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## The biological clock genes in farm animals: A Scoping review

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### Abstract

The biological clock is a 24-hour cycle that is influenced by light and darkness, which are key factors in determining whether one feels alert or sleepy. Typically, the biological clock regulates how the body works. It is a system that is heavily utilized during the evolution of living things in order to help them adapt to the cyclic succession of their environment. For instance, metabolic processes coordinated with the circadian clock enable animals to ramp up feeding-related functions and adapt to changes in day-night length. The circadian rhythm is crucial in mediating the timing of seasonal breeding and other annual physiological fluctuations that are controlled by length, in addition to ambient light and food accessibility. Today, in the field of livestock, where we purposefully manipulate the photoperiod for production and management, this is crucial. However, the effects on the environment and the health of animals are frequently disregarded. The circadian clock is based on a group of transcriptional regulators that interact with one another in negative feedback loops and is present in almost all animal cell types. The suprachiasmatic nucleus, which functions as the body's internal clock, primarily regulates the physiological rhythm. SCN, or suprachiasmatic nucleus by continuing to cycle through periods of activity, rest, feeding, and fasting despite the absence of light. Many genes work together to accomplish this. One of the genes that produce proteins that can reversibly suppress the stimulation of the transcription of the Clock and BMAL1 genes in mammals is the cryptochrome (PER) gene (CRY). These play a crucial role in maintaining the circadian rhythm of mammals and enable the cycle to restart when the procedures are changed. While Jane studies retinoic acid receptor-related orphan receptors (RORs), Per and CRY REV-ERBs (REV-ERB) control BMAL1 gene transcription by controlling the BMAL1 gene's transcription. These genes work together to control mammals' biological clocks.

**Keywords:** Biological clock genes, melatonin, ARNTL, NR1D1 gene

### 1. Introduction

#### 1.1 Melatonin's function in regulating the circadian clock

Melatonin secretion is a key hormonal marker of seasonal physiological changes and shifts in day length in cattle. It represents a photoperiodic signal that the brain receives internally and then reflects outward. (Wagner *et al.* 2008) [21]. Sheep are more susceptible to circadian hormone signals, especially melatonin, than other mammals because they breed seasonally (Piccione, *et al.* 2005) [13]. It generates enduring signals during coordination in the winter and ephemeral signals during coordination in the summer, resulting in seasonal variations of circadian physiology. It's interesting to note that young neonates don't secrete melatonin like lambs do, suggesting that the normal melatonin rhythm takes time to develop in various animal species. (Dupré *et al.* 2007) [5]. We propose that it is crucial to understand the roles and regular alterations of the aforementioned hormones in native species. More importantly, a deeper comprehension of the molecular processes underlying regular gene expression and the interplay between these intricate hormonal signals will advance our understanding and inspire the development of fresh targets and management tactics for livestock.

#### 1.2 gene (ARNTL (BMAL)

Gene (ARNTL (BMAL) is thought to be photosensitive to long-term photosensitization with or without melatonin in sheep, where it reduces brown adipose tissue in newborns. (Seron-Ferre, *et al.* 2015) [15].

Depending on the circumstances, it reaches its peak during either a long or short day. This gene reproduces more quickly and 2.5 hours earlier when photoperiods alternate quickly than when they do so slowly (Varcoe *et al.* 2014)<sup>[20]</sup>. In contrast, this gene causes the secretion of prostaglandins to increase in cows. (Isayama *et al.* 2014)<sup>[7]</sup>. Prostaglandins are produced through a chemical reaction in the same location as where they are needed, unlike hormones that are secreted from glands in the body and travel through the blood to other parts. An example of this is their formation in tissues that have been injured and are oozing blood to support the process of clotting and inflammation in that. The precise location within the body that is fixed and does not move. (Isayama *et al.* 2014)<sup>[7]</sup>.

### 1.3 CRY1 gene

A circadian gene whose expression is elevated at night or connected to a higher level of melatonin (Wagner *et al.* 2008)<sup>[21]</sup>.

### 1.4 Gene PER1

The biological clock gene that increases prolactin secretion is one of the biological clock's genes. The morning is when it reaches its peak in terms of gene expression after nighttime increases (Johnston *et al.* 2004)<sup>[8]</sup>.

**1.5 PER2 gene:** Young newborns with a particular circadian clock gene have less brown adipose tissue (Seron-Ferre *et al.* 2015)<sup>[15]</sup>. Its presence is correlated with insulin and glucose levels in blood plasma (Varcoe *et al.* 2014)<sup>[20]</sup>. Additionally, it falls off during long days or when the blood plasma contains high levels of the hormone melatonin (Lincoln *et al.* 2002)<sup>[9]</sup>.

### 1.6 NR1D1 gene

An increase in melatonin levels in the blood works to inhibit the reproduction of this gene, which is one of the circadian clock genes and has a connection to melatonin secretion (Varcoe *et al.* 2014)<sup>[20]</sup>.

### 1.7 Gene Clock

One of the biological clock genes works to increase estradiol while decreasing blood glucose and insulin levels (Shimizu *et al.*, 2011)<sup>[17]</sup>.

### 1.8 Daily organization of seasonal activity

In the management of seasonal activity on a daily basis in many tissues, metabolic adaptations are closely related to the regulation and rhythm of circadian clock genes. They also regulate the transcription of crucial genes in the liver, adipose tissue, and gonads (Hu, *et al.* 2017, Adamovich, *et al.* 2014, Xie *et al.* 2020<sup>[6, 1, 22]</sup>). The smooth transition from pregnancy to lactation in dairy cows is largely influenced by circadian physiology.

While it also has an impact on nutrition due to nocturnal variations and its impact on metabolism. According to (Cardoso *et al.* 2017)<sup>[2]</sup>, these genes have an impact on lipid synthesis, uptake, transport, storage, and catabolism.

**1.9 Expression of circadian genes and related physiological processes in sheep:** All ruminants, including sheep and goats, engage in seasonal breeding (Shinomiya *et al.* 2014)<sup>[18]</sup>. They are known as short-day (SD) animals because they breed in the fall. In contrast, a reduction in the

number of nighttime hours, such as during the summer, has a significant impact on how long day (LD) animals react (Shinomiya, *et al.* 2014)<sup>[18]</sup>. Waveforms of SCN gene expression were seen in the SD breeding sheep when they were exposed to a long photoperiod of more than 16 hours of light, just like in LD animals. As a result, the clock genes PER1, PER2, and FBX121 had high levels of expression, similar to what was observed in long-day animals (Dardente *et al.* 2016)<sup>[4]</sup>. Through the acclimatization of Soay sheep to LD photoperiods, studies revealed that Soay sheep exposed to a long lighting period had a significant impact on estrus activity (Wagner *et al.* 2008)<sup>[21]</sup>. Additionally, it was discovered that the kisspeptin gene (KISS-1), which is extremely important for sheep sexual activity, is encoded in the hypothalamus region of sheep. 8 hours of darkness and 16 hours of light have an impact on this gene (Johnston *et al.* 2004)<sup>[8]</sup>. While prolactin secretion is increased 4-5 times in response to 16 hours of light compared to prolactin secretion in SD animals, plasma melatonin rhythms are seen to be in sync with various light/dark cycles (Wagner *et al.* 2008)<sup>[21]</sup>.

(PER1) and neuroendocrine (TSH) output in PT, as well as the expression of the kisspeptin gene in the hypothalamic arcuate nucleus (Wagner *et al.*; 2008)<sup>[21]</sup>. Another study on sheep found that the central nervous system suffers when the photoperiod changes quickly (for example, the expression of the melatonin gene and peripheral rhythm, which disrupt Glucose balance in sheep blood and impact sexual activity (e.g., gene expressions of circadian clock genes in skeletal muscle), (Varcoe *et al.* 2014)<sup>[20]</sup>. A rapidly varying photoperiod environment with the peak occurring during the day and the lowest point at dawn appears to cause a decrease in blood sugar levels. According to the timing of seasonal shifts along the hypothalamic-pituitary-gonad pathway, this may reflect an adaptive sheep mechanism. Another study on sheep found that the central nervous system suffers when the photoperiod changes quickly (for example, the expression of the melatonin gene and peripheral rhythm, which disrupt Glucose balance in sheep blood and impact sexual activity (Varcoe *et al.* 2014)<sup>[20]</sup>, (e.g., gene expressions of circadian clock genes in skeletal muscle). A rapidly varying photoperiod environment with the peak occurring during the day and the lowest point at dawn appears to cause a decrease in blood sugar levels. According to the timing of seasonal shifts along the hypothalamic-pituitary-gonad pathway, this may reflect an adaptive sheep mechanism. Indeed, a variety of physiological processes in sheep exhibit diurnal variations. For instance, the liver collagen concentration exhibits a strong diurnal rhythm, rising from dawn to dusk (at most 14 hours after illumination), and falling at night. The lowest level of plasma leptin is reached 12 hours later (4 hours before the lights are on), while the peak is reached in the middle of the photoperiod (8 hours after the lights are on). (Chakir, *et al.* 2015)<sup>[23]</sup>. Additionally, the ewes' motor activity peaks at noon and troughs at noon and 8 p.m.; it is inversely correlated with melatonin secretion, plasma glucose level, and body temperature.

## 2. Conclusion and Future Directions

1. Genes whose protein products are necessary for the creation and regulation of circadian rhythms are referred to as essential circadian genes. Both mammals and other living things contain it.

2. The manifestation of endogenous circadian rhythm in behaviour and physiology is caused by the rhythmic expression of circadian genes in neurons of the suprachiasmatic nucleus SCN.
3. Tiny nuclei in the centre of the brain control circadian rhythms. SCN stands for suprachiasmatic nuclei. The cores serve as command posts. The daily "clock" seems to be set primarily by light.
4. These genes have a significant impact on reproductive and reproductive traits in farm animals, which are traits that increase productivity.

**3. Conflict of Interest:** Not available

**4. Financial Support:** Not available

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