Using genomics for surveillance of veterinary infectious agents

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Summary
Factors such as globalisation, climate change and agricultural intensification can increase the risk of microbial emergence. As a result, there is a growing need for flexible laboratory-based surveillance tools to rapidly identify, characterise and monitor global (re-)emerging diseases. Although many tools are available, novel sequencing technologies have launched a new era in pathogen surveillance. Here, the authors review the potential applications of high-throughput genomic technologies for the surveillance of veterinary pathogens. They focus on the two types of surveillance that will benefit most from these new tools: hazard-specific surveillance (pathogen identification and typing) and early-warning surveillance (pathogen discovery). The paper reviews how the resulting sequencing data can be used to improve diagnosis and concludes by highlighting the major challenges that hinder the routine use of this technology in the veterinary field.

Keywords
Genomics – High-throughput sequencing – Infectious disease – Metagenomics – Next-generation sequencing – Surveillance – Typing – Veterinary pathogen – Whole-genome sequencing.

Introduction

The regular emergence and re-emergence of infectious diseases poses a significant challenge to both animal and human health. Globalisation, climate change and agricultural intensification all favour the emergence and spread of infectious disease (1, 2, 3). It is well established that infectious animal diseases can have a major economic impact at both the national (high-impact diseases) and domestic (enzootic diseases) levels, as well as on public health (zoonoses). A comprehensive literature survey revealed that 58% of all infectious diseases of humans and 73% of emerging infectious diseases of humans originate from animals (4). Responding to these challenges requires a more holistic and collaborative approach to animal and human health (www.onehealthinitiative.com).

The timely detection of undefined or unexpected pathogens is a key factor in disease control. A wide range of diagnostic tools are now available to identify and/or type pathogens based on their phenotypic or genetic properties (5). Traditional typing methods based on phenotypic differences, such as serotyping, biotyping, phage typing and antibiograms, have been used for many years. However, the advent of molecular biology in the 1980s led to the development of new methods for comparing pathogens at the molecular level, including amplicon sequencing of discriminative regions, serotype/genotype-specific polymerase chain reaction (PCR), pulsed-field gel electrophoreses, variable-number tandem repeat typing and multilocus sequence typing (MLST). Continuous technological improvements in this field have led to a major shift from phenotypic to genotypic typing of pathogens (5). More recently, the emergence of high-throughput sequencing (HTS) platforms has made it possible to interrogate genome-wide genetic variation in a cost-effective manner. HTS is already being used extensively in virology and is gradually being adopted in bacteriology. In the near future, it is predicted to become a routine tool for outbreak investigations and surveillance systems.

In this review, the authors examine potential applications of high-throughput genomic technologies for veterinary

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pathogen surveillance (Fig. 1). They focus on the two types of surveillance which will benefit most from these new tools: hazard-specific surveillance (pathogen identification and typing) and early-warning surveillance (pathogen discovery). They also describe how the obtained sequence data can be used to improve diagnosis. Finally, they highlight the major challenges that hinder the routine use of this technology in the veterinary field.

Applications

(Nearly) whole-genome sequencing for pathogen identification and characterisation

Current routine surveillance programmes often require high-resolution typing methods to identify pathogens at the species or subspecies level. The ability to quickly and reliably distinguish closely related organisms is the basic requirement for laboratory-based surveillance. Cases with indistinguishable subtypes are more likely to have originated from a common source than those with different subtypes. Currently available HTS technologies can be used to zoom in on a particular genomic region of interest; alternatively, they can be used to characterise the entire genome of a pathogen at an unprecedented level of resolution.

Unsurpassed powerful subtyping tool

Over the past three decades, a wide range of molecular typing tools have been developed that can directly or indirectly exploit variations at specific genomic loci to discriminate between pathogens (6). As none of these methods are universally applicable, the choice of an appropriate typing tool depends on the pathogen under study, the specific epidemiological context, the time and geographical scales, and the available facilities.

Most current molecular typing tools capture only a small portion of the true genetic variation and consequently often lack the discriminatory power to distinguish between

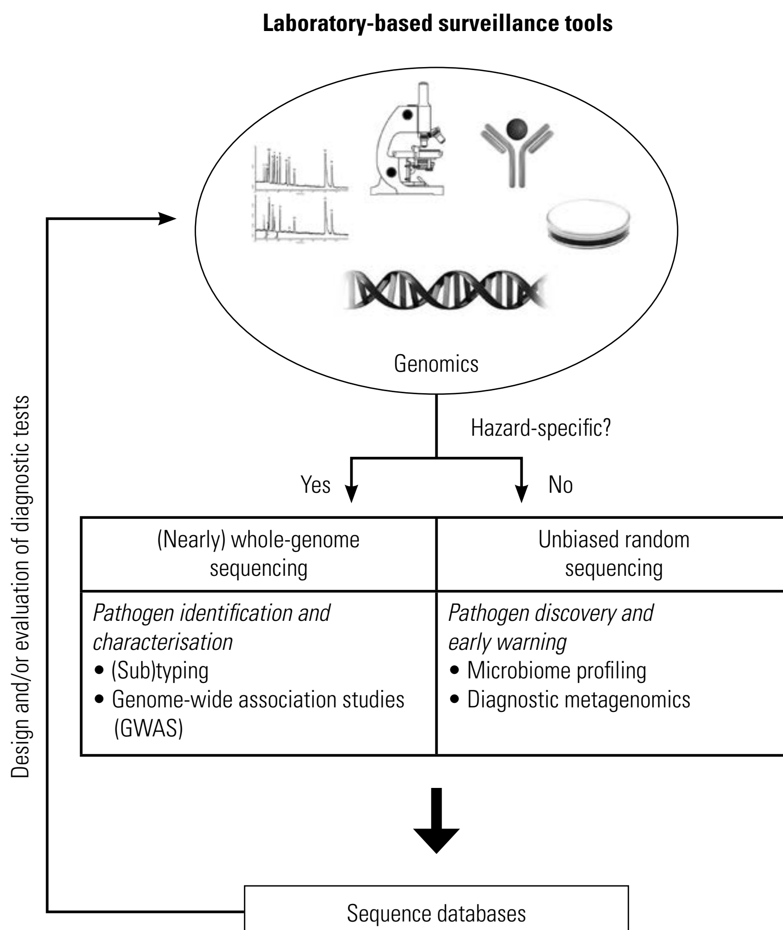

Fig. 1
Schematic overview of potential applications of high-throughput genomic technologies for veterinary pathogen surveillance

closely related or slowly evolving pathogens, such as the so-called 'genetically monomorphic bacteria' (7). The advent of HTS technologies has enabled researchers to measure genetic variation on a genome-wide scale at single nucleotide resolution (8). While the cost of producing a draft genome has dropped enormously, the largely manual process of finishing a genome continues to be expensive. As a result, more than 90% of released bacterial genomes remain in a 'permanent' draft stage. However, a detailed comparison of 133 draft and finished genomes indicated that the amount of missing sequence information is minimal, thus making draft genomes adequate for most purposes (9). One of the main challenges of genome-based typing is the need to condense and translate the observed genetic diversity into meaningful information that accurately describes a particular 'genomotype'. Two approaches are currently used for whole-genome typing of bacteria: single nucleotide polymorphism (SNP) typing and gene-by-gene typing. SNP typing is based on the analysis of a set of specific SNPs with defined allele states such that genetic groups can be defined and phylogenetic relationships inferred. This approach has been successfully used in epidemiological studies of genetically monomorphic bacteria or closely related isolates of the same lineage (10, 11, 12). Gene-by-gene typing extends the concept of conventional MLST to the genomic level. Unlike SNP typing, the gene-by-gene approach is inherently scalable and can be adapted for closely or distantly related pathogens by simply changing the number of loci included in the analysis (13, 14).

Although whole-genome sequencing (WGS) has become a powerful tool for outbreak investigations and studies into human pathogen surveillance, its use in the veterinary field has been restricted to monitoring zoonotic (mainly foodborne) pathogens of major public health concern (15, 16, 17, 18). Several studies have shown the superior discriminative power of genome-based typing methods over traditional molecular typing methods (19, 20). The 2011 outbreak of multidrug-resistant enterohaemorrhagic *Escherichia coli* (EHEC) O104:H4 infection in Germany is an excellent example of the added value of genome-based typing methods. Traditional MLST typing based on seven housekeeping genes indicated that the outbreak strain belonged to sequence type (ST) 678. However, WGS of several *E. coli* O104:H4 ST678 isolates collected worldwide over a period of more than ten years revealed that the outbreak strain differed substantially from the other isolates in both chromosomal and plasmid DNA content (21).

In contrast to its widespread use in the bacteriology field, WGS is not yet being used extensively as a virus subtyping tool in veterinary surveillance programmes. The high genetic diversity of viruses means that most molecular subtyping approaches target one or more highly variable regions within the virus genome. Although these amplicon-based sequencing approaches are very useful for routine subtyping, they do not provide the resolution required to study viral populations that have not diverged substantially (e.g. virus analysis within an outbreak cluster) (22). A more comprehensive approach based on analysis of the entire genome could reveal important information about the origins, evolution and characteristics of each viral population (e.g. genetic reassortment, antiviral resistance and pathogenicity) (23, 24, 25). The added value of WGS is gradually being recognised and WGS-based subtyping is being increasingly integrated into surveillance and outbreak investigations (22, 23, 24, 25).

One of the main problems in virus genome sequencing is the often very low abundance of viral nucleic acids in clinical samples, which necessitates virus enrichment and/or concentration. Proposed strategies to accomplish this involve either selectively capturing viral nucleic acids of interest (26, 27) or removing most of the contaminating host nucleic acids (28). The enriched viral nucleic acids then undergo sequence-independent amplification (e.g. sequence-independent, single-primer amplification [SISPA] [29]) or are directly used for sequencing (e.g. RNA sequencing [RNA-Seq] [30]). Alternatively, target-specific primers can be used to specifically amplify the entire viral genome prior to sequencing. However, designing a robust whole-genome amplification strategy can be challenging, especially for RNA viruses that exhibit high mutation rates (31). Despite these technical challenges, WGS-based typing methods have been published for several economically important viruses, including African swine fever virus (32), avian influenza virus (33), bluetongue virus (34), classical swine fever virus (35), foot and mouth disease virus (36) and porcine reproductive and respiratory syndrome virus (37). Moreover, the OIE–FAO global network of expertise on animal influenzas (OFFLU network) highly recommends WGS for the worldwide surveillance of animal influenza viruses (38).

Unequalled resolution and speed of genetic pathogen characterisation

In addition to identifying and typing pathogens, WGS facilitates genome-wide association studies (GWAS) for dissecting the genetic basis of clinically relevant phenotypes such as antimicrobial resistance (resistome analysis), virulence (virulome analysis), host-range restriction and transmissibility (39). Once a set of markers has been identified, genomic-based surveillance programmes can then be used to monitor the spread and evolution of the pathogen of interest.

Although any measurable phenotype can be analysed using a GWAS approach, most studies have focused on resistome and virulome analysis. The widespread use of antimicrobial agents has led to the emergence of multidrug-resistant pathogens, which is a major concern for both human and animal health. As antimicrobial resistance is an international and multi-sectoral problem, integrated global surveillance

programmes are needed to monitor the antimicrobial susceptibility of foodborne pathogens isolated from animals, food and humans (40). Despite the recommendations of the World Health Organization, the World Organisation for Animal Health and the Food and Agriculture Organization of the United Nations, only a limited number of countries in Europe and North America have implemented integrated surveillance programmes for antimicrobial resistance (41, 42, 43). Recent studies have indicated that genotyping using WGS is a realistic alternative to surveillance based on phenotypic antimicrobial susceptibility testing (44, 45). Moreover, due to its high resolution, WGS can be used to identify novel resistance mechanisms (46, 47) and even to study the evolution of antimicrobial resistance in real time (48, 49, 50). Large WGS studies on antimicrobial resistance have also started to shed light on the interface between humans and animals by identifying interspecies transmission routes (51, 52, 53). Finally, WGS has been successfully used to monitor the genomic events underlying the emergence, evolution and spread of drug resistance in influenza A viruses (54).

Whole-genome sequencing is being increasingly used in (post-)vaccination surveillance programmes to determine vaccine safety and effectiveness. Monitoring the genetic stability of vaccine strains is a cornerstone of vaccine quality control (55). Although reversion to virulence is generally considered a rare event, several studies have demonstrated that inappropriately attenuated or administered vaccines can cause disease under field conditions (56, 57, 58). As our understanding of the molecular basis of attenuation is often rudimentary, whole-genome analysis of viruses used in vaccine manufacture (e.g. progenitor, master seed and vaccine virus) provides the best chance of detecting potential reversions to virulence (59, 60, 61) or loss of protective epitopes (62).

Metagenomics for assessing microbial diversity within healthy or diseased animals

Wildlife has long been recognised as a potential reservoir or amplifier of emerging infectious diseases affecting both humans and domesticated animals (63). Interestingly, the vast majority of recently discovered infectious diseases are caused by viruses, which probably reflects their extraordinary adaptive abilities (64). As the health of humans, domesticated animals and wildlife is inherently intertwined, integrated surveillance programmes are essential to ensure the timely detection of undefined or unexpected pathogens. Direct sequencing of the entire genetic material extracted from a sample without culture or target-specific amplification or capture is referred to as ‘shotgun metagenomics’. The main advantage of metagenomics is that it does not require prior knowledge about the pathogenic agents that might be present in the sample. Although metagenome characterisation by Sanger sequencing has been attempted, the rise of the metagenomics era was closely linked to the development of HTS platforms that can generate millions of reads in a single experiment. Because of its ‘open view’, metagenome sequencing has been extensively used as a diagnostic tool to determine the aetiology of diseases or disease syndromes with no known cause (i.e. ‘diagnostic metagenomics’). A similar approach has been used to monitor changes in pathogen activity in hematophagous arthropods and wildlife that could help to predict spillover and species jump events (65).

Unravelling microbial diversity within key hosts, reservoirs and vectors

Predicting the emergence or re-emergence of zoonotic diseases from metagenomics data requires a thorough understanding of the baseline microbial diversity (i.e. microbiome) in important disease vectors, hosts and reservoirs. Three major experimental approaches can be considered for microbiome studies: high-throughput amplicon sequencing (typically 16S ribosomal RNA [rRNA] or 18S rRNA amplicons for bacteria and parasites, respectively), metatranscriptome sequencing (RNA-Seq) and metagenome sequencing. These approaches all rely on the high sequencing depth offered by the current HTS technologies (66). Although partial 16S rRNA gene sequencing is by far the most popular approach for microbiome studies, its use in pathogen surveillance is limited by its poor taxonomic resolution. Moreover, it often fails to distinguish symbiotic or commensal bacteria from pathogenic bacteria (67). Unlike bacteria and parasites, viruses do not have regions of sufficient sequence conservation to enable surveillance and discovery by a molecular barcoding method analogous to 16S rRNA amplicon sequencing. As a consequence, viral diversity studies have been largely based on metagenome sequencing approaches that combine sequence-independent amplification with HTS.

Haematophagous arthropods (e.g. mosquitoes, midges, flies, fleas and ticks) are efficient disease vectors that can transmit pathogens either mechanically or biologically. Recent arbovirus outbreaks in previously naive populations have demonstrated the potential of these pathogens to spread rapidly and cause substantial economic losses (e.g. Rift Valley fever virus, bluetongue virus and Schmallenberg virus) (68, 69, 70). To date, the microbiota in arthropods is poorly documented. The few reported studies have focused on viral diversity in wild-caught mosquitoes (71, 72) or microbial diversity in ticks (73, 74). Although shotgun metagenome sequencing is still too expensive and labour-intensive to be used as a first-line surveillance tool, Coffey and collaborators (75) have reported a strategy that combined metagenome sequencing with traditional arboviral

surveillance. Instead of directly analysing individual or pooled mosquitoes, they first inoculated mammalian cell lines with mosquito homogenates to enrich for pathogens that could replicate in both insect and mammalian cells. Metagenomic sequencing was then applied only to cell cultures showing a cytopathogenic effect and for which no aetiological agent could be identified by conventional antigenic tests (75). This strategy enabled the detection of two novel rhabdoviruses, two novel bunyaviruses and an arbovirus not previously recognised in Australia.

The increased contact among humans, domesticated animals and wildlife has resulted in a growing number of emergent zoonotic diseases due to spillover events or species jumps. Recent examples are the Middle East respiratory syndrome coronavirus (from bats and/or camelids) and highly pathogenic influenza A (H5N1) virus, Usutu virus and West Nile virus (all from wild birds) (76, 77, 78, 79). In recent years, bats have received increasing attention as potential zoonotic disease reservoirs because of their association with several high-impact zoonoses (80). Only a limited number of studies have focused on wildlife species living in close contact with domesticated animals (81, 82, 83, 84).

Identifying unknown or unexpected pathogens in clinical samples

Similar to electron microscopy, shotgun metagenome sequencing provides a molecular 'catch-all' method for detecting any kind of pathogen (virus, bacterium, fungus or parasite) in nearly any type of sample. These characteristics make it an ideal tool to complement syndromic surveillance programmes, which frequently encounter vague, non-specific clinical signs. The added value of combining metagenomics with syndromic surveillance was clearly illustrated by the recent discovery of an emerging arbovirus in Europe (85). In the late summer of 2011, farmers in the Netherlands and Germany reported a disease in dairy cattle that caused non-specific, transient clinical signs including fever, reduced milk production and, often, watery diarrhoea. Towards the end of 2011, a significant increase in the number of abortions, stillbirths and congenital abnormalities was observed in cattle, sheep and goat herds (86). As all routine laboratory tests failed to identify an aetiological agent, blood samples from both diseased and healthy cattle were analysed by shotgun metagenome sequencing. This revealed a novel orthobunyavirus of the Simbu serogroup: the virus was named Schmallenberg virus after the town where it was first isolated (87). Following its initial identification, specific diagnostic tests were developed which enabled virus detection in other domesticated ruminants and wildlife across Europe (88).

Schmallenberg virus is just one example of the growing number of pathogens that have been discovered using metagenome sequencing (see Table I). Owing to their broad detection range, all metagenomic approaches are likely to reveal a wide range of microorganisms in both diseased and healthy animals. However, most of these will be non-pathogenic, ubiquitous infectious agents (e.g. commensals). As already noted by others, the presence of the genetic material of a microorganism in a diseased individual does not in itself prove causation: determining the aetiology of a disease requires extensive supporting information to fulfil Koch's postulates, or variations thereof (107, 108). The multidisciplinary follow-up studies needed to prove causality are the most time-consuming and arduous, yet the most crucial, part of pathogen discovery.

Designing and evaluating molecular-based diagnostic tests

Although HTS is primarily used for pathogen discovery and typing, the resulting sequence data can also be utilised to improve molecular diagnostics.

Real-time PCR has become the method of choice for the molecular diagnosis of pathogens due to its high specificity, sensitivity and speed (109). Well-designed primers and probes are prerequisites for reliable real-time PCR analysis. Unfortunately, identifying robust signatures with low false-negative and false-positive rates is not trivial, especially for rapidly evolving pathogens such as RNA viruses. The massive increase in the number of publicly available sequences further complicates assay design. To alleviate this problem, a large number of tools have been developed to automate the design of primer/probe signatures, e.g. CODEHOP (110), Primaclade (111), Greene SCPrimer (112), Insignia (113), HYDEN (114), PAMPS (115), PRIMUX (116), FastPCR (117) and Prise2 (118). In contrast, far less effort has been put into developing tools to evaluate existing primer/probe signatures, and only a limited number are currently available, e.g. De-MetaST-BLAST (119), MFEprimer-2.0 (120) and simulate_PCR (121). Several studies have demonstrated that mismatches in the primer or probe regions can substantially reduce assay performance by impairing both primer annealing and extension (122, 123, 124, 125). False-negative results have been reported for highly divergent viruses such as influenza virus (126, 127), porcine reproductive and respiratory syndrome virus (128) and West Nile virus (129). These studies highlight the need to regularly reassess primer/probe signatures against all newly available sequence data. Whether or not an assay needs to be adapted depends on its intended use (i.e. whether it is fit for purpose), but the end-user should at least be aware of the limitations of the assay and account for these when interpreting the results.

Table I
Overview of metagenomics studies that identified novel viruses potentially linked to a disorder or syndrome

Species	Year	Clinical signs or syndrome	Putative pathogen identified	Reference
Cattle	–	Bovine respiratory disease	Bovine astrovirus, Picobirnaviruses	89
	1995–2012	Non-suppurative encephalitis	Bovine astrovirus	90
Pig	–	Post-weaning multisystemic wasting syndrome	Porcine boca-like parvovirus	91
Chicken	2003/2012	Transmissible viral proventriculitis	Picornavirus QIA01	92
	2013	Neurological signs, high mortalities	Avian gyrovirus 2	93
Turkey	2011	Stunting syndrome	Turkey picornavirus	94
Poultry	2004	Poultry enteritis mortality syndrome (turkey) Runting-stunting syndrome (chicken)	Parvoviruses	95
Guinea fowl	2010–2011	Fulminating disease	Avian gammacoronavirus	96
Honeybee	–	Colony collapse disorder	Aphid lethal paralysis-like virus	97
Dogs	–	Severe haemorrhagic diarrhoea	Dog circovirus	98
	2009–2010	Diarrhoea	Canine kobuvirus Canine sapovirus	99
Mink	–	Shaking mink syndrome	Astrovirus	100
Snake	–	Neurorespiratory disease	Sunshine virus (paramyxovirus)	101
Fox	2009	Severe gait abnormalities	Gray fox amdovirus (parvovirus)	102
Gull	2001	Mortality	Gull adenovirus	103
Seal	–	Ulcerative gingivitis and glossitis	Phocine herpesvirus 7	104
	2000	Mortality	Seal anellovirus	105
Possum	–	Wobbly possum disease	Nidovirus	106

Remaining challenges for the (routine) use of genomics for surveillance of veterinary infectious agents

High-throughput sequencing has revolutionised pathogen research and is being increasingly used for surveillance and outbreak investigations. However, a number of challenges still need to be addressed before this technology can become a routine tool in the veterinary field.

One of the main constraints on using HTS technologies is the total cost per analysis, which is still too high for routine veterinary applications. Over the past decade, the 'production' cost (often expressed as price per base pair) has dropped dramatically as a consequence of the massive increase in throughput of the current platforms. Unfortunately, applications in the veterinary field cannot always benefit from the increased capacity and reduced cost due to the relatively small genome sizes of bacteria and viruses. Although multiple samples can be analysed in a single multiplexed sequencing run, postponing the run until sufficient samples are available is not always an option, especially for pathogen discovery and outbreak investigations. One should also bear in mind that the sequencing step represents only a fraction of the total cost: it does not take into account expenses associated with data storage, analysis and interpretation (Fig. 2). 'Non-production' costs such as hardware infrastructure, development of bioinformatics tools and downstream biological analysis should also be included in the cost calculation. Although several options for reducing the 'non-production' costs are available (e.g. outsource sequencing, use cloud-based environments for data analysis), implementing HTS-based applications will always require special expertise that might not be present in small research laboratories.

To take full advantage of the possibilities offered by HTS, the time between sampling and obtaining the final laboratory report must be further reduced. Although a

short turnaround time might be less important for pathogen typing studies, it is crucial for outbreak control, which relies heavily on the timely detection of possible emerging or re-emerging pathogens. Technical advances have already shortened the time needed to obtain raw sequence data, but the rapid extraction of relevant information from the large amount of sequence data remains challenging.

As HTS technologies have matured and become more accessible, the bottleneck has now shifted from the wet laboratory (i.e. extraction, amplification and library preparation) to the dry laboratory (i.e. data analysis and interpretation). The continuous technological improvements and wide range of applications means that there is no 'one-size-fits-all' solution for HTS-based analyses. In fact, the availability of numerous workflows is advantageous for more research-oriented applications such as pathogen discovery. In contrast, routine applications (such as pathogen typing) require a robust, reliable and, above all, harmonised genomics approach for comparing data from different time points and between laboratories. Several initiatives have been undertaken to facilitate data analysis and management. Of these, the 'Global Microbial Identifier' is probably the most exhaustive and ambitious: it aims to develop a global system to aggregate, share, mine and translate genomic data for microorganisms in real time (130).

As for all diagnostic methods, HTS-based methods should be properly validated and integrated in a quality management system to ensure that test results are consistent and reliable. Unfortunately, validation and quality assurance guidelines are not available for HTS-based applications in the veterinary field, which greatly hampers their transition from the research environment to a diagnostic setting. Similarly, external quality assessment programmes to compare and monitor the performance of different laboratories must be established. These programmes would also enable the suitability of existing workflows to be evaluated and help to define appropriate quality metrics. Regardless of the

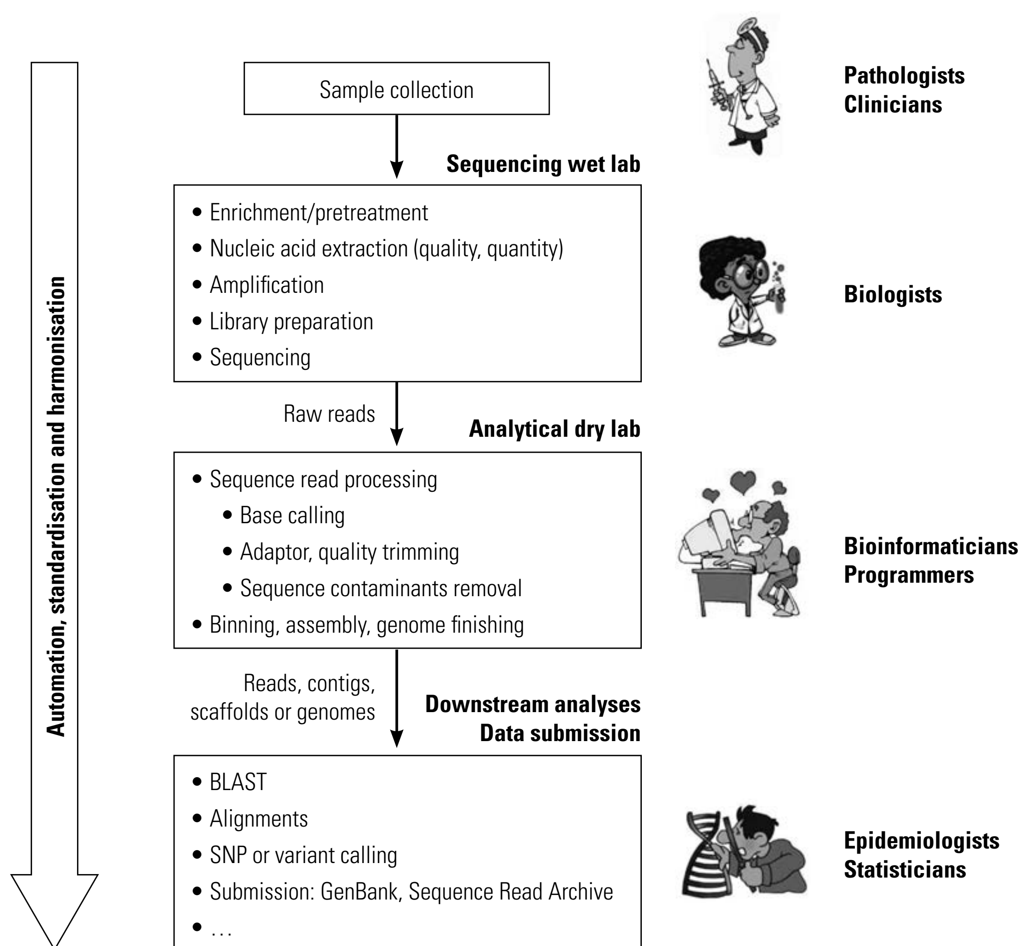

Fig. 2
Schematic overview of the different steps in a typical genomics workflow

intended use, the complexity of HTS workflows requires that all steps from each workflow are documented in a standard operating procedure. These should include all steps performed in both the wet and dry laboratories because the latter make a significant contribution to test results.

Downstream data analyses are necessary for translating primary sequence data into practical information for disease surveillance (Fig. 2). These analyses typically require a multidisciplinary team of experts (e.g. epidemiologists, statisticians, biologists and physicians) and rely heavily on publicly available databases. Numerous databases exist, but often lack adequate curation and contain incomplete metadata. To date, high-quality databases have only been established for influenza viruses (OpenFlu, EpiFlu) and foot and mouth disease virus (OpenFMD). Similar databases are urgently needed for all other economically important veterinary diseases.

Conclusions

Over the past decade, HTS technologies have matured and are now ready to be integrated into the diagnostic laboratory. WGS-based methods have advantages over conventional molecular typing tools in that they allow genetic variation to be measured at a genome-wide scale with single nucleotide resolution. Although such extremely high resolution is not often required, it can reveal crucial information about the origins, evolution and characteristics of closely related pathogens such as genetically monomorphic bacteria or viral populations within an outbreak cluster. HTS also can be used to perform detailed metagenomics analyses and detect unknown or unexpected pathogens. Although HTS holds great promise for pathogen research, it is important to realise that sequence data alone provides little information. It is often more time-consuming and labour-intensive to interpret the sequence data than to generate it. In general, extensive follow-up studies are needed to confirm or reject the initial findings and to place the data in a broader, non-molecular context. To take full advantage of HTS, HTS-based methods should be firmly integrated into existing workflows and should not be seen as stand-alone tools. Several remaining challenges need to be addressed to facilitate this process. The availability of powerful bioinformatics tools and high-quality databases is essential to bridge the existing gaps.

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La génomique au service de la surveillance des agents infectieux vétérinaires

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Résumé

La mondialisation, le changement climatique et l'intensification de la production agricole sont des facteurs pouvant entraîner un risque accru d'émergence d'agents pathogènes infectieux. En conséquence, il est impératif de disposer d'outils de surveillance souples d'emploi au sein du laboratoire pour identifier, caractériser et contrôler rapidement les maladies émergentes et ré-émergentes au niveau mondial. Un grand nombre d'outils sont disponibles, mais ce sont les technologies de séquençage qui ont ouvert une nouvelle ère de la surveillance des agents pathogènes. Les auteurs passent en revue les différentes applications potentielles des technologies génomiques à haut débit dans le domaine de la surveillance des agents pathogènes vétérinaires. Ils examinent plus particulièrement les deux types de surveillance auxquels ces nouveaux outils vont le plus contribuer : la surveillance axée sur les dangers (identification et caractérisation des agents pathogènes) et la surveillance précoce en amont (découverte des agents pathogènes). Après avoir expliqué les perspectives d'amélioration des moyens diagnostiques en ayant recours à l'utilisation des données de séquençage, les auteurs soulignent les principales difficultés

qui entravent l'utilisation systématique de cette technologie dans le domaine vétérinaire.

Mots-clés
Agent pathogène vétérinaire – Caractérisation – Génomique – Maladie infectieuse – Métagénomique – Séquençage à haut débit – Séquençage de nouvelle génération – Séquençage du génome entier – Surveillance.

Utilización de la genómica para la vigilancia de agentes infecciosos veterinarios

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Resumen
Factores como la mundialización, el cambio climático o la intensificación de la agricultura pueden acrecentar el riesgo de que surjan nuevos patógenos microbianos. De ahí la creciente necesidad de contar con herramientas flexibles de vigilancia en laboratorio, que permitan identificar, caracterizar y vigilar enfermedades (re)emergentes de importancia mundial. Aunque ya existen muchas herramientas, las novedosas técnicas de secuenciación han inaugurado una nueva era en la vigilancia de patógenos. Los autores examinan las posibles aplicaciones de las técnicas genómicas de alto rendimiento en el terreno de la vigilancia de patógenos veterinarios, centrándose en los dos tipos de vigilancia para los que más útiles serán estas nuevas herramientas: la vigilancia en función del riesgo específico (identificación y tipificación de patógenos) y la vigilancia de pronta alerta (descubrimiento de patógenos). Por último, tras explicar cómo se pueden utilizar los datos de secuenciación resultantes para mejorar el diagnóstico, los autores concluyen destacando los principales problemas que dificultan un uso sistemático de estas técnicas en el ámbito de la veterinaria.

Palabras clave
Enfermedad infecciosa – Genómica – Metagenómica – Patógeno veterinario – Secuenciación de alto rendimiento – Secuenciación de genoma completo – Secuenciación de próxima generación – Tipificación – Vigilancia.

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