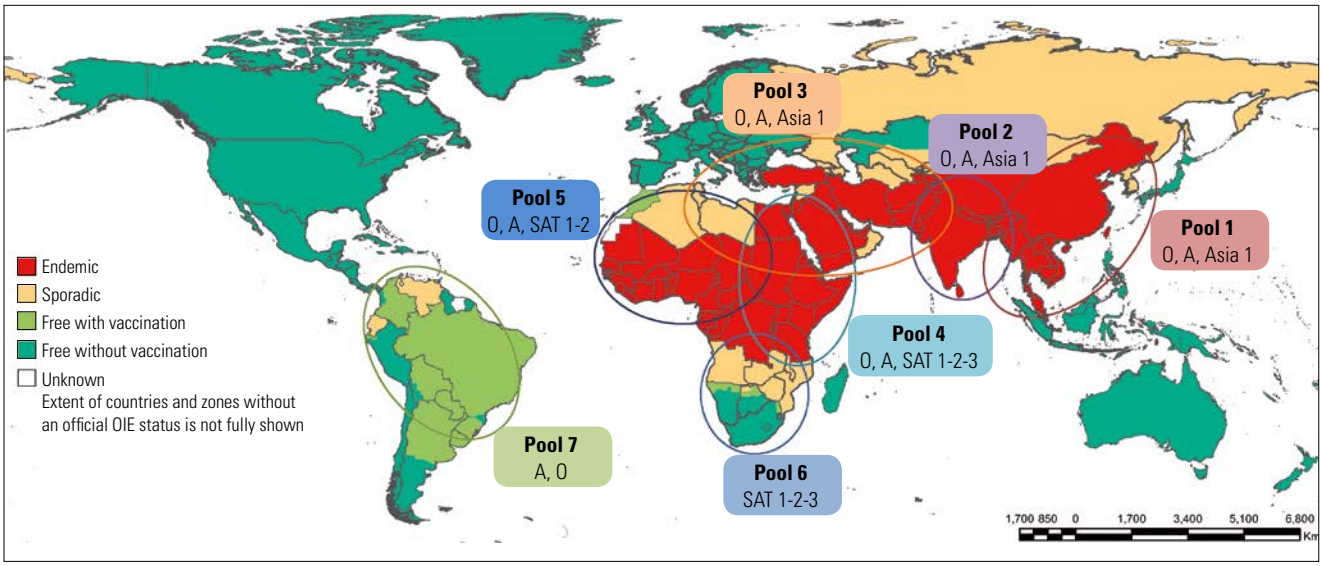


Fig. 1
Global circulation of foot and mouth disease virus
Distribution of the seven endemic pools of foot and mouth disease showing the predominant viral serotypes that are present in each region, as well as the conjectured status of foot and mouth disease in different countries
Periodically, viruses spread between pools and to free regions, and countries at the interfaces between pools (such as in North Africa and Central Asia) often experience foot and mouth disease outbreaks from different regional sources

the recent advancements in sequencing technologies have played a driving role in the utilisation of both partial- (viral protein [VP]1) and whole-genome sequencing (WGS) to address questions relating to FMDV circulation in field settings, and identification of the sources of FMD outbreaks.

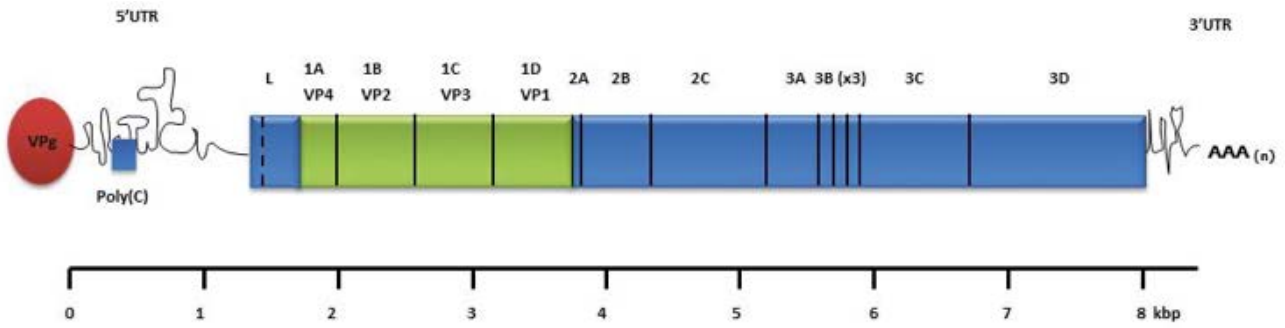
This review outlines how sequencing and genomics have been embraced to drive knowledge and understanding of the epidemiology of FMDV outbreaks and the mechanisms that underpin FMDV evolution. This review also summarises the potential of recently developed technologies, such as next-generation sequencing (NGS), that are now being exploited to develop novel tools to expand our knowledge of FMDV phylogenomics.

Foot and mouth disease virus: genome organisation

The genome of FMDV comprises a single strand of positive-sense RNA approximately 8,300 nucleotides (nt) in length; the virus encodes an enzyme (RNA-dependent RNA polymerase) that facilitates viral RNA (vRNA) genome replication. These enzymes in RNA viruses, such as FMDV, typically have poor fidelity, resulting in frequent changes to the nascent nucleotide sequence of progeny viruses. The viral genome contains a single long open reading frame (ORF) flanked by highly structured 5′ and 3′ untranslated regions (UTR) (Fig. 2), with a long poly-cytosine tract (poly(C), ~250 bases) of unknown function located within the 5′UTR. A large polyprotein, encoded by the ORF, is subsequently cleaved by viral proteases (10) to produce four structural polypeptides (VP1–4), with VP1–3 being exposed on the surface of the virus, encapsulating the RNA genome. Of these, the VP1 protein (also referred to as 1D), encoded by, on average, 639 nt, contains several major antigenic determinants (11, 12) in addition to playing a number of other critical roles, including viral attachment, cell entry and stimulation of immunity.

Molecular epidemiology using partial genome sequences

One of the most important applications for FMDV nucleotide sequence data has been in the field of molecular epidemiology (7), where phylogenetic comparisons of VP1 sequence data are widely and routinely used to monitor outbreaks (13, 14, 15, 16). Although VP1 has become the most commonly used and robust genetic marker for outbreak tracing, other studies have also focused on the phylogenetic analysis of other FMDV genomic regions (17, 18, 19). Phylogenetic analysis of VP1 can be applied to categorise field strains into discrete topotypes and lineages which, despite the tendency for the virus to spread, frequently show geographical clustering based on the historical distribution of the virus (20). The distribution of these different serotypes and topotypes varies according to countries and



AAA: poly(A) tail
kb: kilobases
L, 2A, 2B, 2C, 3A, 3B, 3C and 3D: non-structural proteins
Poly(C): poly-cytosine tract
UTR: untranslated regions
VP1–4: viral proteins
VPg (3B): virus-encoded peptide primer for synthesis of viral RNA

Fig. 2
A cartoon of the foot and mouth disease virus genome

continents and in some areas several serotypes and variants can circulate simultaneously. The nucleotide sequence identity amongst the FMDV serotypes and topotypes has also been investigated (21, 22), with the VP1 coding region having been reported to be considerably more diverse (in the range of 30–50% identity between serotypes) than other regions of the genome (7). The increase in both partial and whole FMDV genome sequence data available in the public domain reflects the increased application of sequence-based studies for the characterisation of field viruses, and the use of such data in attempting to reconstruct transmission pathways during outbreaks (Fig. 3).

The combination of Sanger-based sequencing and phylogenetic analysis has been instrumental in identifying the source of outbreaks from the distribution of diversity within viral populations (23) since the methodology was first employed to investigate diversity in A and O strains in Europe (24) (Table I). In addition to characterising FMD outbreaks in endemic regions of the world (14, 56, 57), genomic data have been used recently to characterise FMD viruses recovered from exotic incursions, including the spread of FMD due to serotype SAT 2 into Egypt (58, 59), to monitor the spread of lineages into new geographical regions (15, 42, 60), in the discovery of novel lineages (13, 61) and to retrospectively analyse the diversity in previous outbreaks (53, 62). Such surveillance highlights the transboundary movements of FMDV, providing critical support for both regional and country-level control programmes.

The following examples show the application of phylogenetic analyses of VP1 sequences in tracing the transboundary spread of FMD viruses:

i) O/SEA/Mya-98, O/ME-SA/PanAsia and A/ASIA/Sea-97 lineages from FMD-endemic parts of mainland Southeast Asia into countries lying to the north, i.e. the People's Republic of China, Mongolia, North and South Korea, eastern parts of the Russian Federation, Chinese Taipei and Kazakhstan (63)

ii) serotype SAT 2 and A/AFRICA/G-VI from sub-Saharan Africa to North Africa and the Middle East (4, 59)

iii) O/ME-SA/Ind-2001d lineage from the Indian subcontinent to the Middle East and North Africa (15).

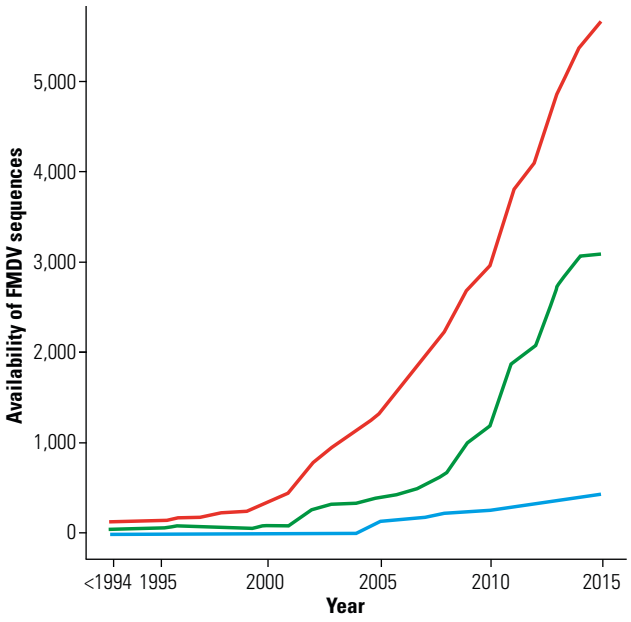


Fig. 3
Increasing number of foot and mouth disease virus sequence submissions to the National Center for Biotechnology Information GenBank since 1994
The figure shows VP1 (green line: comprising all the sequences of <700 nucleotides [nt] mapping to VP1, including partial VP1sequences), whole-genome sequencing for FMDV (blue line: comprising all FMDV sequences >7,000 nt in length, including complete genome and partially complete coding regions), and all FMDV sequences (red line)

In each case, presumed changes in socio-political or trade circumstances have led to repeated and unusual transboundary movements of multiple virus serotypes/topotypes/lineages.

Studies of larger VP1 sequence datasets have permitted more detailed evolutionary analysis to be undertaken to retrospectively trace evolutionary histories between continents and countries and to identify common ancestors (27, 64). In particular, evolutionary models of population dynamics have been used to infer viral demographic signals and changes in population sizes, highlighting the impact of control policies, such as vaccination and culling, in reducing outbreak sizes (65). Therefore, the monitoring of past viral population kinetics and evolutionary dynamics of FMDV can inform and drive the guidance of regional and country-level control policies. While major serotypic determinants reside within the genomic region encoding VP1, a number of studies have looked at comparative genomics of FMDV using both individual components of the FMDV genome (46, 66), and on a genome-wide level, exploring genetic relationships between individual serotypes (53, 67, 68).

Molecular epidemiology: whole-genome sequencing

Genomics can ultimately drive the reconstruction of FMDV movements on multiple scales ranging from intra-host, to farm, to region, to country, and also to a wider global picture (69), thus providing a more detailed breakdown of the virus transmission chain (i.e. 'who infected whom'), with this knowledge directly supporting decision- and policy-makers in outbreak management. Although the VP1 coding region of FMDV is useful for such characterisation of field outbreaks at both regional and country levels, it is relatively short (only ~8% of the genome length) and, consequently, phylogenetic trees generated from very closely related FMDV sequences recovered within outbreak clusters are typically flat, with poor resolution (Fig. 4) (41, 71). For this reason, the use of WGS to discriminate between closely related organisms has become commonplace and has subsequently been applied to both human (72, 73) and animal pathogens (74, 75). Novel advances in genome sequencing technologies have enabled a much increased

Table I
Selected publications describing recent outbreaks and molecular epidemiology of foot and mouth disease virus using genomics and sequencing of both partial genomes (e.g. VP1) and whole genomes

Virus pool	Serotype	Partial-genome sequencing	Whole-genome sequencing
Pool 1	O, A, Asia 1	Abdul-Hamid *et al.* (14)	Abdul-Hamid *et al.* (28)
		Valarcher *et al.* (25)*	Yang *et al.* (29)
		Hui and Leung (26)	Zheng *et al.* (30)
		Di Nardo *et al.* (27)	Valdazo-González *et al.* (31)
Pool 2	O, A, Asia 1	Valarcher *et al.* (25)*	Subramaniam *et al.* (13)
		Yuvaraj *et al.* (32)	Subramaniam *et al.* (35)
		Nandi *et al.* (33)	Ullah *et al.* (36)
		Subramaniam *et al.* (34)	Valdazo-González *et al.* (37)*
Pool 3	O, A, Asia 1	Knowles *et al.* (15)	Jamal *et al.* (40)
		Valarcher *et al.* (25)*	Valdazo-González *et al.* (41)
		Schumann *et al.* (38)	
		Brito *et al.* (39)	
Pool 4	O, A, SAT 1, SAT 2, SAT 3	Hall *et al.* (42)*	Balinda *et al.* (16)
		Wekesa *et al.* (43)	Valdazo-González *et al.* (37)*
		Wekesa *et al.* (44)	Carrillo *et al.* (46)
		Dhikusooka *et al.* (45)	
Pool 5	O, A, SAT 1, SAT 2	Sangare *et al.* (47)	
		Hall *et al.* (42)*	
		Ehizibolo *et al.* (48)	
		Gorna *et al.* (49)	
Pool 6	SAT 1, SAT 2, SAT 3	Bastos *et al.* (50)	Carrillo *et al.* (46)*
		Phologane *et al.* (51)	Logan *et al.* (52)
		Hall *et al.* (42)*	
Pool 7	O, A	König *et al.* (53)	Carrillo *et al.* (46)*
		Malirat *et al.* (54)	
		Malirat *et al.* (55)	

*Cross-pool infections

discriminatory resolution (76, 77) coupled with a higher throughput sequencing of complete FMDV genomes (28, 78). For the first time, this has opened up the potential for using WGS to reconstruct virus transmission trees with extremely high resolution, rapidly revealing the origin of unresolved transmission events within discrete infection clusters. When combined with accurate epidemiological data and a more diverse range of strategies for sampling wildlife in endemic areas, such an approach will enable us to draw more accurate conclusions about the virus transmission chain (79).

Initial WGS studies were undertaken using field samples collected from 21 strategically selected farms from the UK 2001 FMD epidemic, demonstrating that transmission events at farm-to-farm level could be reconstructed (80) using only statistical parsimony-based analyses, thus confirming the initial epidemiological reports of viral spread. Nevertheless, inconsistencies were evident between the transmission histories predicted by the genetic data and those suggested by conventional contact-tracing studies, thus underlining the critical requirement for both accurate sequence information and accompanying contextual information with fully resolved spatio-temporal data when successfully reconstructing transmission trees (9, 80). The WGS approach has also been used to discriminate between natural and unconventional sources of outbreaks (81); one such study investigated the UK 2007 FMD outbreak, with the aim of:

– distinguishing between accidental and natural infection
– tracing the outbreak transmission chain.

The investigation successfully demonstrated the processing of samples in real time, and predicted undisclosed infected

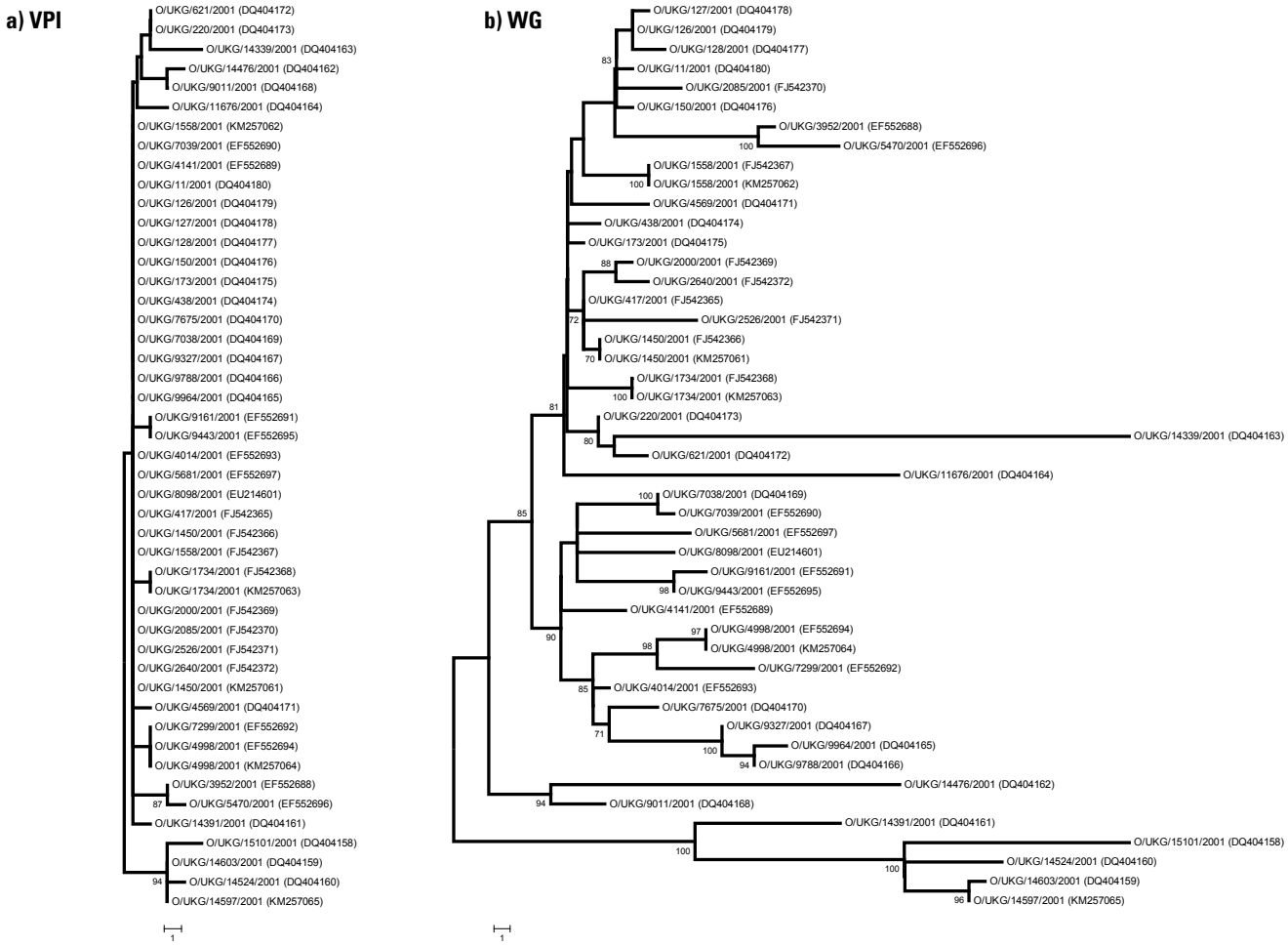


Fig. 4

A comparison between phylogenetic analysis of data generated from the same foot and mouth disease virus isolates collected during the 2001 foot and mouth disease epidemic in the United Kingdom using VP1 only or WG (whole genome)

Maximum likelihood trees were produced using MEGAv.6.06 (70)

premises prior to their discovery by serological surveillance (71). Using consensus-level WGS from each farm, the presence of cell-culture-specific adaptations within field isolates was identified as indicative of an unconventional or laboratory-derived infection/escape. The extent of intra-farm sequence variability was also investigated, identifying nucleotide changes at 56 sites in 36 isolates recovered from the eight infected premises (82). Such studies have provided background information that has increased our understanding of the complexity of FMD epidemiology within farms, and has shown that trees generated using a single consensus from each farm were as accurate as those trees generated using multiple consensus sequences (a finding of potential epidemiological importance, with implications for outbreak management).

Furthermore, WGS approaches have been used to reconstruct the origin and transmission history of FMD outbreaks which occurred during 2011 in Burgas Province, Bulgaria (83). This was an area that was previously FMD-free without vaccination (84). Initial attempts to use VP1 sequences failed to resolve the epidemiological relationships between the infected farms; therefore, whole genome sequences were produced to increase the accuracy of the predicted transmission chains, to a greater resolution. The numbers of nucleotide changes present between, and within, separate clusters provided evidence that undetected FMDV infection had occurred. These conclusions supported laboratory data that subsequently identified three further FMDV-infected livestock premises by serosurveillance, in addition to a number of antibody-positive wild boars on both sides of the border with Turkish Thrace. Like the UK 2001 and 2007 FMD outbreak investigations, this study underlined the importance of combining the accuracy of traditional epidemiological and sequence data in drawing the correct interpretations and conclusions from the data.

Information extracted from genetic sequences, spanning either the VP1 coding region only or the whole genome, has also been used to obtain information on evolutionary mechanisms such as viral mutation rates (Table II). Although the mutational frequency of viruses is seen to vary according to the genome resolution and the study system, FMDV molecular clock estimates obtained from WGS and VP1-only data are similar, even though a wider variability is observed in those extracted from VP1 coding sequences. Furthermore, both epidemic and endemic settings provide a similar evolutionary dynamic. This might suggest that FMDV evolutionary dynamics are driven by a strict, stable and constant molecular clock. Evolutionary rates have also been used to predict/identify the occurrence of fomite transmission (i.e. the re-infection of infected premises [IP]) through the introduction of infected hay, which atypically produced unusually 'slow' evolutionary rates within an outbreak (86).

The new age of genomics: the potential of next-generation sequencing

Next-generation sequencing is a term that encompasses a family of new technologies that show much promise for sequence analysis (95). The advantage of NGS is its ability to generate sequence data directly from amplified single complementary DNA (cDNA) fragments, thereby circumventing the need for DNA cloning of fragments. Furthermore, NGS enables sequencing on a high-throughput scale not afforded by previous Sanger-based technologies, with a choice of several platforms being available to the end-users (96). In spite of these benefits, several issues remain, particularly those concerning running costs and error rates, despite significant recent advancements in the chemistries and protocols for individual platforms (97, 98). Until now, NGS has predominantly been used as a research tool to produce consensus-level WGS and sub-consensus deep sequencing with the aim of elucidating mechanisms of FMD viral evolution. For an RNA virus such as FMDV, the ability of NGS to characterise and monitor the complex viral sequence swarm that surrounds the consensus provides new and exciting tools that can be applied to address questions that underpin the evolutionary biology of the virus. In this context, NGS has primarily been used to characterise intra-host FMDV dynamics and diversity (99) and to define the changes that accrue in viral populations during controlled transmission experiments (100). Previous studies had addressed this at the consensus level using Sanger sequencing, characterising the accumulation and fixation of nucleotide changes within a transmission chain of experimental infection in cattle, with WGS analysis clearly demonstrating sequence divergence during parallel passage via direct and indirect contact (85). Surprisingly, the rate of substitutions between animal hosts was comparable to those reported previously during the UK FMD epidemics in 2001 and 2007, indicating that FMD infection on farms is typically a parallel process. In a follow-up study, NGS was utilised to sequence amplicons (generated by long-reverse-transcriptase PCR) on an Illumina GA2 (99). This was then repeated for multiple animal hosts in an experimental transmission chain (100). Sequence data suggested that genetic bottlenecks impact upon viral diversity at different tissue lesion sites within the same host, prior to further dissemination among other individual infected animals.

Current efforts are focused upon the development of and requirement for a high-throughput capability, in order to assess the suitability of NGS to process and generate consensus-level whole genome sequences within an outbreak scenario. Methodologies have already been published to

Table II
Comparison of estimated substitution rates between transmission chains reconstructed from foot and mouth disease virus sequence data retrieved from either experimental, endemic or epidemic scenarios using a strict molecular clock evolutionary model

Dataset	Scenario	Sequence type	Serotype	Substitution rate (nt/site/day)	Substitution rate (nt/site/year)	Reference
Cow-to-cow (chain A)	Experimental	WGS	O	2.27×10^{-5}	8.29×10^{-3}	85
Cow-to-cow (chain B)	Experimental	WGS	O	2.86×10^{-5}	1.04×10^{-2}	85
Herd-to-herd (1967)	Epidemic	WGS	O	2.39×10^{-5}	8.74×10^{-3}	86
Herd-to-herd (2001)	Epidemic	WGS	O	2.37×10^{-5}*	8.66×10^{-3}*	87
Herd-to-herd (2007)	Epidemic	WGS	O	2.51×10^{-5}	9.17×10^{-3}	71
Herd-to-herd	Epidemic	WGS	O	2.48×10^{-5}	9.05×10^{-3}	83
Mixed (2007)	Epidemic	WGS	O	2.80×10^{-5}*	1.02×10^{-2}*	82
Isolate-to-isolate	Endemic	WGS	O	1.35×10^{-5}	4.94×10^{-3}	31
Isolate-to-isolate	Endemic	VP1	Asia 1	1.57×10^{-5}	5.74×10^{-3}	88
Isolate-to-isolate	Endemic	VP1	A	1.09×10^{-5}	4×10^{-3}	89
Isolate-to-isolate	Endemic	VP1	O	7.56×10^{-5}	2.76×10^{-3}	16
Isolate-to-isolate	Endemic	VP1	O, A, C, Asia 1, SAT 1, SAT 2 & SAT 3	6.79×10^{-6}	2.48×10^{-3}	90
Isolate-to-isolate	Endemic	VP1	SAT 2	6.71×10^{-6}	2.45×10^{-3}	42
Isolate-to-isolate	Endemic	VP1	O	4.87×10^{-6}	1.78×10^{-3}	91
Isolate-to-isolate	Endemic	VP1	O, A, C, Asia 1, SAT 1, SAT 2 & SAT 3	3.99×10^{-6}	1.46×10^{-3}	67
Isolate-to-isolate	Endemic	VP1	SAT 2	3.56×10^{-6}	1.30×10^{-3}	92
Isolate-to-isolate	Endemic	VP1	O	3.01×10^{-5}	1.10×10^{-2}	93
Isolate-to-isolate	Endemic	VP1	A	2.90×10^{-5}	1.06×10^{-2}	94
Isolate-to-isolate	Endemic	VP1	O	2.90×10^{-5}	1.06×10^{-2}	27
Isolate-to-isolate	Endemic	VP1	O	2.74×10^{-5}	1×10^{-2}	89

* Value has been re-estimated from the original data
nt: nucleotide
WGS: whole-genome sequencing

obtain WGS for FMDV and other polyadenylated RNA viruses (52); however, although significant progress has been made, the practicalities of high-throughput sequencing require further validation. Factors including sample-to-sample contamination, processing time and the development of simple analysis workflows, as well as the financial resources required to undertake these types of study, remain obstacles to be circumvented. Furthermore, with the increase in the use of NGS-based technologies with RNA viruses, such as FMDV, the development of analytical tools for such datasets, thereby maximising their usefulness, will become an area of critical importance (9, 101).

Genomics as a tool for understanding viral evolution: viral diversity and recombination

In addition to understanding viral population diversity, genomics has also enabled the fine dissection of viral evolutionary mechanisms (102, 103), with recombination being of particular interest as a source of outbreak diversity. Studies with recombinant viruses have previously demonstrated the generation of recombination

events within the FMDV genome (104), and have highlighted the fact that particular regions of the FMDV genome appear to be more prone to intertypic recombination than others. Recombination events are rarely observed in the capsid proteins (46), and are more frequently observed in the non-structural coding regions (105). Studies with field isolates have also reported these observations through the analysis of WGS, confirming these observations with several serotypes, including A and Asia 1 (18, 40, 60), and reconfirming that the non-structural regions are more likely to be involved in recombination events, particularly in regions where co-circulation of the multiple serotypes and/or topotypes is present.

Future directions and conclusions

One of the greater challenges facing the application of genomics to outbreak tracing lies in the construction of transmission trees from phylogenetic data, particularly through integration of spatio-temporal epidemiological data (9, 87, 106). Such methods, integrating both phylogenetic and epidemiological data in transmission networks in order to maximise usage of currently available data, could in theory increase statistical power while reducing bias (107).

Furthermore, as the technology advances, the development of the 'third-generation sequencing' platforms (such as the Pacific Biosystems PacBio RS/single molecule, real-time [SMRT] sequencing platform) has yet to be exploited (108). These methodologies open up new possibilities, such as providing the capability for minimal library preparation and long reads (up to 10 kilobases), thus enabling true linkage to be established between variants within single genomes. Despite this, high error rates remain an issue that has plagued their development, although recent technological progress continues to reduce them to a level more comparable with existing NGS platforms (109). Oxford Nanopore Technologies and their MinION nanopore sequencer have generated particular interest within the scientific community (110). The USB-sized MinION offers the exciting potential of bringing genomics firmly into the realm of FMDV diagnostics. With the first studies regarding viral population sequencing to consensus level having been published (111, 112), the MinION's portability, combined with advances in global positioning system (GPS) technologies, could result in high-resolution WGS being coupled with highly accurate spatio-temporal data, which would significantly aid traceability between even the remotest farms in any outbreak.

As the sequencing technology continues to advance (irrespective of whether it is first, second or third generation), genomics will become more closely aligned with FMDV molecular epidemiology, even though financial and technical issues still make future advances challenging, particularly in developing countries where the technologies are most needed (113). Areas requiring development include the significant demands on infrastructure in terms of both expertise and resources, particularly when considering implementation of high-throughput sample processing pipelines and the level of bioinformatics expertise required for data analysis. Furthermore, with the advent of the 'omics' era, improvements in the analysis, archiving and sharing of WGS data are required before sequencing can progress and drive decision- and policy-making. This will involve investment in standardising data processing and analysis in ways acceptable for accreditation, the development of databases and communication tools, which are required to maximise the use of data, and a focus on ethical issues, including ownership, access and security (114). The challenges of combining genomics with other clinical and epidemiological datasets will require careful consideration. As technologies progress and genomics plays a more central role in outbreak tracing, these advances will provide us with some of the solutions required to overcome these issues.

Conclusions

The genomics revolution is changing the way outbreak tracing is approached on fundamental levels, and changing how such information is handled and disseminated. It is also extending the possibilities of what can be done and what is known. Whether VP1 will remain sufficient for future routine handling of outbreaks remains to be seen; this very much depends upon increased throughput and the time spans of the higher-throughput protocols. This will have impacts upon both policies and how outbreaks are managed in the future.

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La génomique et le contrôle des foyers : la fièvre aphteuse

G.L. Freimanis, A. Di Nardo, K. Bankowska, D.J. King, J. Wadsworth, N.J. Knowles & D.P. King

Résumé
Le virus de la fièvre aphteuse est un agent pathogène affectant les animaux d'élevage, avec des conséquences économiques considérables à l'échelle mondiale. La détection des sources des foyers est un aspect important de la lutte contre cette maladie ; l'efficacité de cette stratégie est toutefois compromise par la facilité avec laquelle le virus de la fièvre aphteuse se propage à la faveur des mouvements d'animaux ou de produits d'origine animale infectés, d'aérosols ou de personnes ou matières contaminées. Les auteurs décrivent, au fur et à mesure des avancées des technologies du séquençage, les données de la génomique virale qui ont permis de mieux comprendre la distribution mondiale et la propagation transfrontalière du virus de la fièvre aphteuse et le rôle que ces approches ont commencé à jouer dans les programmes de contrôle et de surveillance. Les auteurs examinent également les applications récentes des plates-formes de séquençage de nouvelle génération pour résoudre des problèmes épidémiologiques et évolutifs importants, en se référant particulièrement à l'avènement des technologies dites «–omiques ».

Mots-clés
Diversité virale – Épidémiologie moléculaire – Génomique – Identification des sources des foyers – Séquençage – Séquençage de nouvelle génération – Séquençage par la méthode de Sanger – Virus – Virus de la fièvre aphteuse.

Genómica y brotes: fiebre aftosa

G.L. Freimanis, A. Di Nardo, K. Bankowska, D.J. King, J. Wadsworth, N.J. Knowles & D.P. King

Resumen
El virus de la fiebre aftosa es un patógeno animal que reviste importancia planetaria. A la hora de combatir la enfermedad es útil poder determinar el origen de los brotes, tarea que sin embargo puede verse frustrada por la facilidad con que el virus es capaz de diseminarse siguiendo los desplazamientos de animales o derivados animales infectados o por aerosoles o fómites (por ejemplo personas u objetos contaminados). Los autores hacen hincapié en la utilización de datos de genómica vírica para ayudar a aprehender la distribución mundial y los movimientos transfronterizos del virus de la fiebre aftosa, lo cual es posible gracias a los avances que han conocido las técnicas de secuenciación, así como en la función que pueden cumplir estos métodos dentro de los programas de control y vigilancia. También examinan la reciente aplicación de dispositivos de secuenciación de próxima generación para abordar importantes problemas epidemiológicos y evolutivos, refiriéndose especialmente al advenimiento de las técnicas «ómicas».

Palabras clave
Diversidad vírica – Epidemiología molecular – Genómica – Rastreo de brotes – Secuenciación – Secuenciación de próxima generación – Secuenciación de Sanger – Virus – Virus de la fiebre aftosa.

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