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Interleukin-2 ((IL-2) gene polymorphism and association with heat tolerance in Nigerian goats

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ABSTRACT

Interleukin-2 (IL-2) serves as a potent immuno-modulator, and plays a unique role in both the activation and maintenance of immune responses and in lymphocyte development. Gene polymorphism in IL-2 gene in three major Nigerian goat breeds [West African Dwarf (WAD), Red Sokoto (RS) and Sahel (SH)] was analysed by restriction fragment length polymorphisms (RFLP). The restriction enzyme, DraI was utilized. The association between the polymorphic site and some heat tolerant traits were also investigated in a total of 157 animals comprising 59 WAD, 69 RS, and 29 SH goats of both sexes. The IL-2 sequence displayed a 98% nucleotide identity with the referenced Cahi-IL-2 AY603404.1 orthologous sequence in GenBank. The phylogenetic trees revealed largely species-wise clustering, while the RS and SH goats were closer compared to the WAD goats. DraI genotype frequencies were in Hardy-Weinberg Equilibrium ($P < 0.05$). The expected heterozygosity (H), which is a measure of gene diversity in the goat populations, ranged from 0.26 to 0.28. The heterozygote (TA) had a comparative advantage over the homozygote (AA) in terms of rectal temperature (39.21 ± 0.08 (TT) and 38.86 ± 0.13 (TA); $P < 0.05$). The SH goats also displayed greater resistance to thermal stress compared to the RS and WAD goats. There were varying sex and interaction effects on the thermal indices. The present findings may find application in the selection of superior animals for resistance to heat stress as well as provide insight to questions about evolution, ecology and conservation of Nigeria indigenous goats.

1. Introduction

Cytokines have generally been discovered and characterized as components of the peripheral immune system. Although far from fully understood, the role of cytokines as immune-modulators in the peripheral immune system is well documented (Dhama et al., 2015). That several cytokines and their receptors are constitutively expressed in the central nervous system of healthy organisms also supports the notion that cytokines may have originally evolved for functions other than signaling in the peripheral immune system (Opp, 2005). Cytokines have been shown to play important roles in different aspects of animal health and production (Marcos-Carcavilla et al., 2007; Lühken et al., 2009; Szydlowski et al., 2010; Darlay et al., 2011). Cytokines are mediators of information transfer between cells, and in this way, they regulate physiological and pathological mechanisms in the body (Turner et al., 2011). They are potentially of use in diagnosis. IL-2 is the prototype member of a family of cytokines that have pleiotropic actions in the immune system (Lin and Leonard, 2003). It was discovered in 1976 as a growth factor present in conditioned medium from phytohemagglutinin (PHA)-stimulated normal human lymphocytes. This was able to

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specifically support the growth of activated normal T lymphocytes in-vitro and was therefore denoted as T-cell growth factor (TCGF). IL-2 stimulates natural killer (NK) cells, and lymphocyte-activated killer (LAK) cells. It shows strong B-cell growth factor activity and can stimulate monocytic lineage cells (Pintaric et al., 2008; Nagarajan et al., 2011). It also stimulates progesterone production in granulose cells (Kumar and Esha, 2011). The insulin-dependent diabetes susceptibility locus 3 (*idd3*) in the NOD mouse has been shown to map to the IL-2 gene (Yamanouchi et al., 2007). Luhken et al. (2005) reported the presence of transcription factor binding sites in the second intron of the IL-2 gene of cattle. The SNPs in these sites might influence the binding of transcription factors leading to varied production patterns in different genotypes. Genotypes arising from IL-2 polymorphism have been reported to have significant associations with milk production traits. This can also serve as a major tool for combating disease susceptibility and improving overall productivity of livestock populations in the tropics by selecting and breeding the most suitable genotypes (Prakash et al., 2011).

The goat (*Capra hircus*, L.) represents one of the most important farm animal species. It is reared in all continents with an estimated world population of about 900 million of animals, out of which 55.1 million are reared in Nigeria (FAOSTAT, 2011). The Nigerian goat is still genetically unimproved, and the pressure of modern genetic improvement has increased the need to better understand natural genetic variation in Nigerian goat breeds, as well as formulate germplasm conservation and improvement policies. Although the three major breeds of goats in Nigeria namely, West African Dwarf (WAD), Red Sokoto (RS) and the Sahel goats have been characterized using morphological traits (Yakubu et al., 2011), protein polymorphism (Imumorin et al., 1999; Yakubu et al., 2014), microsatellites (Okpeku et al., 2011) and major histocompatibity complex DQB1 markers (Yakubu et al., 2013), there is no information on genetic characterization involving interleukin genes.

Therefore, this study aimed at investigating molecular genetic variation and phylogenetic diversity of IL-2 gene in Nigerian goat breeds and the association of its SNPs with heat tolerance traits. The molecular markers (SNPs) emanating from the association between IL-2 allelic variations and heat tolerant traits in this study would lay the ground work for appropriate molecular selection strategies for sustainable production and effective management of tropical goats especially in Nigeria, sub-saharan Africa characterized by high environmental temperatures.

2. Materials and methods

2.1. Animals and blood collection

Blood samples were obtained from a total of 157 animals (about 2 years of age) comprising 59 West African Dwarf (WAD), 69 Red Sokoto (RS) and 29 Sahel (SH) goats of both sexes sampled across various farms in Nigeria (Fig. 1). The ethical guidelines of the International Council for Laboratory Animal Science and Cornell University, Ithaca, NY, USA were strictly followed. Genomic DNA was extracted from the collected blood samples using the ZymoBead™ Genomic DNA kit (Zymo Research Corp. Irvine, CA, USA). The quantification of the DNA yield as well as the assessment of its quality was done using Nanodrop ND-100 UV/Vis Spectrophotometer (Nanodrop Technologies, Inc., DE, USA).

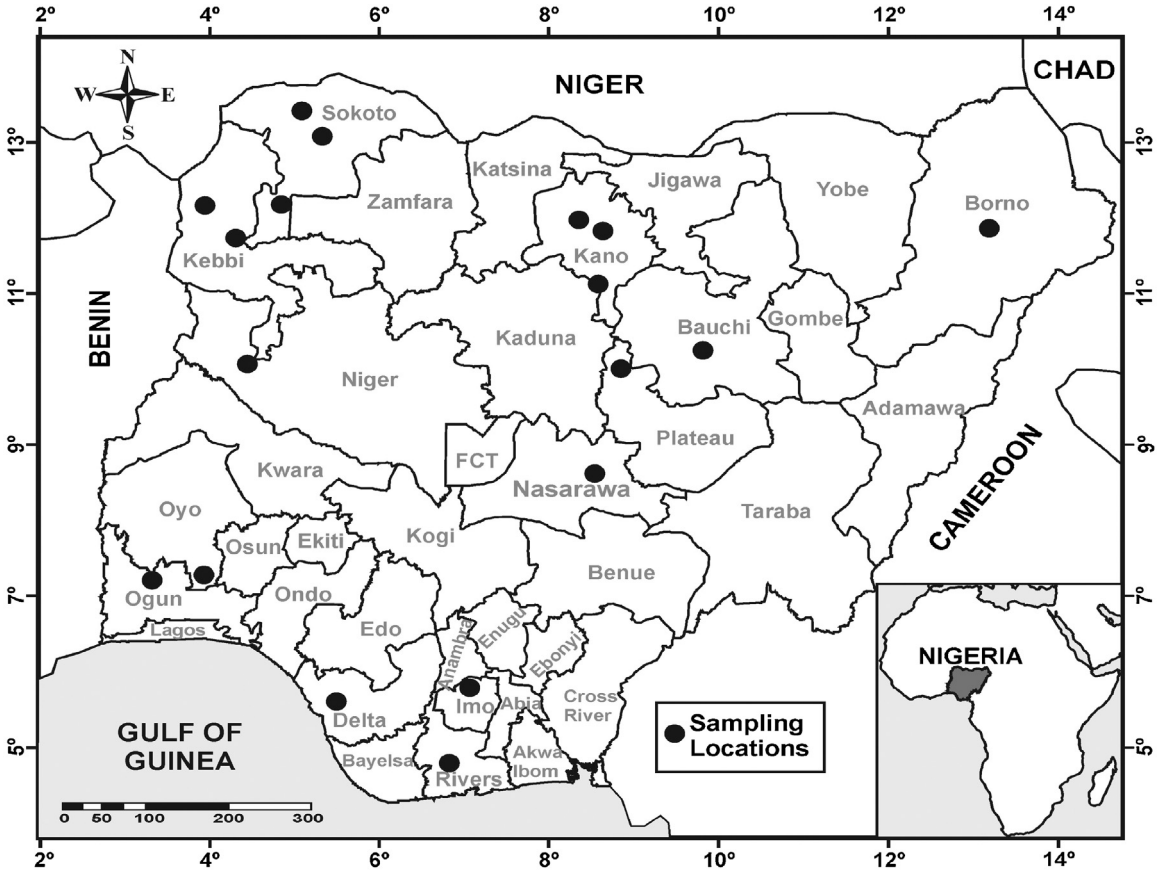

Fig. 1. Map of Nigeria showing sampling locations.