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Scientific Journal of Veterinary Advances (2020) 9(1) 289-298 ISSN 2322-1879

doi: 10.14196/sjva.v9i1.2630

CODEN (USA): SJVAAS

Contents lists available at Sjournals

Scientific Journal of Veterinary Advances

Journal homepage: www.sjournals.com



Review article

Genetics and its role in the control of animal diseases: A brief review

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ARTICLE INFO

Article history,
Received 14 December 2019
Accepted 15 January 2020
Available online 22 January 2020
iThenticate screening 16 December 2019
English editing 14 January 2020
Quality control 21 January 2020

Keywords,
Control
Diseases resistance
Genetics
Genes

ABSTRACT

Veterinary genetics is an emerging branch of genetics which has strong potential application in the control and prevention of livestock disease. Unlike the other methods, control of animal disease through genetic means would be cost effective and does not require continuous investment. This is due to the fact that once a desirable genetic resource is identified and/or achieved, it can be exploited for several generations without any additional input. In the present review, two general approaches or principles to be considered in the control of livestock disease through genetic means are reviewed. The first one is exploitation of the hosts genetic resource, which could be achieved through selection and propagation of those animals having no genetic defects and naturally resistant to a particular disease. Such animals can be prepared through use of transgenic animal technology in which genes for disease resistance have been incorporated. The second approach is genetic control of pathogens by employing several techniques. This includes control of vectors using conventional sterile insect release method, Y-autosome translocation or use of compound chromosomes, and identification and cloning of genes in pathogens responsible for the production of potent antigens which can be used in vaccine development via the application of recombinant DNA technology. Selecting cattle most resistant to the development of infectious diseases will decrease costs of production and should therefore be included in the overall breeding objective.

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1. Introduction

The science of genetics is concerned with determining the mode of inheritance or the transmission of biological properties from generation to generation. The science of development of genetics can be considered with respect to three main eras. These are really on the rediscovery of Gregor Mendel's, the existence of microbial genetics and the discovery of structures of DNA by James Watson and Francis crick. This provide stimulus for development of genetics at molecular level (Kaplan, 2004). In livestock, the use of ever-more sophisticated breeding selection strategies will affect animal breeding (Rothschild, 2004) and considerable effort is now being made to apply these selection tools to produce animals with an increased ability to resist or combat disease (Hanotte et al., 2003; Jorgenson, 2003). This paper argues that the application of transgenic animals for the benefit of animal is becoming increasingly likely due to the combination of new methodologies that enable the efficient production of genetically modified animals, exciting new tools to alter gene activity and advances in our fundamental understanding of causative agents and the disease process. The timely development of novel projects will demonstrate the feasibility of generating GM livestock that are resistant to disease (Clark and Whitelaw, 2003).

In veterinary medicine, considerable effort has been made to control or eradicate spread of disease among domestic animals by employing several methods, which include chemotherapy, isolation and quarantine of susceptible groups or individuals, the applications of principles of hygiene and vaccination. Many diseases, however, cannot practically be controlled by these means and increasing the use of drugs to eliminate or destroy pathogens or their vectors. The regular use of therapeutic agents increases the resistance of pathogen to the drug as well as produce drug residues which have public importance (Rothschild, 2004).

The control of disease is one of the major problems encountered in efficient production of livestock (Rothschild, 2004). Effective and satisfactory control of some disease by the development of genetically resistant stock is found to be possible these days. The exploitation of genetic resource in the control of animal disease might be technically effective method. Due to this fact, it appears important to discuss veterinary genetics, which encompasses those aspects of genetics that are relevant and applicable in the control of animal disease (Axford and Owen, 1990).

There have been considerable advances in animal breeding and genetics, relevant to animal disease control. These advances are of considerable veterinary interest, noting that observed animal performance is the outcome of the interaction between the animal's genetic makeup and the specific environment it was exposed to. Logically, therefore, improved genetics has the potential to complement current approaches to animal disease control. Improvement in animal health through genetic selection is advantageous, because genetic gain is cumulative and permanent, as the genes introduced into a population can persist for many generations (Berry et al., 2011). Genetic and genomic studies of disease resistance are becoming ever more widespread. This has translated into some notable examples of success in terms of describing and understanding the genetic control of between-animal differences in resistance, and also in the utilization of these results to breed animals for increased resistance (Bishop and Woolliams, 2014). Therefore, the objectives of this paper were to overview genetic basis of diseases resistance in domestic animals and also to highlight principles and potential application of genetics in controlling livestock diseases.

2. Basic concepts of genetics

"Genetics is the study of heredity, the process in which a parent passes a certain genes onto their children". It means offspring inherit their biological parents' genes that express specific traits, such as some physical characteristics, natural talents, and genetic disorders (Kaplan, 2004). The science of genetics is concerned with determining the mode of inheritance of the transmission of biological properties from generation to generation. The science of development of genetics can be considered with respect to three main eras. These are the rediscoveries of Gregor Mendel's work: inheritance and genetic mapping, microbial genetics emerged in mid-1940 and the role of DNA as the material was firmly established and the discovery of the structure of DNA by James Watson and Francis Crick in 1953 provided the stimulus for the development of genetics at the molecular level and, this work culminated with the establishment of the complete genetic code in 1966. The stage was now set for the appearance of new genetics (Kaplan, 2004).

3. Genetic resistance to diseases

3.1. Genetic basis to diseases resistance

Different mammals often differ in their degree of resistance or susceptibility to certain disease. For example, Horses are not susceptible to FMD virus (Abdela, 2017), dogs are not susceptible to Corynebacterium pyogenes but cattles and sheep are the chief host of these bacteria. The animals are categorized depending on resistance to certain disease into: species, breed, age and sex (Baker, 1998).

3.2. Species

For a variety of anatomical, physiological and biochemical reasons, many pathogens do not develop at all apart from their natural hosts; this is typified by, the remarkable host specificity of various species of Emeria. In many instances, however, a limited degree of organisms, example Staphylococci, Mycobacterium tuberculosis, Fasciola hepatica and Trichinella spiralis have wide range of host or universal distribution. The best example of species difference in resistance to diseases due to genetic difference is the superior ability of Zebus (Bos indicus) to tolerate high environmental temperatures than European (Bos Taurus) species (Duncan, 1999).

3.3. Breed

Within a single species, genetic variation occurs. The best example is trypanotolerance displayed by the West African humpless cattle, such as N'Dama breed, which survive in areas of heavy tsetse challenge. Other example of difference in susceptibility to diseases conditions among breeds of the same species include the superior abilities of Leghorns to resist both Salmonella pullorum and Salmonella gallinarum infections than the heavy breeds and the Zebu similar ability to resist tuberculosis than Ankole cattle (Duncan, 1999).

3.4. Age and sex resistance

Numerous infection are limited to one sex or the other because of anatomical or physiological differences between the two examples, one cannot expect mastitis in males; females fowls are more susceptible than males to Lymphomatosis (Duncan, 1999). Many animals are more resistant to primary infections with most pathogens as they reach maturity, for examples Ascarid infections in animal are most likely to develop to potency if it is more than three months of age; likewise, sheep of more than three months of age are relatively resistant to Nematodidrus, and in similar fashion, dogs gradually develop resistance to infection with Anclostoma caninum over their first years of age. In mastitis (by Streptococcus agalactiae) and contagious bovine pleuropneumonia in cattle and Leucosis in fowl, it is generally thought that there is an inverse age resistance for young animals as compared to older native animals (Baker, 1998).

3.5. The components of genetic resistance

3.5.1. Animals

Resistance to pathogens may refer to all mechanisms contributing to a disease (escaping infection by maturing before the epidemic develops), expression of inducible detrimental effect of the pathogen, such as acquisition of avoidance behavior defenses and modification of life history traits. A more specific definition of resistance refers to the biochemical and physiological changes preventing proper parasite establishment, survival, and/or development. This may further be divided into resistance and tolerance to pathogens (Tour et al., 2004).

True resistance or resistance to infection reduces or prevents infection. It is sometimes called qualitative resistance because animals are either resistance or susceptible, without intermediate levels. Complete resistance is rare, is usually specific to an individual pathogen and is usually receptor-related. Examples of such relative resistance and tolerance to pathogens are K88 E. coli receptor in swine or the gene coding for receptor to Avian Sarcoma and Leucosis viruses. This type of resistance is called "major-gene" or "single gene" resistance because animals with this type of resistance usually have one or a few specific, well defined genes that confer a high level of resistance to the specific pathogen. Often, the gene offers the animal resistance to only one specific pathogen. If other pathogens are present, the animal needs different "major genes" to resist each parasite (Berthier et al., 2006).

Tolerance or resistance to disease describes the reaction of an animal to an infection. It is often called quantitative because there are an intermediate levels ranging from resistant to susceptible. It is the resistance to

disease development and may be classified into three categories: it may refer to a complete level of tolerance (no development of disease), to the ability of an animal to maintain a reasonable level of productivity when it is diseased (true tolerance), and to the ability of affected individual to require minimal treatment to maintain acceptable performance (resilience). For examples, it has been shown that 20.7% of Holistein experimentally challenged with the same dose of S. aureus did not establish infection in any of the quarters and that 20% had all quarters infected. Usually, tolerance may be unknown. It usually effective against several pathogens and does not give an animal as high a level of resistance (Schukken et al., 1999).

Another level of resistance is the clearance, or the ability of the infected host to get rid of the pathogen. It is well known that duration of infection may be quite different across different animals infected with the same infectious doses. For examples, geometric mean duration of environmental Streptococcal infection is 12 days with a range from 1 to 370 days (Todhunter et al., 1995).

3.5.2. Pathogens

Resistance and tolerance of an animal have their counterparts in the microbial agent: Pathogenicity and virulence.

3.5.2.1. The virulence of pathogen

It is directly related to the ability of the organism to cause disease despite host resistance mechanisms. It is the rate at which parasite exploit host tissue and is affected by numerous variables such as the number of infecting bacteria, the route of entry into the body, specific and non-specific host defense mechanisms and the virulence factor of the bacterium. It can be expressed by the number of organisms needed to provoke the disease stages or by the number of organisms needed to cause infection (Lunney, 2005).

3.6. Development of resistant animals

The strategy for advancing genetic control of disease can be established through the following initiatives: the selection of locally adapted breeds, the implementation of cross-breeding methods geared at introducing genes significant in the expression if genetic resistance/ tolerance towards pathogens, and the selection of individuals highly resistant to pathogens (Bishop and Mackenzie, 2003).

3.7. Locally adapted breed and diseases resistant animals

A number of approaches to the genetic management of disease can be applied, depending on the nature of problem and the resources available. Strategies may include choosing the appropriate breed for the production environment which is naturally resistant to the diseases and adapted to the environment. The following examples are common diseases and their perspective resistant and tolerant host (Hill et al., 2005).

3.8. Trypanosomiasis

Parasite resistance associated with control based on trypanocidal drugs, and sustainability problems involved in the implementation of tsetse control progammes, have increased interest in the use of integrate control methods including the utilization of disease tolerant breeds of livestock. The most trypanotolerant breeds includes N'Dama and West African Shorthorn cattle, as well as Djallonke sheep and goats. Despite smaller size, studies have shown that these breeds are more productive than susceptible animals under moderate to high tsetse challenge (Agyemang et al., 1997). Severity of infection varies with the host in most wild animal and some domestic ones establish a balance with the parasite and remain as clinically normal carriers for long periods. Specifically, some breeds of cattle indigenous to Africa can tolerate light to moderate challenge with tsetse flies by limiting the multiplication of trypanosomes in their blood and by apparently warding off the infection, especially T. vivax (Leta et al., 2015).

The only surviving indigenous Taurine type cattle breed in Ethiopia is the Sheko that exhibt better trypanotolerant attributes than the other three breeds (Abigar, Horro and Gurager), with lower trypanosome prevalence, less severe anemia after infection, and fewer trypanocidal treatment annum than the other breed. Moreover, the Sheko breed maintained its physiological functions under prevailing Trypanosomosis challenge and compared favorably with the other breeds in its reproductive performance. While the Abigar manifested high sensitivity and frequent death to PCV depression, Horro had strong resilience to PCV depression with better response to Berenil 1 treatment assistance (Lemecha et al., 2006).

3.9. Ticks borne diseases

Ticks are a widespread problem for livestock producers, particularly in the tropics. Ticks themselves weaken animals by the withdrawal of blood to cause tick paralysis through the injection of toxin secreted in the saliva, damage hides, and provide sites for secondary infections. Moreover, they also spread a number of serious diseases, the most notable being Anaplasmosis, Babesiosis, Theileriosis and Cowdriosis (Abdela, 2016; Abdela and Bekele, 2016; Abdela and Jilo, 2016).

Resistance or tolerance to ticks, and to a lesser extent, to tick-borne diseases, is well documented. It is well known that Bos indicus cattle are much more resistant to ticks than Bos taurus cattle raised under the same circumstances (Abdela, 2016; Abdela and Bekele, 2016). Study of comparison of tick resistance of three breeds of cattle in Ethiopia, of two indigenous (Arsi and Boran) and Boran-fresian cross breed cattle following natural tick infestation at Abernossa ranch, clearly showed that the Arsi local breed have demonstrated the highest tick resistant level and the Boran cross breed has been classified intermediate (Bock et al., 1999).

3.10. Selection for increased resistance to diseases

There have been many investigations on the extent of genetic variation in response to pathogens and parasites across a broad range of non-laboratory animals (Cheng, 2005).

3.11. Pathways of infection

The bigger pictures of infectious disease can involve various pathways of infection in relation to a host population and a reservoir of infection; there are pathways from reservoir to host, from host to host, and from reservoir to reservoir. Not every pathogenic disease is involved in all pathways, but it is very useful in these terms of when contemplating the overall impacts of genetic management of disease. If, for example, selection in the host population can reduce not only infection within the host population, but also the flow of infection to the reservoir (e.g. with selection for resistance to internal parasites whose life cycle involves some time outside the host), then the reservoir will become a less important source of infection. Selection for resistance can also have impact on the populations' exposure to the same reservoir that has not been selected. In other words, these pathways help in understanding the broader consequences of selection for resistance (Bishop and Mackenzie, 2003).

3.12. Pathogen evolution

Common sense shows that the greater the success of artificial selection in increasing the level of resistance in a population, the greater will be the natural selection imposed on the pathogen to evolve in such a way as to overcome the resistance. The greater the number of the gene and mechanism involved in resistance, the less likely is the pathogen to evolve to overcome the resistance. Resistance that has evolved naturally during the course of evolution of a breed will probably present greater challenges to a pathogen than the resistance that has been created by artificial selection within a population during a relatively few generations. This latter argument raises the issue of introgression of resistance genes from naturally resistant breeds to commercial populations (Bishop and Markezie, 2003). Another issue is the extent to which genetic variation itself is a buffer against effective evolution of pathogens. The lower the level of genetic diversity in the host population, the greater the chance of extreme outcomes providing a warning against aiming for selection for homozygosity at all loci affecting resistance (Springbett et al., 2003).

3.13. DNA markers for disease resistance

Obviously, a major hurdle to the widespread application of selection for resistance to disease is that the requisite exposure to pathogens or parasites is often neither practicable nor acceptable on welfare grounds. Consequently, there is a very strong incentive for identification of DNA markers for disease resistance, which has stimulated a considerable research effort around the conducting genome scans and testing candidate genes (Kaplan, 2004).

Conducting genome scans for resistance to disease require no prior knowledge of genes that could be involved. All that is needed in a population in which there is variation is resistance, and a set of DNA markers that together cover all regions of all chromosomes. A powerful population for this purpose comprises the segregating generation (F2 or later) resulting from a cross between two populations that differ as far as possible in level of resistance, either from divergent selection or from widely discrete breeds. More common is genome scans

conducted within breed or populations on which detailed disease-resistance performance is seen. The result of genome scans for resistance is the identification of regions of chromosomes so-called quantitative trait loci (QTL) that contribute to variation in resistance. Candidate genes are genes whose known function suggest a possible role in the trait of interest. In this case, is disease resistance. Examples included genes encoding immunoglobulins, cytokines, histoglobulins and pathogen receptors, and genes that have been shown to be associated with resistance (Rupp and Boichard, 2003).

A major class of candidate genes comprise the major histocompatibility complex (MHC), a set of closely linked genes that encode peptides that act as identity cards for the cell, enabling cell of the immune system to distinguish between self and non self (the latter usually indicating infection). The atypically extensive polymorphism at these loci defines solely neutral explanations, and results in even the most ardent neutralist coming down on the side of selection (Cheg, 2005). Strong associations between particular MHC alleles and resistance/susceptibility to diseases would be found in animals and that once found, such associations could be used for marker-assisted selection (MAS) for resistance (Woolastont and Windon, 2001).

3.14. Genetically modified resistant animals

Genetically modified animals resistant to disease would provide valuable models to investigate disease progression and controlling the disease (McCcreath et al., 2000). The principle has led to a faster rate of change because it has focused attention on economically important traits. It has provided systemic approach to the exploitation of cross breeding. It has also be shown to maximize progress in the animal production as whole distinct from individual. Better understanding has also be shown for effective system of testing genetic merit and to refine the techniques of performance and progeny testing. Some support has been given to the process by technical advance such as those for accessing disease (Hassan et al., 2004).

3.15. Development of transgenic animals

Transgenic animal are those animals that have transgene from genes of natural diseases resistant animal and which exhibit resistance to diseases without losing their production capacity. Although, robust and successful, conventional breeding is limited in animals produced by mating two selected individuals which are genetic mixtures of the two parents. Thus, unknown or undesirable traits can be co-selected inadvertently. In addition, only those genetic loci present in the parent can be selected, which severely limits the extent of genetic improvement. Gene addition through transgenic technology potentially offers a route to overcome these limitations. Genetic modification offers alternative strategies to traditional animal breeding. This technology likely has specific application where genetic variation does not exist in a given population or species and where novel genetic improvements can be engineered. With either approach, the intention would be to enhance the ability of an animal to mount an appropriate immune response against the pathogens (which could require dampening down the immune system at strategic stages) or to generate an effective system that would directly block pathogen entry or directly destroy the pathogens. Indeed, a combination of strategies may prove to be the most successful approach. The strategies of improving immune response (a new strategies for which experimental examples are only now being tested) could be used in instances where specific gene alleles confer resistance in species. There are some techniques to develop such animal (McCcreath et al., 2000).

3.16. Microinjection

The main purpose of the microinjection method is to expose the transgene before cell differentiation begins, thus allowing it to be prevalent in the organism before the organism begins to develop. If the process works as planned, all cells in all tissues of the soon to be organism will contain this crucial gene. An egg and sperm are fertilized in vitro, and before two pro-nuclei fuse inside the new zygote, the male pronucleus is microinjected with the recombinant DNA. A fine point glass pipette immobilizes on one side, while on the other side, the foreign DNA is inserted into the male pronucleus with an ultra-fine needle. The pronucleus visibly swells as it is microinjected (Wheeler et al., 2008).

Following microinjection, the embryo is cultured unto the blastocyst stage in vitro, then, placed back into a pseudo-pregnant female or foster mother. The embryo develops the same way as a typical embryo into a fetus, and normal pregnancy is observed. This microinjection procedure is the most efficient way today to create transgenic animal lines, even though only about 25% of these embryos actually produce transgenic offspring. The

reason for this low efficiency is unknown, but likely includes destruction of the embryo during microinjection, and spontaneous abortion of the fetus (Eide, 1997).

3.17. Embryonic stem cell injection

The second method for creating transgenic animals is somewhat similar to the first method discussed, but involves making embryonic stem (ES) cells transgenic instead of a male pronucleus. An embryo is created by in vitro fertilization (IVF) but instead of being injected with foreign DNA, the embryo is cultured unto the blastocyst stages. The blastocyst stage occurs about 5-7 days after fertilization. The blastocyst consists of an inner cell mass of embryonic stem (ES) cells and an outer trophobast. The word blastocyst means "bud" or "sac" reffering to the fetus which at the time is only a cellular sac with a central cavity. The ES cells are isolated then injected with foreign DNA. Once it has been determined that the transgene is present in the ES cells, they are injected into another blastocyst. That blastocyst is then implanted into surrogate mother as before to create transgenic pups (Archibald, 2003).

As with transgenic DNA microinjection, with this procedure, every organ system of the animal usually contains transgenic DNA, including the reproductive system and ES cells can be pre-screened to ensure transgene insertion prior to injection into the blastocyst, which improves efficiency. This method is particularly important for studying the development of transgenic organism while being able to control their genes, and works very well with mice. However, the DNA microinjection method works better on a wider variety of species (Cheng, 2005).

3.18. Genetic control of pathogens

3.18.1. Control of vectors

The control is the introduction of genetic factors to pest populations that reduce or eliminate the pest problems by mating (Christophides, 2005). It involves the rearing, radiation or chemical sterilization and release of males to introduce large amount of dominant lethal mutation into the wild pest species (Coleman and Alphey, 2004) or treatment of the natural population with an agent (chemosterilant) which will induce sterility in the native insects. Cytoplasmic incompatibility is one of the genetic control techniques in which cytoplasmic factor transmitted through the egg, kills the sperm of the incompatabile male after its entry into egg. Ionizing radiation or chemical sterilants induce dominant lethal mutation in the sperm that are used to sterilize males. Genetic control is a potential technique that may be subdivided into population suppression or population replacement in which genetic traits are introduced into the wild population by mating (Christophides, 2005).

Sterile insect technique (SIT): This technique is a population suppression method that eliminates a range of agricultural pests and disease vectors. Population replacement involves the development of genetically modified strain of target vector that may be spread throughout the wild vector population. The method relies on the large number of the target insect in specialized production centers, the sterilization of the male pupae or adult fly and the sustained and systematic release of sterile males over the target area in numbers large enough in relation to the wild females. Mating of the sterile insects with virgin, native females will result in offspring (Hassan et al., 2004). With each generation, the ratio of sterile to wild insects will increase and the technique becomes therefore more efficient with lower population densities inversely-density dependent (Christophides, 2005).

The SIT is intrusive to the environment, has no adverse effects on non-target organism, is species-specific and can easily be integrated with biological control method such as parasitoids, predators and pathogens. There is no development of resistance to the effects of the sterile males provided adequate quality assurance is practiced in the production process and the sterile insects cannot be established in the released areas as with other biological control programme (Lewin et al., 2004). The release sterile insects are however, only effective when the target population density is low, it requires detailed knowledge on the biology and ecology of the target pest, the insect should be amenable to mass rearing. In addition, the SIT necessitates efficient release and monitoring method, which have to be applied on the area-wide basis (Tompkins et al., 2004).

One technique for the automatic sexing of larvae involves generating by irradiation of a reciprocal translocation between a Y-Chromosomes and a selection of chromosomes 5 carrying a dieldrin resistance gene, R. Strains translocation in conjunction with a normal chromosomes 5 with the susceptible gene, S consists of only resistant males and susceptible females, making the male to be released as part of an SRIM programme. The fact that the released males are all carrying a dieldrin resistant gene does not matter, because they have all been sterilized by radiation prior to release (Christophides, 2005).

3.18.2. Recombinant DNA technique to control pathogens

One of the main objectives of working with recombinant DNA is to produce an unlimited number of copies of particular segment of DNA. This process is used currently in DNA recombinant vaccine development. The vaccine development over the years has been to identify the important antigens responsible for protection and to produce them in purest form. But only recently has recombinant DNA technology (rDNA, genetic engineering) become available to help to produce defined antigens, or antigenic determinants, on a large scale and in a cost-effective manner. The isolation of these antigenic determinants on the surface of infectious agents represents the first step in trying to produce a more specific antigen. Since these determinants occur in repeating subunits and their production is controlled by specific genes in the nucleus of the organisms, these genes may be used to produce antigenic determinants (Albert and Boothe, 1998).

By isolating the specific gene (DNA) that encodes for the surface antigenic determinant, and by using a plasmid (a piece of DNA that occurs naturally in bacteria and yeast) to insert this gene as a bacteria, yeast, or mammalian cell, the gene recombines with the cell's own genes to produce the antigenic determinant along with other cellular products (Tompkins et al., 2004). The antigenic determinant may be isolated and used as an immunogen. This immunogen will be recognized by the immune system as being foreign and will stimulate the production of antibodies or a cellular response that will protect the animal or prepare the animal's immune system for future infection with the infectious agent (Yonash et al., 2005).

Antigenic determinants can be produced by growing the cells on a large scale and collecting arid purifying the antigen as it is expressed. The antigen may have improved characteristics as compared to the antigen derived from the whole organism. These characteristics are purity, safety, and stability. Also, the risk of having the vaccine contaminated with infectious material used in production of the whole organism is reduced. All these characteristics help in developing improved vaccines (Bakri et al., 2005).

4. Conclusion

The knowledge of genetic variation in hosts leads to the exploration of resistance lines which will be economically important in infected areas, where production losses due to disease are severe. This circumvents the problems created due to drug resistance and it also helps in further studies on the mechanism of disease resistance. Development of natural disease resistant animal helps to increase the frequency of desirable genes in a population, which will be a source that could be exploited indefinitely without further investments unlike other disease control means. Veterinary genetics has strong potential application, for countries like Ethiopia. But much research work should be done regarding the livestock breeds available, the existence of difference in resistance or susceptibility to a particular disease among the livestock disease breeds in order to establish resistant lines and to propagate those genes responsible for resistance. Pedigree record of animals by farmers or breeders should be encouraged to identify and control animal diseases or inherited disorders. Using genetically modified or genetically engineered animals is now a reality, for the time being, however, somewhat difficult to use in the developing countries like ours. However, it is important to have concern on the application as it will hopefully be in routine use in the future. Genetic control of pathogen using different techniques should be practiced in order to overcome the risk of pathogen resistance to drug, loss of economy to chemotherapy as well as to reduce residual effect of drug which have public importance. Combination of new methodology that enables the efficient production of genetically modified (GM) animals with exciting new tools to alter gene activity makes the applications of transgenic animals for the benefit of animal (and human health) increasingly possible.

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How to cite this article: Deneke, Y., 2020. Genetics and its role in the control of animal diseases: A brief review. Scientific Journal of Veterinary Advances, 9(1), 289-298.

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