

# Circadian Genes and Economic Traits in Livestock Animals

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## Abstract

Circadian rhythms are oscillators of endogenous autonomic activity in all living organisms and regulate economic traits such as reproduction, milk characteristics and growth performance in farm animals. These rhythms are directly or indirectly controlled by the circadian clock in a 24-hour cycle. It has evolved as an adaptive system for living organisms in a cyclical natural environment. A regular circadian rhythm can be associated with good health, well-being, strong immunity, and high economic characteristics. The interaction between circadian rhythmicity and the physiology of farm animals is becoming an important focus of animal science. Understanding the circadian genes (*CLOCK*, *BMAL*, *PER1*, *PER2*, *CRY1*, *CRY2*) and actions regulating circadian oscillation in farm animals is important to improve management and increase economic traits. The study aimed to summarise the research on the effects of circadian rhythm genes on productivity and to highlight the importance of this topic.

## Introduction

Circadian rhythms are vital to the existence of all life forms, directing sleep/wake cycles and metabolic processes (Rhodes *et al.*, 2022). In mammals, the primary internal clock is located in the hypothalamic suprachiasmatic nucleus (SCN). The circadian rhythms of mammals are primarily synchronized with the natural light-dark cycle (Takahashi *et al.*, 2008). Circadian mechanisms are essential for regulating the timing of daily processes and annual physiological and behavioral variations that are controlled and synchronized by day length (Li *et al.*, 2021). Key clock genes driving circadian rhythms consist of positive and negative components that together form an autoregulatory feedback loop (Plaut and Casey, 2012). Circadian rhythms operate at the post-transcriptional and post-translational levels, but the clock still requires high-quality translation to function properly (Ferreira and Takahashi, 2019). Fundamental clock genes are well preserved across

mammalian species. In their study of 11 circadian genes, Derdante *et al.* (2009) found that 10 of these clock genes are highly conserved in sheep compared to other animals. Brain and Muscle ARNT-Like 1 (*BMAL1*), Circadian Locomotor Output Cycle Kaput Protein Hood (*CLOCK*) and Neuronal PAS Domain Protein 2 (*NPAS2*) genes regulate positive circadian rhythm control, whereas the Period (*Per*) and Cryptochrome (*Cry*) genes are involved in negative control (Plaut and Casey, 2012). The circadian timing system in livestock is hierarchically organized and comprises central and peripheral clocks. The master clock directs and synchronizes the peripheral clocks in every tissue of the body. This indicates that each tissue has its clock, and the circadian expression of tissue-specific transcriptomes near to them assists in the digestion system and physiology of the organism (Trujillo and Casey, 2016).

## Economic Treat Related Circadian Studies in Livestock

Studies have focused on investigating the effect of circadian rhythm genes on animal performance, primarily those related to ovarian activity, milk yield and reproduction. Many functional activities in farm animals, such as reproduction, are closely related to circadian rhythm. Many studies in male and female animals have shown that circadian rhythm is a regulator of reproductive biology (Han *et al.*, 2021). In cattle and mammals, the estrus cycle, LH levels, ovulation, production, sperm maturation, fertilization, artificial insemination, and litter size have also been reported to be related to circadian clock activity (Han *et al.*, 2021). However, any disruption in circadian rhythm has been reported to have negative effects on the ovulation cycle, fertility rate, miscarriage rates and fetal development (Gotlieb, 2020). Long-term effects of circadian rhythm disruption include both physical and mental health. These effects are even recognized as triggers of diseases such as cancer and depression. In animals, disruption of the circadian rhythm increases the effects of disease and stress, while stress and disease also disrupt the circadian rhythm, creating a vicious negative cycle (Wagner *et al.*, 2021).

## Estrus Cycle-Ovulation Studies

Reproductive cycles in many animal species are seasonally regulated in a daylight-dependent manner. Murphy *et al.* (2015) have demonstrated that sheep ovaries exhibit rhythmic expression of molecular clock genes (*Clock*, *ARNT1*, *CRY1*, *CRY2*, *PER1*, *PER2*). Consequently, ovarian tissue, like peripheral tissue, has a time-sensitive function and a reproductive clock cycle. The researchers analyzed the genetic factors that affect the rate of ovulation and litter size in ewes. It was noted that specific single gene mutations can impact these parameters, and it may be crucial to extensively identify these mutations, including period genes, to compare their reproductive effects across seasons. However, there is a dearth of comprehensive research on this topic, as observed by Notter (2008). Furthermore, the location of timer cells responsible for seasonal control of the gonadal axis is not thought to be in the pituitary gland in the brain. The evidence suggests that reproduction is seasonally controlled by light and melatonin activity. However, the subsequent regulation occurs through rhythmic circadian genes expressed in tissues instead of the suprachiasmatic nucleus. Long-term regulation of these genes also controls appetite, food intake, and body weight in sheep, with the *Per/Cry* complex being especially potent (Lincoln *et al.*, 2003). Circadian regulation is closely linked to metabolism (Takahashi, 2017). Han *et al.* (2021) examined the possible involvement of *BMAL1*, *PER1-2*, and *CRY1-2* genes in the ovine ovarian tissue clock between the luteal and follicular phases. They found that these genes are differently expressed in various phases of

reproductive and non-reproductive tissues, demonstrating that the estrus cycle affects clock gene expression.

## Mammary Gland and Milk Yield Studies

Lactation is a physiological process subject to numerous factors and is crucial for milk production in animals bred for this purpose. Mammary tissue expresses vital clock genes (*BMAL1* and *CLOCK*), and their role in mammary gland development and lactation is currently under investigation. The expression of fundamental circadian clock genes has varied significantly across several lactation stages within the mammary gland, as shown by a study conducted by Casey *et al.* (2014). Transcriptome analysis revealed that 7% of genes communicated within the lactating tissue display circadian rhythms, based on research conducted by Maningat *et al.* (2009). Key circadian clock genes contribute to cell improvement, development, and multiplication, apoptosis and intracellular signaling cascade, as demonstrated by Trujillo and Casey (2016). The mammary clock also regulates the expression of genes responsible for milk synthesis, milk fat and lactose (Casey *et al.*, 2014).

Chronic exposure of non-pregnant, non-lactating dairy animals to day-night shifts during late pregnancy had a detrimental effect on circadian rhythms, insulin and glucose homeostasis, and negatively affected udder development. Introduction of pregnant dairy cattle to day-night stage shifts for 14 days led to changes in the liver and mammary transcriptomes. Chronic disruption of the circadian rhythm can have negative implications for the well-being, welfare, and milk production capacity of cattle. Analysis of the transcript profile of udder tissue suggests that circadian disruption reduces udder remodeling and lipid transport, and adversely affects liver lipid metabolism (Casey *et al.*, 2021).

## Conclusion

Circadian rhythm is closely related to biological rhythms in animal production, which play a crucial role in traits like lactation yield, reproduction, and ovulation. The above summary depicts the relationship between circadian rhythm genes and yield traits in biologically rhythmic animals. The association of these genes with yield traits in seasonally rhythmic animals is apparent but requires further in-depth research to clarify.

## Author Contributions

First Author: Conceptualization, Writing -review and editing; Second Author: Investigation, Visualization and Writing -original draft.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article. We

have no financial or personal relationships with individuals or organizations that could inappropriately influence our work. Furthermore, we confirm that the content presented in this manuscript is original and has not been previously published elsewhere.

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