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COMPUTATIONAL ANALYSIS OF FUNCTIONAL EFFECTS OF SINGLE NUCLEOTIDE POLYMORPHISM ON OVINE INTERFERON TAU

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ABSTRACT

The objective of this study was to evaluate the functional effects of Single Nucleotide Polymorphism(SNP) in ovine interferon tau using computational methods. Data on ovine interferon was retrieved from data base of National Center for Biotechnology Information ((GenBank). Functional effects of substitution of Leucin by Proline at position 26 of interferon protein chain was predicted using Protein Variation Effect Analyser, Panther server and Poly phen 2 (Polymorphism phenotyping). 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. It can be concluded that substitution of Leucin by proline at position 26 of the protein sequence of 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 produced 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 so as 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 been implicated as causative factors of pregnancy failure in domestic animals (Kelsey *et al*., 2014). 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 result 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 (GenBank) and subjected to various computational analysis to predict the effects of Single Nucleotide Polymorphism (SNP) in interferon tau.

Predicting effects of Single Nucleotide Polymorphism using Panther

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 analyser 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 were averaged within and across clusters to generate a final Provean score. Provean score equal to or below a predefined threshold indicate a deleterious effect of the amino acid substitution. Provean score above the threshold indicate a neutral effect (Choi and Chan, 2015).

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	Prediction	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.

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.

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. Proteins interact with other biomolecules to perform their functions. Single Nucleotide Polymorphism could lead to changes in protein stability, folding, flexibility and functional sites thereby causing alterations in protein functions (Koukouritake et al.,2014). Changes in protein stability resulting from Single Nucleotide Polymorphism could be due to geometrical constraints, physico chemical effects or disruption of hydrogen bonds Amino acid substitution have significant effects on protein interaction network. Single Nucleotide Polymorphism resulting in amino acid substitution result in significant impact on phenotype by alteration of protein structure. It may exert deleterious effect on structure, function and stability of proteins. It may also disrupt gene regulation leading to adverse effect on cellular integrity (Romasky et al., 2002). The 3 dimensional structure of protein is determined by its amino acid sequence which is related to its function. An alteration in amino acid sequence can result in structural changes in the protein leading to alteration of function (Ung et al., 2006). The connectivity between residues in a protein is defined by the internal protein structural network, structural changes result in variation in connectivity of the elements within the system leading to changes in functional sites (Tan et al., 2019).

CONCLUSION

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. Single Nucleotide Polymorphism on interferon tau could have significant influence on embryo establishment in sheep. 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. Association studies of Single Nucleotide Polymorphism in interferon tau and embryonic mortality is recommended as this will provide better understanding on the potential of interferon tau as a biomarker for reproductive performance in sheep.

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