

DREAM COMPLEX INHIBITORS FOR TREATING CIRDACIAN RHYTHM-INDUCED DISEASES

Keywords: DREAM inhibitors, harmine, circadian rhythm disruption, sleep deprivation, restoring cellular and organismal homeostasis

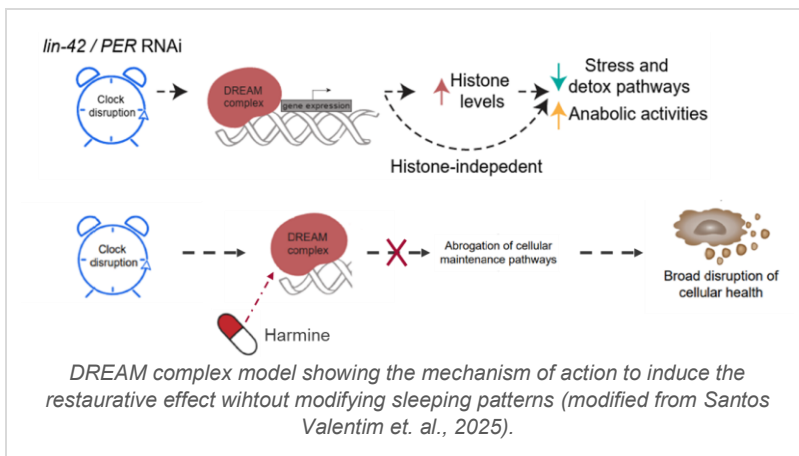
INVENTION NOVELTY

PER1-targeting siRNA or Harmine-like inhibitors restore cellular and metabolic function in circadian rhythm disruption models without modifying sleep patterns.

VALUE PROPOSITION

- **Sleep cycle independent effect:** DREAM inhibition shifts cells toward a sleep-phase, repair/maintenance state supporting a downstream-of-clock mechanism and enabling timed dosing
- **Target engagement:** In *C. elegans*, co-RNAi of DREAM subunits or harmine rescues paralysis in proteotoxic-stress models; in mouse cortex, sleep deprivation keeps DREAM high and disrupts the same pathways; human retinal cells replicate pathway rescue with harmine, demonstrating cross-species conservation
- **MoA:** Lowering DREAM decreases chromatin-compaction markers, rebalances OXPHOS/mitochondria, detoxification, tunes ribosome/transcription programs, and increases DNA-repair programs

Functional evidence suggests that the restorative benefits of sleep can be mimicked by DREAM inhibitors without changing sleep patterns.



TECHNOLOGY DESCRIPTION

- **Modality:** Genetic (siRNA) and pharmacological inhibition (harmine) transiently reduces DREAM complex activity
- **Dosing paradigm:** Evidence supports time-restricted administration to align with physiological low-DREAM times and mitigate daytime DNA-damage response
- **In vitro cellular activity:** Harmine restores OXPHOS/mitochondrial and ribosome programs in *PER1*-disrupted human cells; DREAM subunit knockdown or pharmacologic inhibition lowers chromatin-compaction markers and normalizes detox/repair signatures

COMMERCIAL OPPORTUNITY

The technology is available for co-development and in-licensing partnerships.

DEVELOPMENT STATUS

Proof-of-concept established for DREAM modulation restoring cellular function under circadian disruption.

PATENT SITUATION

A European patent was filed in December 2023 (EP23218648) followed by a PCT application (WO2025133144) in 2024.

FURTHER READING

Original publication – [Santos Valentim et al., 2025. biorXiv.](https://doi.org/10.1101/2025.01.15.431111)