

REVIEW OF CANDIDATE GENES TOWARDS SELECTIVE BREEDING AGAINST SOME MAJOR DISEASES AFFECTING CATTLE, SHEEP AND GOATS IN NIGERIA

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ABSTRACT

Compilation and review of some candidate genes that can be employed in characterization of indigenous livestock in Nigeria for resistance to common diseases were undertaken in this study. The diseases that affected livestock (cattle, sheep and goats) in 2018 and 2019 were presented.

Keywords: Candidate gene, resistance to disease, cattle, sheep and goats

INTRODUCTION

Genetic variation of resistance to internal parasites has been demonstrated in numerous species, including humans and several livestock species (Kloosterman *et al.*, 1992 and Quinnell, 2003). However, the genetic architecture underlying such traits is poorly understood (Kemper *et al.*, 2011). Livestock diseases adversely affect animal production throughout the world. Livestock keepers and other stakeholders involved in promoting animal health can draw on a number of approaches to reducing these negative effects (<http://www.fao.org/3/a1250e/a1250e05.pdf>). Some of the strategies being used to reduce the negative effects of diseases on productivity of farm animals include vaccination, elimination of disease vectors and appropriate management methods. These approaches are sometimes constrained and become less sustainable. Identification of animal genetic resources (AnGR) for resistance to some major diseases of livestock (cattle, sheep and goats) is one of the high end solutions that can provide sustainable reduction to economic losses due to diseases. For many livestock diseases, evidence has been found for genetic variation in the extent to which host animals are susceptible. This paper was aimed at reviewing some candidate genes that can be employed in characterization of indigenous livestock in Nigeria for resistance to common diseases.

Major livestock diseases reported in Nigeria by 2018 and 2019

Reported cases of livestock diseases were shown in Table 1. These reports were documented through the Agricultural Performance Survey (APS) of NAERLS (NAERLS, 2018 and 2019). Contagious bovine pleuropneumonia (CBPP) was reported in six (6) States in 2018 and 2019. Foot and mouth disease was reported among cattle populations in many States of Nigeria. Foot and mouth disease (FMD) is a severe, highly contagious viral disease of cattle. It also affects sheep and goats. Other diseases and pests that affect cattle in Nigeria in 2018 and 2019 were babesiosis, fascioliasis, foot rot, helminthiasis, rinderpest, tick infestation and tuberculosis.

Peste des petits ruminants (PPR) affected sheep and goats in all the agro-ecological zones in Nigeria. The disease was reported to have affected sheep and goats in 16 States in 2018. Plate I showed the estimated loss of sheep and goats to PPR disease in 2018. Other pests and disease that affected sheep and goats in 2018 and 2019 were fleas, foot rot, helminth worms and mange.

Candidate gene for resistance to foot and mouth Disease

Integrin subunit Beta 6 (ITB6) gene was reported to be associated with resistant to foot and mouth disease in cattle (Gowane *et al.*, 2013). This gene encodes a protein that is a member of the integrin superfamily. Members of this family are adhesion receptors that function in signaling from the extracellular matrix to the cell. Integrins are heterodimeric integral membrane proteins composed of an alpha chain and a beta chain. Integrin alpha-V: beta-6 (ITGAV: ITB6) is a receptor for fibronectin and cytotactin. It recognizes the sequence R-G-D in its ligands. Internalization of integrin Alpha-V/ beta-6 via clathrin-mediated endocytosis promotes carcinoma cell invasion. It acts as a receptor for fibrillin-I (FBNI) and mediates R-G-D-dependent cell adhesion to FBNI.

The Major Histocompatibility Complex (MHC) gene is a candidate gene considered important for the immune system and disease resistance traits. MHC is a cell surface molecule involved in antigen presentation by glycoprotein receptors (Dukkipati *et al.*, 2006). The MHC involves a series of highly

polymorphic genes which are responsible for the initiation of the immune response when an animal is challenged by pathogens or parasite (Santucci *et al.*, 2007). The major histocompatibility complex (MHC) is a cluster of tightly linked genes that play an important role in the immune system (Klein, 1986). The products of these genes are involved in the induction and regulation of immune response. The MHC spans approximately 4Mb of human genome, 1.5Mb in mice and approximately 2.5Mb of cattle genome (Lewin, 1996). In cattle, it is located on chromosome 23. The structure and organization of MHC genes of cattle, known as the bovine leukocyte antigen (BoLA) complex, are very similar to those of the human MHC.

Table 1: Reported cases of major diseases affecting cattle, sheep and goats in Nigeria

Species	Diseases	Reported cases by States	
		2018	2019
Cattle	CBPP	Adamawa, Anambra, Gombe, Lagos, Nasarawa, Plateau, Taraba	Bauchi, Borno, Kogi, Kwara, Taraba, Zamfara
	Helminthiasis	Adamawa, Benue, Kano, Niger, Rivers	Benue, Edo, Kwara, Rivers
	FMD	Adamawa, Bayelsa, Gombe, Kano, Katsina, Taraba, Osun, Oyo, Rivers, Sokoto	Borno, Kano, Kogi, Oyo, Rivers, Taraba, Zamfara
	Babesiosis	Niger	Kwara
	Foot rot	Edo	Edo
	Mastitis	Nil	Osun
	Tuberculosis	Nil	Benue, Kano, Ogun
Sheep/Goats	PPR	Abia, Adamawa, Anambra, Benue, Ebonyi, Edo, Gombe, Kano, Katsina, Nasarawa, Niger, Osun, Oyo, Plateau, Rivers, Taraba	Anambra, Benue, Borno, Cross River, Ebonyi, Edo, Ekiti, FCT, Imo, Kogi, Osun, Oyo, Plateau, Rivers, Taraba, Zamfara
	Helminthiasis	Adamawa, Benue, Edo, Kano, Plateau, Rivers, Taraba	Bayelsa, Benue, Cross River, Edo, Kwara, Plateau
	Babesiosis	Imo	Ebonyi
	Foot rot	Bayelsa	Akwa-Ibom
Sheep	Brucellosis	Nil	Zamfara
Goat	Leptospirosis	Nil	Zamfara

CBPP: Contagious bovine pleuropneumonia; PPR: Peste des petits ruminants

Source: NAERLS APS Report 2018 and 2019.

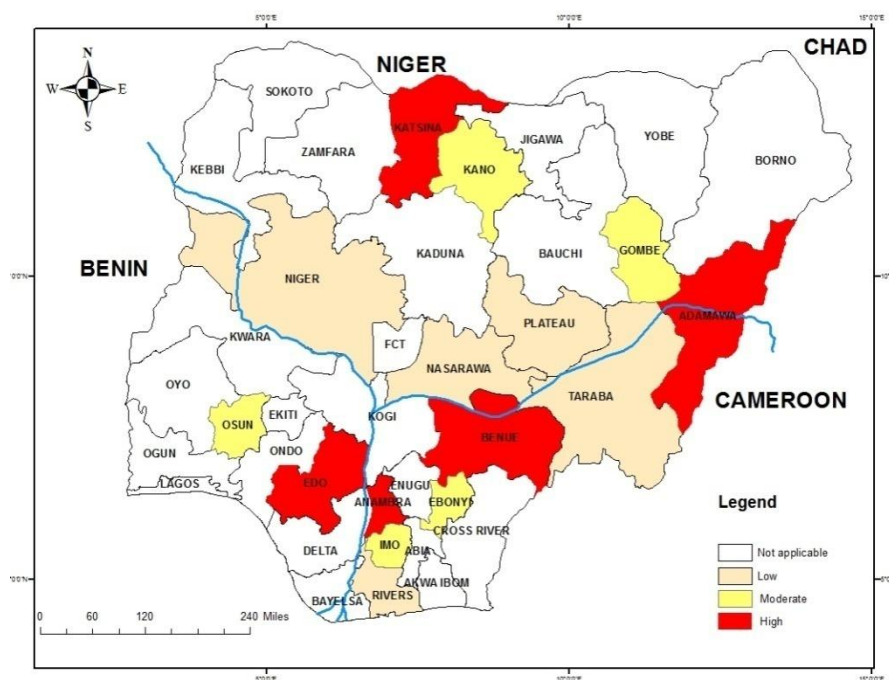


Plate I: Estimated loss of sheep and goats to peste des petits ruminant disease in 2018
(Source: NAERLS, 2018)

Candidate gene for resistance to peste des petits ruminants

Toll-like receptor (TLR) gene are vital for the detection of invading pathogens and are commonly expressed in antigen presenting cells and other immune cells (O'Neill, 2006). Toll-like receptors are type 1 transmembrane protein expressed in almost all cell types and activate the innate immune system upon sensing pathogen associated molecular patterns (PAMPs). Intracellular TLR that sense viral nucleic acids include TLR3 (double stranded RNA), TLR7 and TLR8 (single stranded RNA) and TLR9 (CPG motifs in DNA) (Prajapati *et al.*, 2017). The cell specific location and basal expression levels of TLR mRNA could indicate the natural pathogen-associated molecular patterns (PAMPs) load of that tissue as well as the innate host resistance to pathogens. In addition to the differential expression profiles of Toll-like kinase (TLK), ligand induced downstream cytokine profiles and/or levels could also play a role in the innate disease resistance (Manaswini *et al.*, 2018).

Candidate gene for resistance to mastitis

Toll-like receptor gene 4 (TLR4) plays an important role in bovine mastitis resistance (Wang *et al.*, 2015). The protein encoded by TLR4 gene is a member of the toll-like (TLR) family which plays a fundamental role in pathogen recognition and activation of innate immunity (TLR immunity). TLRs are highly conserved from drosophila to humans and share structural and functional similarities. They recognize pathogen-associated molecular patterns that are expressed on infectious agents, and mediate the production of cytokines necessary for the development of effective immunity.

Candidate gene for resistance to tuberculosis

Caspase recruitment domain 15 (CARD15) gene in cattle plays an important role in tuberculosis (TB) resistance (Prajapati *et al.*, 2017). CARD15 gene encodes for a cytosolic protein implicated in bacterial recognition during innate immunity. Paratuberculosis represents a major problem in farmed ruminants and at the present is considered a potential zoonosis. The disease is caused by *Mycobacterium avium* subspecies (Pinedo *et al.*, 2009).

Candidate gene for resistance to other types of livestock diseases

The Natural Resistance Associated Macrophage Protein 1 (NRAMP1) gene, also known as Solute Carrier family 11 member A1 (SLC11A1) gene is a member of large family of metal ion-transport proteins and it was the first positional cloned gene related to infectious disease susceptibility in mouse (Vidal *et al.*, 1993). Since SLC11A1 is associated with pH dependant transport of divalent cations (like Fe^{2+} , Mg^{2+} , etc.) through the phagosome membranes, are essential for many cellular functions.

Under normal physiological conditions, SLC11A1 gene delivers bivalent metal cations from the cytosol into acidic endosomal and lysosomal compartments where the Fenton and Haber-Weiss reaction generate toxic antimicrobial radicals for direct antimicrobial activity against phagocytosed microorganisms (Goswami *et al.*, 2001). SLC11A1 gene have pleiotropic effects on macrophage function, that include increased chemokine KC, tumour necrosis factor- α , interleukin-1 β , inducible nitric oxide synthase and major histocompatibility complex class II expression; all are important in resistance to intracellular pathogens (Awomoyi, 2007).

There are so many experimental evidences regarding the association of SLC11A1 gene polymorphisms with resistance to infectious diseases in human beings as well as animals. In mouse SLC11A1 gene confers resistance to intracellular pathogens like *Mycobacterium spp.*, *Salmonella spp.* and *Leishmania spp.* (Vidal *et al.*, 1995)

Toll-like receptors (TRL-2 gene) initiate inflammatory responses following the recognition of a wide repertoire of pathogens including bacteria, fungi, protozoa and viruses. They are composed of an extracellular leucine-rich repeat domain responsible for detecting pathogen-associated molecular patterns, a membrane spanning region and an intracellular Toll/Interleukin 1 receptor domain which invokes signal transduction. Toll-like receptor 2 is the most diverse of these receptors as it recognizes infectious agents from a range of pathogenic groups.

Bovine leukocyte antigen (BoLA-DRB3) complex are very similar to those of human MHC. BoLA complex is found in two separate regions of the chromosome rather than a single cluster of genes seen in most mammals. The larger gene cluster is located at BTA23 band 22 and apparently contains all of the bovine class I and class III sequences and gene encoding both subunits of the classical class II proteins DQ and DR. The remaining BoLA class III loci (DIB, DNA, DOB, DYA, DYA, TCPI, LMP2, LMP7 and TAP2) are located in a cluster near the centromere at BTA23 band 12-13 (Rothschild *et al.*, 2000). The DRB3 locus and its gene products are among the best defined in cattle. The associations between BoLA alleles and disease class I association include resistant to mastitis (Mejdell *et al.*, 1994).

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