



Cry me a werewolf: the molecular synchronization of werewolf transformation to the circalunar cycles.

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*When the night has come
And the land is dark
And the moon is the only light we'll see
The werewolf will morph
under the full moon
And someone will be doomed!*

Werewolves are humans who unwillingly transform into monstrous wolves that howl at the full moon and devour livestock and other humans. Despite its popularity in European folklore, scholars cannot agree on one cause of lycanthropy. Some argue that werewolves are cursed humans that had made a pact with the Devil, some that they are “Hounds of God” sent to protect humankind²; others argue that they are humans that are bitten and infected by another werewolf, and there are still others that argue that they inherited lycanthropy from their family. Whether werewolves are “made” or “born”, they all have something in common: they transform under the light of a full moon. The human-to-werewolf morphosis under moonlight suggests that werewolves are synchronised to the circalunar cycle, which is the 29.5 days that the moon requires to complete one orbit around Earth. But how could a werewolf unconsciously sense changes under the moonlight and synchronise their canine morphosis to the full moon?

The circalunar cycle has a significant impact on the natural world. At some level, circalunar cycle also affects humans. In fact, emerging evidence unveils a possible effect of moon cycle on various aspects of human health, suggesting possible influence of the circalunar cycle on some humans’ features^{4,5,6}. During the circalunar cycle, changes in the moon-Sun-Earth positional axis trigger various environmental fluctuations, such as moonlight intensity³. Together with circadian cycles (24 hours), various organisms use the circalunar moonlight changes to synchronise their behaviour to the

lunar month, in particular behaviors such as mating and sexual maturation. As various biological systems synchronise to the circalunar cycle for mating purposes, it is arguable that werewolves also synchronise their canine morphosis to the circalunar cycle to find and to mate with other co-species, and use the moonlight changes as an environmental cue. If organisms are able to entrain their molecular clock to the circalunar cycle, it is only plausible that there needs to be a molecular component that is able to distinguish moonlight changes during the lunar month. Cryptochrome (CRY) is a core molecular clock component that has been suggested as a possible synchronizer of the molecular clock to moon cycles in marine animals, as it is not only able to distinguish between solar and lunar light, but also between changes in moonlight intensity during the lunar month⁷. However, this is not the case for humans and other mammals, whose CRYs are transcriptional repressors in the core molecular clock, and they are not light receptors as in other non-mammalian vertebrates and invertebrates⁸. Therefore, it is possible that werewolves preserved an additional CRY variant that is photosensitive and specifically modulates the circalunar synchronisation of lycanthropic morphosis.

During nights of full moon, werewolves undergo a fast growth of muscles, bones, skin, fur, claws and teeth that is quickly reversed at sunrise. If CRY is a molecular synchronizer for werewolf morphosis, it should also directly or indirectly be involved in modulating those phenotypical changes. Although focusing only on human hair, recent studies suggested that photo-activation of CRY promotes keratinocytes' growth⁹, the main component of hair, skin, and nails. Furthermore, cry seems to foster the circadian differentiation and regeneration of myogenic stem cells¹⁰, which mediate adult muscular regeneration, and osteogenesis¹¹. As CRY is involved in those pathways in humans, it is possible that werewolves' CRY variant might also foster an abnormally fast growth of keratinocytes, myogenic regeneration and osteogenesis through similar pathways under the full moon.

In conclusion, lycanthropy is unlikely the result of a curse or a disease, but it is rather due to a photo-sensitive variant of the molecular clock component CRY, preserved only in werewolves' descendants. This CRY variant might have an evolutionary benefit for werewolves, as it is possible that allows them to transform only under the full moon, consequently allowing them to recognise and mate with other werewolves. Therefore, if you meet two werewolves in the woods under full moon, think before shooting them with a silver bullet: they might just be having their first date!

References

- ¹ Adapted from the song "Stand by me" by Ben E. King (1962).
- ² Donecker, S. (2012). The Werewolves of Livonia: Lycanthropy and Shape-Changing in Scholarly Texts, 1550–1720 *Preternature: Critical and Historical Studies on the Preternatural*, 1(2), 289-322, doi: <https://doi.org/10.5325/preternature.1.2.0289>.
- ³ Raible, F., Takekata, H., & Tessmar-Raible, K. (2017). An Overview of Monthly Rhythms and Clocks. *Frontiers in neurology*, 8, 189. <https://doi.org/10.3389/fneur.2017.00189>.
- ⁴ Casiraghi, L. et al (2021). Moonstruck sleep: synchronization of human sleep with the moon cycle under field conditions. *Sci Adv.* 7. <https://doi.org/10.1126/sciadv.abe0465>.
- ⁵ Helfrich-Forster, C. et al. (2021). Women temporarily synchronize their menstrual cycles with the luminance and gravimetric cycles of the Moon. *Sci Adv.* 7. <https://doi.org/10.1126/sciadv.abe1358>.
- ⁶ Wehl, T.A. (2018). Bipolar mood cycles associated with lunar entrainment of a circadian rhythm. *Transl Psychiatry* 8, 151 (2018). doi: <https://doi.org/10.1038/s41398-018-0203-x>.
- ⁷ Poehn, B. et al. (2022). A Cryptochrome adopts distinct moon- and sunlight states and functions as sun- versus moonlight interpreter in monthly oscillator entrainment, *Nature Communications*, 13(5220). DOI: 10.1038/s41467-022-32562-z.
- ⁸ Partch, C. L., Green, C. B., & Takahashi, J. S. (2014). Molecular architecture of the mammalian circadian clock. *Trends in cell biology*, 24(2), 90–99. <https://doi.org/10.1016/j.tcb.2013.07.002>.
- ⁹ Buscone S, Mardaryev AN, Westgate GE, Uzunbajakava NE, Botchkareva NV. (2021). Cryptochrome 1 is modulated by blue light in human keratinocytes and exerts positive impact on human hair growth. *Exp Dermatol.*;30(2):271-277. doi: 10.1111/exd.14231. Epub 2020 Nov 22. PMID: 33141439.
- ¹⁰ Lowe, M., Lage, J., Paatela, E., Munson, D., Hostager, R., Yuan, C., Katoku-Kikyo, N., Ruiz-Estevez, M., Asakura, Y., Staats, J., Qahar, M., Lohman, M., Asakura, A., & Kikyo, N. (2018). Cry2 Is Critical for Circadian Regulation of Myogenic Differentiation by Bclaf1-Mediated mRNA Stabilization of Cyclin D1 and Tmem176b. *Cell reports*, 22(8), 2118–2132. <https://doi.org/10.1016/j.celrep.2018.01.077>.
- ¹¹ Yuan, G., Hua, B., Yang, Y., Xu, L., Cai, T., Sun, N., Yan, Z., Lu, C., & Qian, R. (2017). The Circadian Gene Clock Regulates Bone Formation Via PDIA3. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research*, 32(4), 861–871. <https://doi.org/10.1002/jbmr.3046>