

Review

Genetics of wildlife diseases and its impact on biodiversity conservation

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Abstract

Diseases of wildlife origin have great impact on the conservation of the vast global biodiversity and also take a toll on domestic animals' and human health. Diseases of wildlife have the capacity to be of utmost concern because they can affect the economy and public health if not attended to promptly. An amazing 60% of emerging infectious diseases are zoonotic and many of the recent cases have been proved to originate from wildlife. Knowledge of genetics is important to curtail the emergence of overwhelming wildlife diseases. Understanding the genetics of these diseases is important to give a better understanding of how they can be prevented and controlled to forestall the decimation of wildlife populations and consequent effect on biodiversity. Being armed with the knowledge of both, host and pathogen or parasite genome, would go a long way to pursue the solutions to wildlife diseases and their transmission. This review is geared towards promoting the incorporation of genetics and genomics and its diverse concepts and techniques into the process of detection, characterization, control and prevention of wildlife diseases.

Keywords: Biodiversity, Parasite, Pathogen, Wildlife diseases, Wildlife genetics, Zoonosis

Introduction

The role of genetics in tackling the hazardous effect of wildlife diseases cannot be overemphasized. Understanding the genetics of both host and pathogen will go a long way to proffer solution to the increasing incidence of emerging and re-emerging zoonoses of wildlife. It has been observed that many pathogens have developed resistance to vaccines and even the act of culling has also increased virulence (Vander Wal *et al.*, 2014). Knowledge of genetics is important to curtail the emergence of overwhelming wildlife diseases (Vander Wal *et al.*, 2014). Neutral genetic variation gives an understanding of how a pathogen is able to successfully spread through a population of organisms and how future infection can be prevented or curbed (Vander Wal *et al.*, 2014). When genetic concepts such as genetic markers, genomic techniques are used in combating wildlife diseases, it will promote prevention, curtail spread, and ultimately stunt disease propagation whereby optimizing the intervention available (Vander Wal *et al.*, 2014).

The role of genotype and its interaction with the environment cannot be overemphasized in the place of conferring protection on or susceptibility to a disease. An amazing 60% of emerging infectious diseases are zoonotic (Jones *et al.*, 2008; Blanchong *et al.*, 2016). The outbreak of zoonotic diseases such as Ebola has

helped in increasing the awareness of the public to the link between wildlife and human health even though the relationship is age long (Blanchong *et al.*, 2016). Factors such as climate change and habitat fragmentation have increased the emergence and re-emergence of various wildlife diseases. Wildlife diseases are known for their effect on conservation of biodiversity (Blanchong *et al.*, 2016). This review is tailored towards promoting the incorporation of genetics and genomics and its diverse concepts and techniques into the process of detection, characterization, control and prevention of wildlife diseases. This has a weighty significance for the conservation of biodiversity.

Genetic approach to tackling diseases of wildlife

The basis of the inclusion of genetics in the search and diagnosis of wildlife diseases is to explore all angles to putting a check on the ever growing world of pathogens (Blanchong *et al.*, 2016). Genetics gives diverse measures of attending to a disease depending on the nature of the problem (McManus *et al.*, 2014). This could range from choosing best individuals with resistant or tolerant genomes, cross-breeding, introduction of desirable genes and so on. Populations with evident genetic diversity are better protected against infection from pathogens or parasites (De Bruin *et al.*, 2008).

Genetic techniques that can be used in unraveling various wildlife diseases include sequencing genomes of microbes, determination of their strongly conserved regions, taking cognizance of the gene or genes that produces the virulent factor in pathogens, and searching out variations such as single nucleotide polymorphisms (SNPs) due to factors such as mutations, which tell us a lot about the similarities or differences observed in the different strains or classes of microbes and host organisms (Deurenberg *et al.*, 2017; McManus *et al.*, 2014; Mcqueen *et al.*, 2015). SNPs are polymorphisms that can be used to study variations in coding regions for proteins and non-coding regions of DNA where regulatory functions are embedded (Mcmanus *et al.*, 2014). SNPs serve as genetic markers used in classifying variations among species and strains. Apart from whole genome sequencing, other approaches such as mitochondrial DNA (mtDNA) sequencing, amplified fragment length polymorphisms (AFLP), variable number tandem repeats (VNTRs), also known as microsatellites, can be used in understanding infection, susceptibility and even transmission of the diseases (Blanchong *et al.*, 2016; Schoenebeck and Ostrander, 2014, Miller and Taylor, 2016). Comparative genomics will also be of immense use because it is already established that some parasites and pathogens have multiple host that they successfully infect (Britton *et al.*, 2015; Mcqueen *et al.*, 2015). Analysis of such comparative genomics gives the mutual grounds of infection and transmission. Genome wide association studies (GWAS) and next generation sequencing (NGS) techniques has opened up a new set of opportunities in understanding the role of genetic variation in the pathogenesis of diseases (Mcqueen *et al.*, 2015).

The coexistence and co-evolution of host and pathogen or parasite are events that occur consistently among living systems (Brunner and Eizaguirre, 2016). The co-evolution has helped in shaping the genomes of both parties to favour co-existence (Mcmanus *et al.*, 2014). The co-evolution can alter host's traits, immunity, abundance and the pathogen/parasite's transmission rates and virulence (Brunner and Eizaguirre, 2016). This could lead to resistance and tolerance to the disease on the part of the host or new shades of virulence or ability to infect other wildlife species or humans on the part of the pathogens (Blanchong *et al.*, 2016). On a positive note, host-parasite or host-pathogen age long interaction, promotes maintenance of genetic diversity (Brunner and Eizaguirre, 2016).

Biek and Real (2010) suggest that population genetics will also be an efficient tool in the quantifying of disease dynamics from an individual to the general population. This is why they admonish that landscape genetics and epidemiology should go hand in hand to have a better understanding of infectious diseases and the age long host-parasite co-evolution. The disease dynamics can also be categorized from the host genetic structure. Genetics, genomics, next generation sequencing techniques and bioinformatics also have a part to play in vaccinology (Quiroz-Castañeda *et al.*, 2016). Adequate genetic and immunologic knowledge of host,

pathogen or parasite is required to develop a successful vaccine (Silver and Watkins, 2017). A good genetic understanding serves as a leverage to better understand and explore the immunologic responses or activities of a host when exposed to parasite or pathogen. For instance, Silver and Watkins (2017) stressed the importance of an in-depth study of major histocompatibility complex class I (MHC-I) alleles (a very important gene in disease resistance) in activating the cells that control HIV (human immunodeficiency virus) and SIV (simian immunodeficiency virus) replication, in order to be able to understand the immune responses. Both HIV and SIV are of wildlife origin and are public health threats worldwide.

Role of Genetics in pathogen and parasites detection and treatment

Various traditional techniques such as microscopy, cell culture, growth on media, as well as immunology techniques such as serology have been used in the detection of the causal agent in the past (Silvy, 2012; Blanchong *et al.*, 2016). In recent years, more sensitive and equally accurate genetic techniques such as polymerase chain reaction (PCR), reverse transcriptase PCR, real time quantitative PCR and sequencing can be used to detect pathogens from animals (cloacal swab or blood sample) or the environment (eDNA samples) (Blanchong *et al.*, 2016). These approaches give quality result without expending so much labour as is done with the traditional methods and can as well quantify the pathogen load. Molecular analysis of vectors' blood meal, mitochondrial genes, ribosomal RNA markers are all molecular methods that have been used in identifying disease transmitting vectors while nuclear genetic markers can be used for animal to animal transmission to see relatedness (Blanchong *et al.*, 2016; Mcmanus *et al.*, 2014). Traditional typing of blood which have proved difficult in some species of pathogens such as *Leucocytozoon* sp. had been made possible by the use of molecular methods (Hellgren *et al.*, 2004).

The sequencing of parasite or pathogen genomes in recent years has served as a major breakthrough in providing new drugs and better vaccines to tackle the menace of diseases in wildlife and livestock (Britton *et al.*, 2015). With the high rate of resistance to drugs e.g. antihelmintic drugs, the tools of genetics and genomics are needed to identify new and more effective drugs and potent vaccines (Britton *et al.*, 2015). Some pathogens affect both man and wildlife and this ability can be understood genetically to state the factors that bring about susceptibility on the part of the host and virulence on the part of the pathogen (Ly and Ikegami, 2016). An example is the bunya viruses which are diverse with some being virulent while others are not. An example of the virulent type is the rift valley fever virus and it has been discovered that its virulence is caused by its non-structural (NS) protein, whose major function is to inhibit cellular general transcription activity by interacting directly with transcription factors (Ly and Ikegami, 2016).

Britton *et al.* (2015) reports that small RNAs such as microRNAs (miRNAs), which perform regulatory roles in gene expression, can be used as regulators for parasite (e.g. nematode) development and used to monitor host parasite interactions thereby serving as diagnostic markers for infection. Small RNAs have been seen to be conserved in some species and unique in some. This means small RNAs are gradually evolving and could provide answers to questions pertaining to parasite transmission and adaptation to various environments (Britton *et al.*, 2015). Marek's disease virus (MDV) also known as gallid herpes virus is an alpha herpes virus with diverse forms of severity of symptoms with different virulent strains (Mcperson and Delany, 2016). The increasing virulence of MDV has become an object of concern because higher virulence is associated to response to vaccines. It is observed that this is due to reduced genetic diversity in the poultry industry. Incorporating the molecular, cytogenetic and genomics knowledge of MDV has equipped researchers with knowledge on the infection and pathogenesis of the virus. The study of the integration of the virus into the host genome gives the location where the pathogen integrates its genome into the host to perform its adverse function. Mota *et al.* (2007) reports that with a cytochrome b multiplex polymerase chain reaction, host of parasite bugs can be identified from bugs blood meal and *Trypanosoma cruzi* can also be identified simultaneously. This identification is even possible ten weeks after bug feeding has taken place (Mota *et al.*, 2007).

Host genetic makeup and their resistance/tolerance to diseases

The knowledge of the genetic structure of wildlife populations cannot be brushed aside because it gives an insight into transmission and susceptibility to diseases. Resistance and tolerance are the major mechanisms of defense the host possesses to defend itself against severity of a disease (Blanchong *et al.*, 2016). The susceptibility to a disease can also be unraveled genetically (Mcqueen *et al.*, 2015). Wildlife populations that are inbred, leading to reduced genetic diversity ultimately have reduced adaptive potentials and are thus more susceptible to diseases than groups with high levels of genetic diversity (Blanchong *et al.*, 2016). Knowledge of genetic variation among various breeds of animals can serve as a means of coming up with breeds that will be able to substantially resist or tolerate the infection of a pathogen or parasite (McManus *et al.*, 2014). It is also important to note that plants (flora) are inclusive in the bracket of host that are affected by pathogens and parasites (Rodríguez-Nevado *et al.*, 2017).

Genetic evaluation alongside other factors has been embraced to reduce the manifestation of disease in dairy cattle so as to improve the welfare of the cattle (Pryce *et al.*, 2016). Pryce *et al.* (2016) concluded that genetic variation in metabolic disease traits makes direct selection possible to reduce the occurrence of the disease. Global warming along with the concomitant climate change with a surviving genotype in an environment will give a better production yield and possibly a sustainable increase in such an environment (Brunner and Eizaguirre, 2016; Mcmanus *et al.*, 2014). The immune system of such individual/population can also be explored for the good of all. The knowledge of the function of Major Histocompatibility Complex (MHC) genes in chicken has given a better understanding of the species immune responses, tolerance and infection to various diseases and vaccinations (Miller and Taylor, 2016). Information from the dog genome project reports that various genomic techniques such as mitochondrial sequencing, SNP chips, genome wide association studies (GWAS) are used in locating loci or genes that lead to a disease or disorder in the mammal (Schoenebeck and Ostrander, 2014). Specific alleles at immune genes may contribute to understanding resistance to disease. This has been found in avian malaria in house sparrows (Loiseau *et al.*, 2011) and chronic wasting disease in cervids (Robinson *et al.*, 2012). Pathogens' genetic variation may affect the rate of transmission, and interactions with the host immune system can affect their evolution. This was true for avian influenza in mallards (Latorre-Margalef *et al.*, 2013), and rana virus in amphibians (Echaubard *et al.*, 2014). NGS techniques can also help in revealing more knowledge on zoonotic transmission of microorganisms (Deurenberg *et al.*, 2017).

Exploits of genetics in wildlife diseases detection and interventions

The knowledge of genetics has been applied to the field of wildlife diseases over the years. It has been used to identify and characterise pathogens, identify reservoir hosts and disease origins, understand transmission, distribution and spread of diseases as well as identify genes associated with resistance/tolerance to diseases (Hillet *et al.*, 2012; Leiseret *et al.*, 2013; Lorchet *et al.*, 2010; Robinson *et al.*, 2012; Robinson *et al.*, 2013; VanderWaal *et al.*, 2014).

Migrating birds who breed in the temperate and winter in the tropics can be a vehicle for the movement of pathogens from one region to the other (Hellgren *et al.*, 2007). An example is given of the introduction of the plasmodium parasite into the Hawaiian Islands which led to the loss of some native susceptible bird species. With the use of the PCR technique, Hellgren *et al.* (2007) reported that introduction of parasite to resident bird species is more frequent in the *Plasmodium* genera and rare in the *Haemoproteus* and *Leucocytozoon* genera. Using genetic techniques, Ayoub *et al.* (2013) shown that new zoonotic diseases are being transmitted from the mangabey to humans. Availability of genetic information on host and parasites in connection with their ecological interactions and geographical distribution can help to predict patterns of disease emergence, spread and control (Biek and Real, 2010). This will have a great effect on the conservation of wildlife populations while protecting public health.

Animals and humans have diseases (pathogens) that infect both of them with symptoms and features of the disease and infection similar in both organisms. The study of the genetics of wildlife pathogen will go a long way to shed light on diseases and disorders that are of public health concern. The study of genes in humans has also served as an eye opener to the cause of some diseases in the animal setting. An example is the LG1 gene studied in human with respect to epilepsy, it was also found to be the root cause of epilepsy in some animals (Pakozdy *et al.*, 2015). Knowledge of the genetics of animal disorders such as cancer and aging in canine has helped in improving and paving way for therapeutic interventions for human problematic diseases and disorders (Blanchong *et al.*, 2016; Ceciliani *et al.*, 2016; Kaeberlein *et al.*, 2016; Schoenebeck and Ostrander, 2014). Another good and helpful example is SIV (Simian Immunodeficiency Virus), the virus that causes AIDS in macaques, it is being studied because it has a high sequence homology with HIV that causes the same disease in humans (Silver and Watkins, 2017). The sooty mangabey viruses is being continuously transmitted to humans, causing new zoonotic diseases (Ayouba *et al.*, 2013). Similarities were observed in its MHC-class I epitope and other factors. Also, Marek's disease virus (MDV) in chickens, human herpes virus 6 (HHV-6), and Epstein-Barr Virus share common features which make chickens a model organism to study human diseases caused by these viruses (Mcpherson and Delany, 2016).

Conclusion

Tackling the challenge of the ever growing and changing complex field of wildlife diseases need a multi-disciplinary and multidirectional approach, so as to maximize the interventions available and to also bring to the barest minimum the effect of wildlife diseases on wildlife, domestic animals and human health as well. Collaborations from geneticist (molecular, population), bioinformatician, immunologist, ecologist and wildlife managers should be encouraged so as to allow the integration of data to tackle diseases of wildlife and humans. Professionals in the upcoming genomic technologies should be embraced to protect wildlife health and biodiversity at large.

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