Computational analysis of data on the functional and structural effects of single nucleotide polymorphisms (SNPs) on inbred ovenbirds

Musa S. I. [1][*]. Yahaya K. O.[2], Yahaya A. [3]

[1,2] Department of Animal Science, Nasarawa State University, Keffi, Shabu- Lafia Campus, Nigeria

[3]Department of Animal Science and Technology, Federal University of Technology, Owerri, Nigeria

Corresponding email : dribmazara@yahoo.com

Abstract

The objective of this study was to evaluate the functional and structural effects of single nucleotide polymorphism (SNP) on ovine interferon tau using computational methods. Data on ovine interferon was retrieved from data base of National Center for Biotechnology Information (Gen Bank). Functional effects of substitution of Leucin by Proline at position 26 of interferon protein chain was predicted using Protein Variation Effect Analyzer, Panther server and Poly phen 2 (Polymorphism phenotyping) respectively. Provean score of - 5.828 was obtained, indicating a deleterious effect of the amino acid substitution. Panther server indicated damaging effect of the SNP with Pdel (probability of deleterious effect) of 0.5. Similarly, Poly phen 2 showed damaging effect of the amino acid substitution. Mudpred 2 server indicated loss of sulfation to be the mechanism of structural change. It can be concluded that substitution of Leucin by proline at position 26 of the protein sequence interferon tau resulted in deleterious effect on the functionality of ovine interferon tau. Studies in single nucleotide polymorphism on ovine interferon tau can provide better understanding of biomarkers associated with efficiency of maternal pregnancy recognition in the ovine species.

Key Words : Ovine; Interferon; SNP; Prediction

Introduction

Interferon tau is the agent of maternal pregnancy recognition in ruminants. It is the anti luteolytic factor by the conceptus in ruminants (**Fuller and Thomas, 2011**). Pregnancy establishment and maintenance requires a functional corpus luteum, which is achieved by pregnancy recognition signals. Maternal recognition of pregnancy is a phenomenon whereby luteolysis of the corpus luteum is abrogated to ensure continuous production of progesteron which is essential for maintenance of pregnancy (**Fuller, 2013**). Interferon tau act on the uterine endometrium to inhibit expression of estrogen receptors and oxytocin receptors thereby abrogating oxytocin dependent pulsative release of prostaglandins. Early embryonic death is a major cause of infertility in farm animals, this may result from impaired interaction between maternal endometrium and the conceptus (**Kabir, 2017**). Failure of uterine endometrium to interact with interferon tau or failure of foetus to produce adequate amounts of interferon have implicated as causative factors of pregnancy failure in domestic animals (**Roberts, 1991**). Interferon tau polymorphism have been identified in ruminants with varying anti proliferative and anti luteolytic activities (**Alan and Lydia, 2017**). Amino acid sequence and composition determine the 3D structure and functionality of a protein (**Vasem et al., 2021**). Structural alteration in a protein results in changes in allosteric sites and altered connections between elements within protein structure (**Guarnera et al., 2017**). Embryonic mortality account for significant proportion of pregnancy losses in sheep with embryonic death occurring during the preimplantation stages

(**Pavitra et al., 2020**). A number of genetic and chromosomal abnormalities have been implicated as causative factors of early embryonic death (**Dupont et al., 2010**). The objective of this study is to evaluate the functional effect of single nucleotide polymorphism in ovine interferon tau in which leucin is substituted by proline at position 26 of the protein sequence. Investigation on single nucleotide polymorphism in interferon tau will provide highlight on biomarkers associated with early embryonic loss in the ovine specie.

Materials and Methods

Data on ovine interferon tau with 195 amino acid sequences and accession no >NP_001116871.1 (**Brooks and Spencer, 2015**) was retrieved from the data base of National Center for Biotechnology Information (Gen Bank) and subjected to various computational analysis to predict the effects of Single Nucleotide Polymorphism (SNP) in interferon tau.

<u>Predicting effects of Single Nucleotide Polymorphism using Panther</u>

Protein analysis through evolutionary relationship (PANTHER, version 15.0) was used for the analysis. The server estimates the likelihood that a non-synonymous SNP will cause a functional impact on the protein as described by **Musa, 2021**.

Analysis of effects of SNP using Provean server

Protein variation effect analyzer was used to predict the effect of single nucleotide polymorphism in ovine interferon as described by **Musa, 2020**. A delta alignment score was compared for each supporting sequence; the scores are averaged within and across clusters to generate a final Provean score. Provean score equal to or below a pre-defined threshold indicate a deleterious effect of the amino acid substitution. Provean score above the threshold indicate a neutral effect.

Prediction of SNP using Poly phen 2 (Polymorphism phenotyping 2)

Poly phen 2 (Version 2) predicts the impact of amino acid substitution on the function of a protein using physical and comparative consideration (**Adzhubei et al., 2010**)

RESULTS AND DISCUSSION

The result of prediction of single nucleotide polymorphism in ovine interferon using Panther server is shown in table 1.

Table 1: Prediction of Single Nucleotide Polymorphism using PANTHER

Substitution	Preservation time	Result	Pdel
L 26 P	361	Probably damaging	0.5

Preservation time (million years), Pdel- probability of deleterious effect

The results indicate damaging effect of substitution of leucin by proline at position 26 of the protein chain. The amino acid substitution has a deleterious effect on the function of interferon tau as an agent of maternal pregnancy recognition

which may lead to increase incidence of early pregnancy loss.

Prediction of effect of SNP using PROVEAN server is shown in table 2.

Musa et al., 2023

Table 2: Prediction of effect of Single Nucleotide Polymorphism using PROVEAN

Variant	Provean score	Prediction
L 26 P	-5.816	**DELETERIOUS**

The default threshold is -2.5, variants with score equal to or below the threshold are considered deleterious

Table 3: Prediction of effect of SNP using Poly phen 2

Protein	position	AA1	AA2	PREDICTION
Interferon	26	L	P	**Damaging**

Prediction of effect of single nucleotide polymorphism using poly phen 2 indicate damaging effect of the amino acid substitution.

Table 4: **Prediction of structural effects of Single Nucleotide Polymorphism using Mudpred2**

Molecular mechanism	Mutpred 2 Score	P-Value	Substitution
Loss of Sulfation	0.876	0.03	L 26 P

Mutpred2 score > 0.75 is considered highly pathogenic

The molecular mechanism of pathogenicity is indicated as loss of sulfation as shown in table 4. A mutpred 2 score of 0.876 is considered highly pathogenic as reported by **Vikas et al., 2020**.

The effects of single nucleotide polymorphisms are attributed to the impact in protein structure, the structural changes may alter the function of the protein as observed in this study. It can be concluded that substitution of Leucin by proline at position 26 of ovine interferon tau sequence resulted in adverse effect on the functionality of ovine interferon. Investigations of single nucleotide polymorphism in ovine interferon can provide information on biomarkers associated with implantation of the embryo and pregnancy establishment in the ovine species.

REFERENCES

Adzhubei, I.A., Schmidt, S., Peshkin, L., Ramensky, V.E., Gerasimova, A. and Bark, P. (2010).A method and server for predicting damaging missense mutations. Nature methods 7(4):248-249

Alan, D.E. and Lydia, K.W. (2017). The evolution of interferon tau in reproduction. Reproduction, 154(5): 1-10

(**Brooks and Spencer, 2015**) Apsent refernce

Dupont, C., Segars,J., DeCharney, A., Bavister, B.D. and Armont, D.R. (2010). Incidence of chromosomal mosicism in morphorlogically normal non human primate pre implantation embryo. Fertility and Sterility, 93 (8): 2545-2550

Fuller, W.B. (2013). Pregnancy recognition signalling mechanism in ruminants and pigs. Journal of Animal Science and Biotechnology, 4(23)

Fuller, W.B. and Thomas, I.S. (2011). Hormones and reproduction of vertebrate mammals, 73-94, texas A AND M University, Texas, USA

Guarnera, E., Tan, Z.W., Zheng, Z. and Berezovsky, I.N. (2017). Allosigma: Allosteric signallin and mutation analysis server. Bioinformatics 33 (24), 3996-3998

Kabir, A.R. (2017). An insight into maternal recognition of pregnancy in mammalian species. Journal of Saudi Society of Agricultural Sciences. 16(1): 1-6

Musa, S.I. (2020). Structural and functional effects of single nucleotide polymorphism in canine cytochrome b5 reductase in silico. Veterinary Medicine and Public Health Journal2(3):73-76

Musa, S.I. (2021). In silico analysis of the effects of amino acid substitution in Kiss 1 receptor. Saudi Journal of Biomedical Research, 5(8): 236-238

Pavitra, C., Barbara, B. and Tormasz, S. (2020). Embryonic mortality in sheep : A review. Turkish Journal of Veterinary and Animal Science, 44 (2): 167 - 173

Robert, R.M. (1991). Embryonic loss and conceptus interferon production. In Straus, JF, Lytttle CR (EDS), Uterine and embryonic factors iearly prgnancy. New York Plenua Press, 21-31

Vasem, M.P., Nagarajan, N. and Narayanaswamy, S. (2021). Influence of disease causing mutation on protein strcture networks. Frontiers in Moleculer Biosciences,

Vikas, P., Jorge, U., Jose, L., Kymberleigh, A. and Predrag, R. 9 (2020). Inferring the molecular and phenotypic impact of amino acid variants with Mutpred 2. Nature Communications, 11(5918): 1-13