

## RESEARCH HIGHLIGHT

# Melatonin Receptor 1A (MTNR1A) gene sequence characterization and SNP identification in Tropical sheep breeds of India

Vijay Kumar Saxena<sup>1</sup>, Bipul K Jha<sup>1</sup>, Amar Singh Meena<sup>2</sup>, Harvinder K Narula<sup>3</sup>, Davendra Kumar<sup>1</sup>, S.M.K Naqvi<sup>1</sup>

<sup>1</sup>Molecular Physiology Laboratory, Division of Physiology and Biochemistry, Central Sheep and Wool Research Institute, Avikanagar, Rajasthan 304501, India

<sup>2</sup>Division of Animal Biotechnology, Central Sheep and Wool Research Institute, Avikanagar, Tonk, Rajasthan 304501, India

<sup>3</sup>Arid Region Campus, Central Sheep and Wool Research Institute, Bikaner, Rajasthan 334006, India

Correspondence: Vijay Kumar Saxena

E-mail: [drvijaysaxena@gmail.com](mailto:drvijaysaxena@gmail.com)

Received: March 18, 2015

Published online: May 13, 2015

**Sheep is considered to be short day seasonal breeder. Sheep does show varying behavior in terms of seasonal reproduction between temperate and tropical latitudinal regions. MTNR1A gene has been studied widely for being linked to seasonality in sheep. Recently, through our studies we have characterized the MTNR1A gene in Tropical arid sheep breeds and could find out that the GG and CC genotypes are having higher prevalence in the tropical arid breed population with reference to two SNP markers 'G612A' and 'C606T' respectively.**

**To cite this article:** Vijay Kumar Saxena, et al. Melatonin Receptor 1A (MTNR1A) gene sequence characterization and SNP identification in Tropical sheep breeds of India. *Receptor Clin Invest* 2015; 2: e731. doi: 10.14800/rci.731.

Melatonin is an important hormone secreted by pineal gland and it functions as the prime sensor of the neuroendocrine system for the photoperiodic environmental cues. Sheep in temperate latitudes still continue to display significant seasonal reproductive behavior, although sheep breeds of tropical climatic regimes are considered largely aseasonal or intermittently polyestrous [1]. It is the phenomenon of photoperiodism which drives their reproductive cycle comprising of a season of high sexual activity during short days (increasing dark period) and an anestrus season or a period of atypical sexual activity that occurs during long days (decreasing dark period). The mechanism of action of melatonin in regulating seasonal reproductive behavior is still a major question striking all of us with a full might. It may be due to temporal seasonal variation in expression of the receptors of melatonin in pars tuberalis, where the maximum numbers of MTNR1A receptors are present. It may also be due to change in the affinity of binding of melatonin due to progressive sequence

differences or its differential regulation may be influenced by the epigenetic or gene interaction mechanisms. Domestication of animals pruned this inherited trait, as the animals are being selected for increased production, been provided with advanced husbandry practices including proper shelter management. Unlike most domestic livestock species, sheep are widely known to display marked seasonality in their breeding activity. Important question which is to be addressed is ascertaining those factors which are responsible for difference in seasonal reproductive behavior among the temperate and tropical sheep breeds. Melatonin receptor 1A (MTNR1A), a high-affinity melatonin receptor is G-coupled protein type receptor and it has been supposed to be a candidate gene for influencing seasonality in sheep. Melatonin receptor gene (MTNR1A) sequence consists of two exons (Exon I and Exon II) spanned by an intron [2] and its Exon II which is responsible for coding a majority portion of the receptor. Several studies of this gene in different animal species have found relationships with

seasonal reproduction activity<sup>[3,4]</sup>. Two SNP markers in the sheep MTNR1A gene at positions 606 and 612 of exon II have been found to be associated with seasonal reproduction. Association studies conducted in sheep breeds of different regions like Merino d'arles<sup>[4]</sup>, Small tail Han sheep<sup>[5]</sup>, Awasi<sup>[6]</sup>, Sarda<sup>[7]</sup>, Dorset<sup>[8]</sup> have found association of the 'G612A' and 'C606T' SNPs with seasonal reproduction status of animals. We in our recent study, have tried to find the genetic variability in the tropical arid breeds (Magra and Marwari), which are mostly aseasonal in their breeding activity and to study comparative prevalence of above two important SNPs G606C and C612A in them. The major purpose of the study was to have a comparative account in terms of sequential genetic variability in the MTNR1A gene in tropical arid sheep breeds vis-à-vis temperate sheep breeds, which do demonstrate significant seasonal reproductive behavior. We have characterized the melatonin receptor gene of the Tropical arid sheep breeds (Magra, Marwari and Chokla) and submitted sequences to the NCBI database. We have also found that the C606T and G612A SNP markers are present in tropical sheep breeds but with a significantly lower minor allele frequency in comparison to what have been demonstrated in temperate sheep breeds by several authors. GG and CC genotypes are dominantly prevalent in the tropical arid breed population<sup>[9]</sup>. We could also notice that there are few unique SNPs in the tropical arid sheep breeds. We could identify a unique conformational destabilizing mutation G931C in Chokla sheep breed which was acting as kink in the helical structure of G-coupled receptor owing to substitution of alanine by proline. Polyphen-2 analysis was performed to assess the potentiality of this mutation in terms of its ability to effect the conformation of the receptor, and the mutation was found to be potentially damaging<sup>[10]</sup>. Two other non-synonymous mutations (G706A, C893A) were observed in Chokla sheep breed. G706A lead to substitution of valine by isoleucine Val125I (U14109) in the fifth transmembrane domain. C893A leads to substitution of alanine by aspartic acid in the third extracellular loop. We have noticed that the two important SNPs C426T and G555A were observed in temperate sheep breeds and they were absent in Chokla, Magra and Marwari breeds of sheep<sup>[9,10]</sup>. Thus, distinctive SNPs pattern has been observed between these tropical and temperate sheep breed but it will be too early to link them clearly with the differential reproductive behavior manifested by them.

### Conflicting interests

The authors have declared that no competing interests exist.

### Acknowledgements

The research is funded by Department of Biotechnology, Government of India (Grant/Project No.BT/PR14462/AAQ/01/442/2010).

### References

1. Rosa HJD, Bryant MJ. Seasonality of reproduction in sheep. *Small Ruminant Research* 2003; 48:155-171.
2. Reppert SM, Weaver DR, Ebisawa T. Cloning and characterization of a mammalian melatonin receptor that mediates reproductive and circadian responses. *Neuron* 1994;13:1177-1185.
3. Carcangiu V, Mura MC, Pazzola M, Vacca GM, Paludo M, Marchi B, et al. Characterization of the Mediterranean Italian buffaloes melatonin receptor 1A (MTNR1A) gene and its association with reproductive seasonality. *Theriogenology* 2011; 76, 419-426.
4. Pelletier J, Bodin L, Hanocq E, Malpoux B, Teyssier J, Thimonier J, et al. Association between expression of reproductive seasonality and alleles of the gene for Mel(1a) receptor in the ewe. *Biol Reprod* 2000; 62:1096-1101.
5. Chu MX, Cheng DX, Liu WZ, Fang L, Ye SC. Association between Melatonin Receptor 1A Gene and Expression of Reproductive Seasonality in Sheep. *J Anim Sci* 2006;19:1079-2084.
6. Faigl V, Arnyasi M, Keresztes M, Kulcsar M, Reiczigel J, Danko G, et al. Seasonality of reproduction and MT1 receptor gene polymorphism in Awassi sheep. *Reprod Domest Anim* 2008;43:11.
7. Mateescu RG, Lunsford AK, Thonney ML. Association between melatonin receptor 1A gene polymorphism and reproductive performance in Dorset ewes. *J Anim Sci* 2009;87: 2485-2488.
8. Carcangiu V, Mura MC, Vacca GM, Pazzola M, Dettori ML, Luridiana S, et al. Polymorphism of the melatonin receptor MTNR1A gene and its relationship with seasonal reproductive activity in the Sarda sheep breed. *Anim Reprod Sci* 2009;116:65-72.
9. Saxena VK, Jha BK, Meena AS, Narula H.K, Kumar D, Naqvi SMK. Assessment of genetic variability in the coding sequence of Melatonin receptor gene (MTNR1A) in Tropical Arid sheep breeds of India. *Reproduction in Domestic Animals* 2015; doi: 10.1111/rda.12503.
10. Saxena VK, Jha BK, Meena AS, Naqvi SMK. Sequence analysis and identification of new variations in the coding sequence of melatonin receptor gene (MTNR1A) of Indian Chokla sheep breed. *Meta Gene* 2014; 2:450-458.