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Genomic variations in the 2'-5' oligoadenylate synthetase 1 (OAS1) gene in zebu cattle and its crossbreds of Indian origin

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ABSTRACT

In the antiviral host defense mechanisms, the role of mammalian OAS/RNASEL pathway is very significant. These enzymes are interferon-inducible and activated by binding to double-stranded RNA (dsRNA) which are present in virus infected cells. The OAS proteins functions through its receptor, the 2–5Adependent ribonuclease (RNaseL) and activated OAS-RNaseL system degrades viral and cellular RNA and subsequently inhibits protein synthesis. Polymorphisms in the human and equine OAS gene cluster have been previously utilized for case-control analysis of virus-induced disease. But no polymorphisms have yet been identified in the bovine *OAS1* genes for use in similar case-control studies. The promoter and coding regions of the OAS1 gene was amplified and screened for polymorphisms by PCR-SSCP and sequencing in Sahiwal and Frieswal animals. Two SNPs have been identified in the promoter region of OAS1 gene, which have predicted to create/delete sites for transcription factors. Specific amplification of the exonic regions of the OAS1 gene have identified 26 SNPs and one dinucleotide repeats, among them 14 are mis-sense variants. These polymorphisms are the first to be reported in OAS1 gene and will facilitate future case-control studies of cattle susceptibility to infectious diseases.

Key words: Cattle, Genomic variations, OAS1 gene, Polymorphisms, Zebu cattle

Interferons (IFNs) are an important part of the mammalian innate immune system (Stark *et al.* 1998). The resistance to viral infections is conferred by IFNs by regulating the transcription of large number of genes (Der *et al*. 1998). Among them, the 22–52 oligoadenylate synthetases (OAS) are important for the antiviral activity of interferons. They were also reported to be involved in other cellular processes (Justesen *et al*. 2000). These enzymes when activated by double-stranded RNA, oligomerize ATP into 2–5-linked oligoadenylate ranging from dimers up to 30–mers. After binding to a latent endoribonuclease, RNaseL forms dimers and becomes active (Dong *et al.* 1995) which leads to degradation of viral and cellular RNA, and subsequently to a drop in protein synthesis in virus-infected cells (Clemens *et al*. 1978, Baglioni *et al.* 1979 and Zhou *et al.* 1993).

The sequences of most members of the mouse 2–5 A synthetase gene family and all members of the human gene family have been reported previously (Justesen *et al.* 2000, Kakuta *et al*. 2002, Perelygin *et al*. 2002). However, analyses of this gene family in other species have been incomplete or nonexistent. The OAS gene clusters among other mammals are strikingly different from the human and murine clusters. The canine (*Canis familiaris*) cluster of OAS genes resembles attributes of both the human and murine OAS clusters (Perelygin *et al.* 2006). The canine OAS gene family also resembles the murine cluster, containing two OAS-like genes, OASL1 and OASL2. Canine OASL1 encodes a full-length protein containing two C-terminal ubiquitin domains while the OASL2 is a pseudogene. The equine OAS gene cluster was mapped to horse (*Equus caballus*) chromosome 8p15 and shown to have an organization similar to that in the human genome: OAS1-OAS3-OAS2 (Perelygin *et al.* 2005). The equine OAS gene cluster was FISH mapped to equine chromosome ECA8p15 and found to contain single copies of each OAS gene in the same orientation as the human cluster (RPH3A-OAS1-OAS3-OAS2) and a single OASL gene (Perelygin *et al*. 2005, Rios *et al.* 2007). On average, exon lengths are more similar to the human genes than mouse. Furthermore, equine OAS2 is differentially spliced into two transcripts (Perelygin *et al.* 2006). The bovine (Bos taurus) OAS gene cluster most resembles the human gene cluster, although not entirely. The bovine cluster was FISH mapped to

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BTA17q24 telomeric to RPH3A (Perelygin et al. 2005, Perelygin *et al.* 2006). Sequencing of bovine CHORI BAC clone 49:I16 identified three OAS1 genes (OAS1X-OAS1X-OAS1Y) and a single OAS2 gene. Sequencing the intergenic region between the OAS1 genes and OAS2 did not identify a bovine OAS3 gene. Polymorphisms in the human and equine OAS gene cluster have associated for susceptibility to various virus-induced diseases. But no polymorphisms have yet been identified in the bovine OAS1 genes for use in similar case-control studies. The present investigation was carried out to identify the genetic variants in the promoter and exonic regions of OAS1 gene in Bos indicus (Sahiwal) and crossbred cattle (Frieswal) of Indian origin.

MATERIALS AND METHODS

Experimental animals and blood sample collection: The present study was conducted on random sample of 250 cows (168 Frieswal and 82 Sahiwal cattle) maintained at Military Farm, Meerut, India, under similar managmental conditions. The Military Farm, Meerut, Uttar Pradesh is located at an altitude of 224.659 meters above mean sea level on 28° 59' 24" N latitude and 77° 42' 0" E longitude. The climate of the farm is tropical. The temperature rises up to 43°C during summer and comes closer to 2–3°C during winter. The rainfall is about 80 cm to 100 cm per annum and mostly seen in June to October. Blood samples were obtained by jugular venipuncture using sodium heparin (10 IU/ml) as an anticoagulant. Immediately after collection, blood samples were stored in a portable refrigerator at 4°C, transported to the laboratory, and stored at –80°C until DNA extraction.

Genotyping: Genomic DNA was isolated by the phenol chloroform extraction method (Sambrook and Russell 2001) and purity was assessed by spectrophotometry. Samples showing an optical density (OD) ratio (260 nm/280 nm) between 1.7 and 1.9 were used for further analysis while samples outside this range were reprocessed. After checking the quality and quantity of the DNA, it was diluted to the final concentration of 50 ng/µl in water and stored at 4°C. The PCR was carried out on about 50-100 ng of genomic DNA in 25 µl/reaction volume. Nine primers covering the entire promoter and exonic regions were designed on nucleotide sequence of the *Bos taurus* OAS1 gene (ENSBTAT00000039861) using Primer3 (v.0.4.0) software. The primers used for amplification, the size of the amplicon, the region amplified and the annealing temperature are shown in Table 1. The PCR programme was made with the following conditions—initial denaturation at 94°C for 5 min, followed by 35 cycles of 94°C for 30 sec, specific annealing temperature for 30 sec, 72°C for 1 min and a final extension at 72°C for 10 min.

The PCR-SSCP method was used to scan for mutations within the amplified regions. Aliquots (10 µl) of the PCR products were mixed with equal amount of denaturing solution (95% formamide, 25 mM EDTA, 0.025% xylene cyanole, and 0.025% bromophenol blue), heated at 95°C for 5 min and immediately chilled on ice. The denatured DNA was subjected to 10% polyacrylamide gel (acrylamide: bisacrylamide = 29:1) electrophoresis (PAGE) in 1× Tris/ Borate/ EDTA buffer with a constant voltage of 90 V for 16 h at a constant temperature. The gel was stained with 0.1% silver nitrate.

Sequencing and analysis: Representative samples of each PCR-SSCP pattern from each breed were custom sequenced (Sci-genome Pvt. Ltd., Kochi) using the automated ABI DNA sequencer and analyzed by Clustal W multiple alignments using Bio Edit software to identify the SNPs responsible for mobility shift which resulted in different banding patterns.

RESULTS AND DISCUSSION

Characterisation of the promoter region of OAS1 gene: The promoter region of the OAS1 gene was predicted with promoter prediction software (Gene2Promoter; Genomatix), which predicts the genomic context of eukaryotic polymerase II promoter regions with high specificity in mammalian genomic sequences. The sequence containing OAS1 gene and its 52 upstream sequence were used as input for this analysis. The identified region was marked as a true positive as a transcription start site was located within the predicted promoter region. Vertebrate transcription factor binding sites were identified with transcription factor analysis software (MatInspector; Genomatix) (Quandt *et al.* 1995). The 601 bp upstream to the coding sequence was identified as the promoter region,

Table 1. Details of primers with product size and annealing temperature

Targeted region	Sequence	Size of the product	Annealing temp (°C)
Promoter FR1	F-CTGCAAGGACCATAGGAGGCTAR-TAGAATCCCAGATTTACTCCTGCCT	363 bp	65
Promoter FR2	F-CCTGCATCAAGGCAGGAGTAAATR-GGTATTTCTGAGCTCCATCACGG	310 bp	60
Exon 1	F-CTCACAGATTCAGGCAGCAGR-TGCTCACCAGCCTCTCTTCT	280 bp	62
Exon 2	F-GAGGCTCTTCTCAATGAAATGTGTR-GGAGCACTCACCTAGGGCAT	351 bp	68
Exon 3	F-AGCTTGTTGTCTCAGAGGGAR-CCAGTTGGTACCAGTGCTTC	260 bp	61
Exon 4	F-ACAGGCTGAATTTGATCCATGAR-ATGTGGGGAGCTAAGCCTTG	351 bp	56.4
Exon 5	F-CTGGTTGCTTTGCCCTTCCR-TGGAAGGAATGGTCTCTAGCT	329 bp	56
Exon 6 Part 1	F-CCTTTCAGCCCCAAGAACACR-GCACAGAATAGCAGGAAGGC	301 bp	60
Exon 6 FR2	F-GCCTTCCTGCTATTCTGTGCR-TGAGCCAGTGACCAGAACAA	342 bp	59

where the location of TSS was at 501st position.

To cover the entire promoter region, the targeted region was fragmented into two and PCR-SSCP was carried out separately. The PCR-SSCP analysis revealed polymorphism in the second fragment where as the first fragment revealed monomorphic pattern in both Sahiwal and Frieswal cows, indicating that this region of OAS1 gene is highly conserved in indigenous cattle as well as in Holstein crossbreds.

Two SNPs were identified in the second fragment of the promoter region, which include A to T transversion (rs715937117:A>T) and A to G transition (rs480985443: A>G). However, as revealed in the PCR-SSCP analysis, there were no SNPs in the first fragment of promoter region. Further, the effect of these SNPs on the transcription binding factors was studied using bioinformatic tool variant analysis and SNP inspector in genomatix suite. For each SNP allele the transcription factor binding sites either deleted or generated by the nucleotide exchange were determined using the tool. The substitution of A to G in the rs480985443:A>G resulted in the loss of sites for two transcription factor viz. Hepatic nuclear factor 4 alpha, DR1 sites and Liver enriched Cut - Homeodomain transcription factor HNF6 (ONECUT). The same substitution also predicted to create one new site for transcription factor CP2-like 1 (LBP-9). Similarly, the A to T transversion (rs715937117:A>T) resulted in the generation of sites for two transcription factors viz. estrogen-related receptor gamma, homodimer DR4 binding site (family estrogen-related receptors) and thyroid hormone receptor, beta (ER5 - everted repeat, spacer 5) (family RXR heterodimer binding sites). The estrogen related receptor transcription factor has clear role in the embryonic placenta development and is associated with tissues of the embryonic structures. Further confirmation using proteomic studies or gel shift assays are required to identify the role of SNP (rs715937117:A>T) on the immune response and fertility traits in cattle.

Characterisation of the exonic regions of OAS1 gene: The PCR-SSCP analyses of exonic regions of OAS1 gene were performed using seven sets of primers. The 6th exon was splitted into two and analysed as two different fragments using two sets of primers whereas all other exons were amplified using one set of primer. The PCR-SSCP analysis of exon 1, exon 3, exon 4 and second fragment of exon 6 revealed no variation in banding pattern, within breeds as well as between breeds. Representative samples from both breeds of different amplicons were custom sequenced and the sequences of both the breeds were compared with the reference sequence of *Bos taurus* cattle by multiple alignments. The sequences of Frieswal and Sahiwal cows were found to be same as the reference sequence with respect to the exon 1 and its intron boundaries of OAS1, which further confirmed highly conserved nature of the sequences in the targeted region as revealed in the PCR-SSCP results. On sequencing of representative samples from Frieswal and Sahiwal cows and on comparison with the reference sequence of *Bos Taurus,* the targeted region of exon three with its intronic boundaries revealed two variations which include one transition (rs133870661:G>A) and one transversion (rs109660830: A>T). In comparison to the reference population, Sahiwal population was homozygotes for both the mutated alleles whereas the Frieswal population showed heterozygotic nature. Both the SNPs were located in the coding region and were mis-sense mutations. The amino acid changes corresponding to the SNPs rs133870661:G>A and rs109660830:A>T were glutamic acid to lysine and asparagine to tyrosine, respectively. The representative samples of exon four from both the breeds were also sequenced. The sequences were found similar to reference sequence except at one position (rs722802843:G>A) in Sahiwal population. This mutation even if it is present in the coding region, has not resulted in any amino acid change. The second fragment of the 6th exon revealed no variation within the breeds selected for the study by PCR-SSCP analysis. But in comparison to the reference sequence, a 3'UTR variant was found, rs522690593:A>G, in Frieswal population. The variant existed in heterozygotic condition in the population. The Sahiwal cows were homozygous at the mutant sites with G nucleotide and the sequence was same as the reference sequence.

The PCR SSCP analysis with respect to the amplicons of exon 2, exon 5 and first fragment of exon 6 showed different banding patterns and the respective samples from different bands from both breeds were sequenced and SNPs were identified by Clustal W multiple alignments. The PCR-SSCP analysis of OAS1 gene with exon 2 and exon-intron boundaries revealed variation in band pattern within Frieswal cows. On sequence analysis, eleven SNPs were identified in comparison to the reference sequence. This includes already reported six SNPs (rs46239856:C>T, rs483262120:A>G, rs463311564:G>A, rs441920411:A>G, rs384536768:G>A, rs382283230:A>G) and five new SNPs, viz. AY243505.1:c.293C>T, AY243505.1:c.327G>A, AY243505.1:c.483A>G, AY243505.1:c.512C>T and AY243505.1:c.490A>C. Out of these eleven SNPs, sequence analysis of each SSCP variant within the studied population revealed only five SNPs. They were rs46239856:C>T, AY243505.1:c.293C>T, AY243505.1: c.327G>A, rs384536768:G>A and AY243505.1:c.512C>T.

The fragment containing exon 5 of OAS1 gene showed variation in the banding pattern of PCR-SSCP analysis in both the Frieswal and Sahiwal population. On further analysis by sequencing and multiple alignments, six substitutions and one dinucleotide (CT) insertion were detected in the population . The substitutions include four transitions (rs381523356:C>T, rs436825533:A>G, rs718949648:G>A, and rs209393388:G>A) and two transversions (rs109020019:T>A and rs380417419:A>C). The insertion of a CT di-nucloetide (rs378942231 or ENSBTAT00000016856.3:c.885–18_885–17dupCT) was also observed. The transition, rs436825533:A>G, was present only in Sahiwal population, whereas the Frieswal population was similar to reference sequence. Out of six substitutions observed in the population, four SNPs were

located in coding region while others were in intronic region. The dinucleotide insertion is also an intron variant. All the four SNPs were located in the coding region were predicted to cause change in the amino acid in the translated product. The transitions rs436825533:A>G were found to cause amino acid changes from lysine to glutamic acid whereas other two transitions rs718949648:A>G, and rs209393388:G>A were predicted to cause the same amino acid change, from arginine to glutamine. The transversion (rs109020019:T>A) which was reported in the coding region also caused the amino acid change from tyrosine to asparagine.

The first fragment with OAS1 exon 6 and exon-intron boundaries showed polymorphism within the studied population. In the fragment, five SNPs were identified which include four transitions and one transversion. The substitutions observed in the fragment were rs209321868:A>G, rs210168578:C>T, rs135845370:G>A, rs519948624:G>A and rs526257115:C>G. Except the substitution, rs209321868:A>G, all others were 3'UTR variants. The transition rs209321868:A>G, was located in the coding region and predicted to cause an amino acid change from tyrosine to cysteine.

The details of all the SNPs and other polymorphism in OAS1 gene of Sahiwal and Frieswal animals and their effects are summarized in Table 2. SNPs may change the encoded amino acids (non-synonymous) or can be silent (synonymous) or simply occur in the non-coding regions. They may influence promoter activity (gene expression), messenger RNA (mRNA) conformation (stability), and sub-cellular localization of mRNAs and/or proteins and hence may produce disease. Therefore, identification of numerous variations in genes and analysis of their effects may lead to a better understanding of their impact on gene function and health of an individual (Shastry 2009).

Linkage disequilibrium analysis: Characterization of the linkage disequilibrium (LD) structure of candidate gene will help in the effective association studies, especially in the complex diseases. The estimated r^2 values between all the SNPs identified in the Frieswal and Sahiwal population are summarized in Tables 3, 4. In the Frieswal population, the LD measure varied between 0.019 and 1.000, whereas in the Frieswal population, it varied from 0.006 to 1.000. The comparatively higher measures of LD in Frieswal population may be due to the higher selection pressure applied on the population for milk production over the

Table 2. Single nucleotide polymorphisms observed in exonic regions of OAS1 gene in Sahiwal and Frieswal animals

Location	SNPs	Type of variant	Change in amino acid
Exon 2	rs462329856:C>T	Splice region variant Synonymous variant	
	rs483262120:A>G	Mis-sense variant	Glutamic acid to lysine
	rs463311564:G>A	Mis-sense variant	Arginine to glutamine
	rs441920411:A>G	Mis-sense variant	Glutamic acid to valine
	rs384536768:G>A	Mis-sense variant	Arginine to lysine
	rs382283230:A>G	Mis-sense variant	Glutamine to arginine
	AY243505.1:c.293C>T	Synonymous variant	
	AY243505.1:c.327G>A	Synonymous variant	
	AY243505.1:c.483A>G	Mis-sense variant	Asparagine to serine
	AY243505.1:c.512C>T	Synonymous variant	
	AY243505.1:c.490C>A	Mis-sense variant	Alanine to glutamic acid
Exon 3	rs133870661:G>A	Mis-sense variant	Glutamic acid to lysine
	rs109660830:A>T	Mis-sense variant	Asparagine to tyrosine
Exon 4	rs722802843:G>A	Synonymous variant	
Exon 5	ENSBTAT00000016856.3:c.885-18_885-17dupCT	Intron variant	
	rs381523356:C>T	Intron variant	
	rs436825533:A>G	Synonymous variant	Lysine to glutamic acid
	rs109020019:T>A	Mis-sense variant	Tyrosine to asparagine
	rs718949648:G>A	Mis-sense variant	Arginine to glutamine
	rs209393388:G>A	Mis-sense variant	Arginine to glutamine
	rs380417419:A>C	Intron variant	
Exon 6 FR1	rs209321868:A>G	Mis-sense variant	Tyrosine to cysteine
	rs 210168578:C>T	3'UTR variant	
	rs135845370:G>A	3'UTR variant	
	rs519948624:G>A	3'UTR variant	
	rs526257115:C>G	3'UTR variant	
Exon 6 FR 2	rs 522690593:A>G	3'UTR variant	

Table 3. Estimated pairwise r^2 values for the SNPs found in the Frieswal population in the OAS1 gene

	rs715937117:A>T	rs480985443:A>G	rs46239856:C>T	AY243505.1:c.293C>T	AY243505.1:c.327G>A	rs38453676 8:G>A	AY243505.1:c.512C>T	rs38152336:C>T	rs109020019:T>A	rs71894968:G>A	rs20939388:G>A	rs38041741 9:A>C	rs20932186 8:A>G	rs 210168578:C>T	rs13584537 0:G>A	rs51994862 4:G>A	rs526257115:C>G
rs715937117:A>T		0.087	0.344	0.344	0.259	0.259	0.344	0.106	0.052	0.079	0.106	0.090	0.019	0.066	0.197	0.066	0.066
rs480985443:A>G			0.258	0.258	0.214	0.214	0.258	0.526	0.541	0.555	0.526	0.372	0.305	0.550	0.069	0.550	0.550
rs46239856:C>T				1.000	0.649	0.649	1.000	0.183	0.208	0.235	0.183	0.285	0.459	0.188	0.075	0.188	0.188
AY243505.1:c.293C>T					0.649	0.649	1.000	0.183	0.208	0.235	0.183	0.285	0.459	0.188	0.075	0.188	0.188
AY243505.1:c.327G>A						1.000	0.649	0.082	0.287	0.297	0.082	0.276	0.459	0.075	0.045	0.075	0.075
rs384536768:G>A							0.649	0.082	0.287	0.297	0.082	0.276	0.459	0.075	0.045	0.075	0.075
AY243505.1:c.512C>T								0.183	0.208	0.235	0.183	0.285	0.459	0.188	0.075	0.188	0.188
rs381523356:C>T									0.903	0.952	1.000	0.759	0.038	0.164	0.050	0.164	0.164
rs109020019:T>A										0.948	0.903	0.685	0.049	0.149	0.047	0.149	0.149
rs718949648:G>A											0.952	0.722	0.052	0.175	0.051	0.175	0.175
rs209393388:G>A												0.759	0.038	0.164	0.050	0.164	0.164
rs380417419:A>C													0.047	0.070	0.031	0.070	0.070
rs209321868:A>G														0.404	0.439	0.404	0.404
rs 210168578:C>T															0.196	1.000	1.000
rs135845370:G>A																0.196	1.000
rs519948624:G>A																	1.000

Table 4. Estimated pairwise r^2values for the SNPs found in the Sahiwal population in the OAS1 gene

	rs71593711 7:A>T	rs48098544 3:A>G	rs38152335 6:C>T	rs43682553 3:A>G	rs10902001 9:T>A	rs71894964 8:G>A	rs20939338 8:G>A	rs38041741 9:A>C	rs20932186 8:A>G	rs 21016857 8:C>T	rs13584537 0:G>A	rs51994862 4:G>A	rs52625711 5:C>G
rs715937117:A>T		0.167	0.145	0.092	0.151	0.157	0.125	0.221	0.056	0.006	0.261	0.008	0.008
rs480985443:A>G			0.251	0.112	0.172	0.225	0.216	0.025	0.014	0.085	0.133	0.043	0.043
rs381523356:C>T				0.027	0.834	0.886	0.937	0.456	0.028	0.318	0.246	0.348	0.348
rs436825533:A>G					0.046	0.007	0.034	0.402	0.011	0.008	0.050	0.045	0.045
rs109020019:T>A						0.955	0.915	0.445	0.099	0.332	0.173	0.371	0.371
rs718949648:G>A							0.958	0.466	0.039	0.305	0.213	0.341	0.341
rs209393388:G>A								0.487	0.016	0.279	0.248	0.312	0.312
rs380417419:A>C									0.035	0.149	0.124	0.167	0.167
rs209321868:A>G										0.483	0.564	0.547	0.547
rs210168578:C>T											0.329	0.882	0.882
rs135845370:G>A												0.373	0.373
rs519948624:G>A													1.000

generations.

The innate immune response confers host resistance by the recognition and limitation of viral infection and replication. The interferon inducible anti-viral 2–5 oligoadenylate synthetase (OAS) enzyme is part of the cellular innate immune response (Baglioni *et al.* 1979), which is induced by Interferon (IFN), a most powerful antiviral cytokine. The oligoadenylate synthase (OAS) proteins have been identified as enzymes that sense exogenous nucleic acid and initiate antiviral pathways. The precise molecular mechanism by which the OAS1 degrades viral and cellular RNA is well explained and it initiates with stimulation of OAS to catalyze the polymerization of ATP to form 2'-5'-linked oligomers of adenylate (2–5As) by a pathogen-associated molecular pattern (PAMPs) such as dsRNA or mRNA (Yaffe *et al.* 1996, Malathi *et al.* 2008). Further 2–5 A functions through its receptor, the 2–5Adependent ribonuclease (RNaseL), that dimerizes into its catalytically active form upon binding 2–5A (Zhou *et al.* 1993, Malathi *et al.* 2008) and activated OAS-RNaseL system degrades viral and cellular RNA and subsequently inhibits protein synthesis (Nilsen *et al.* 1981). It was also proved that OAS-RNaseL system triggers apoptosis via mitochondrial pathway (Mullan *et al.* 2005 and Domingo-Gil *et al.* 2006). It is also known that OAS silencing attenuates interferon induced anti-proliferative and antiviral signaling and stimulates anchorage independent cell growth (Yaffe *et al.* 1996). The exogenous recombinant porcine OAS1 exhibits broad-spectrum antiviral activity through the activation of the IFN system that is independent of RNaseL (Kristiansen *et al.* 2010). The enzyme that comprise the 2,5, oligoadenylate synthetase family (OAS) may play additional roles in the control of cellular growth and differentiation (Johnson *et al.* 2001).

Single nucleotide polymorphisms in OAS1 gene are associated with wide variety of health related disorders such as hepatitis C infection (Knapp *et al.* 2003 and Li *et al.* 2009), West Nile virus infection (Yakub *et al.* 2005), SARS (Hamano *et al.* 2005), Type1 diabetes (Field *et al.* 2005), multiple sclerosis (Fedetz *et al.* 2006) and prostate cancer (Mandal *et al.* 2011). Further OAS is identified as a useful biomarker for various diseases in multiple stages due to the upregulation of OAS family whether it is dependent or independent of IFN stimuli, which include autoimmune diseases and chronic infections, including systemic lupus erythematosus, systemic sclerosis, rheumatoid arthritis and multiple sclerosis (Preble *et al.* 1983, Hertzog *et al.* 1988, Croz 2010, Almeida *et al.* 2014). The OAS1 polymorphisms were also associated with susceptibility to West Nile Encephalitis in horses (Rios *et al.* 2010).

No reports are available on genetic variability in the promoter and coding regions of OAS1 gene in *Bos taurus* and *Bos indicus*. Therefore, characterization of this gene may contribute to better understand the immune response in cattle, especially to various viral infections.

This study characterized the promoter and exonic regions of the OAS1 gene in cattle. Polymorphisms were detected

in the regions studied in both indigenous and crossbred cattle, indicating variability of the loci analysed. Some of the SNPs identified cause amino acid substitutions and would be candidates for association studies with immune response.

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