Delayed Sleep Phase Syndrome and CRY1 gene

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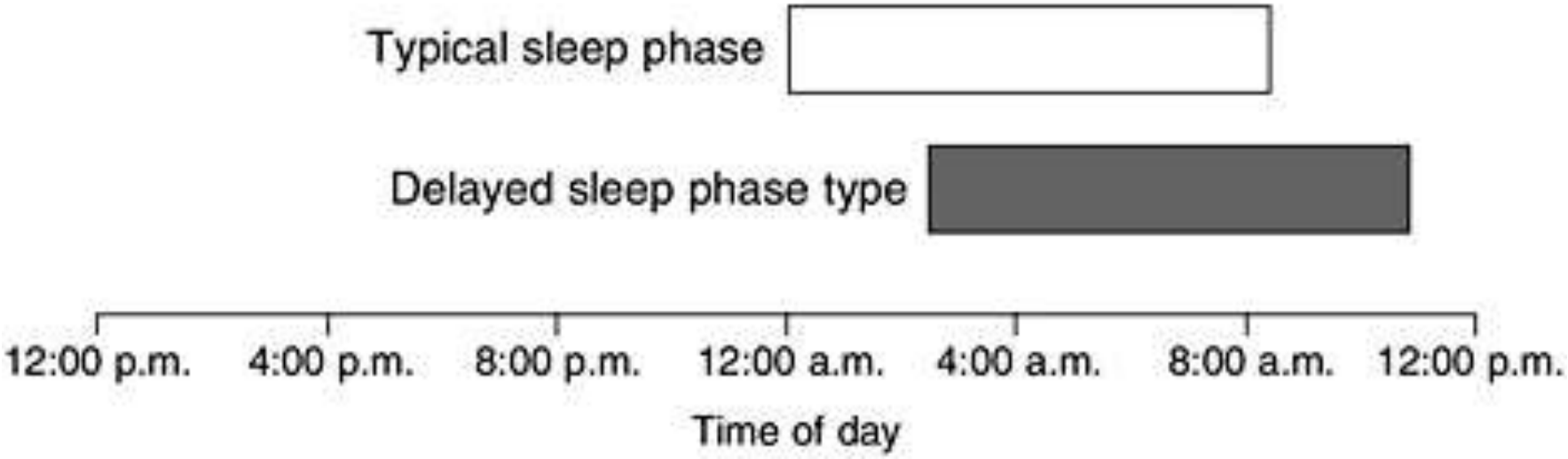
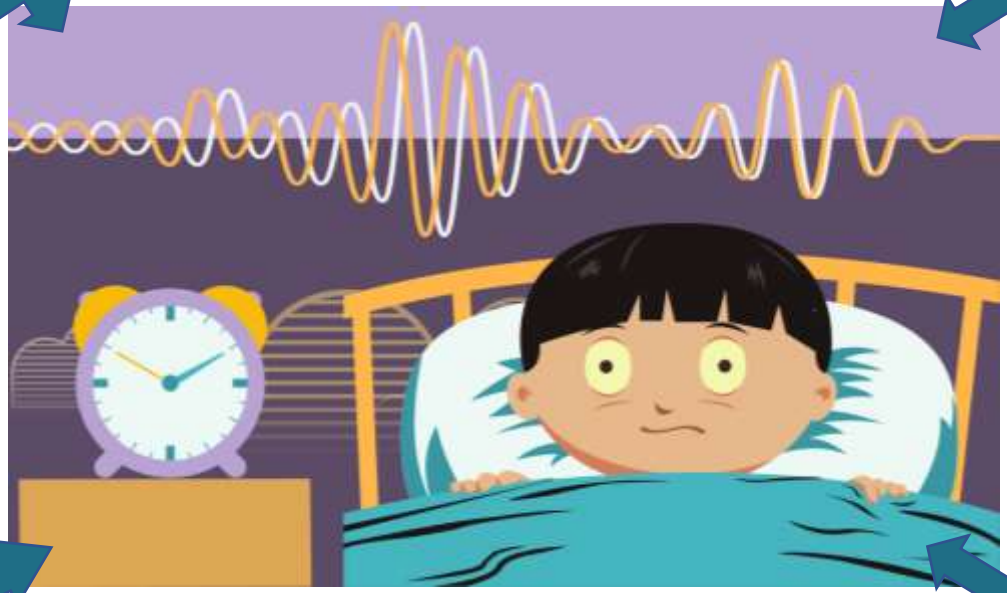
What is Delayed Sleep Phase Disorder (DSPS)?



What are the signs of DSPS?

Trouble falling asleep

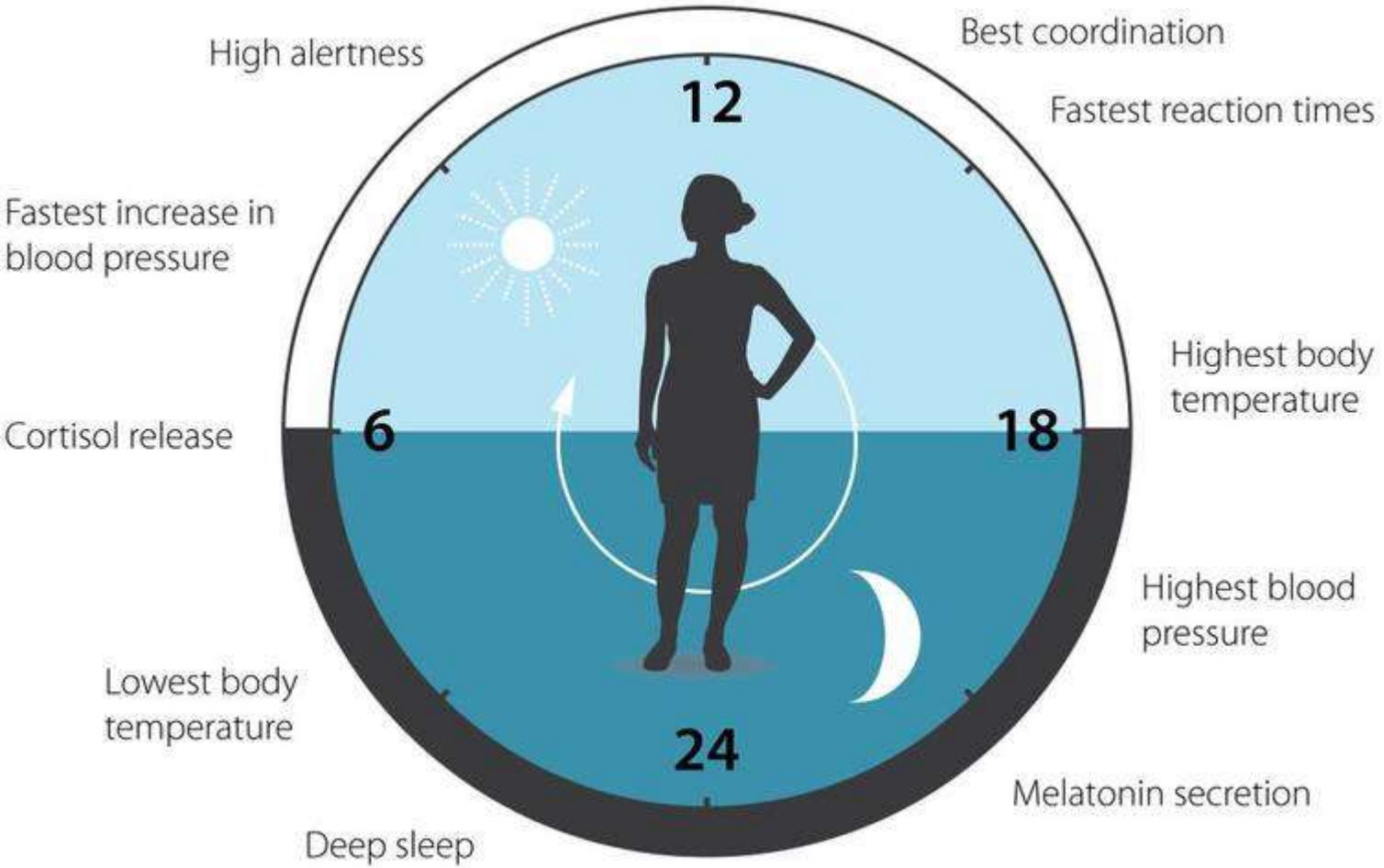
Depression



Behavioral problems

Inability to wake up at desired time (school, work)

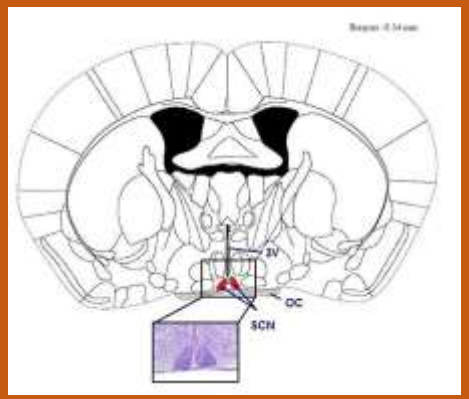
What is the Circadian Clock?



CRY1 gene is associated with DSPS

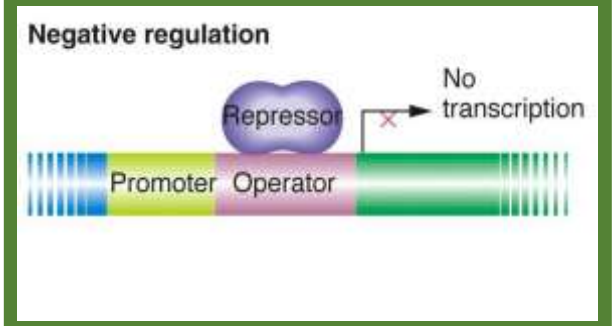
Photolyase | FAD binding domain | 632 AA

Cellular Component



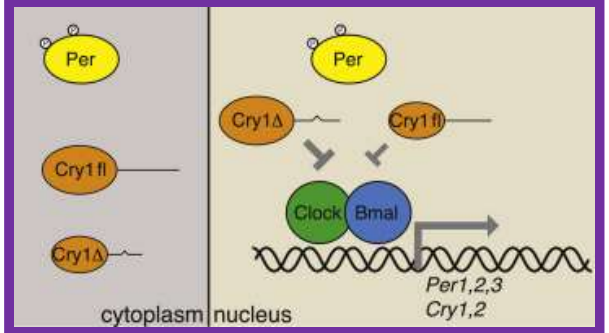
SCN; cell nucleus

Molecular Function



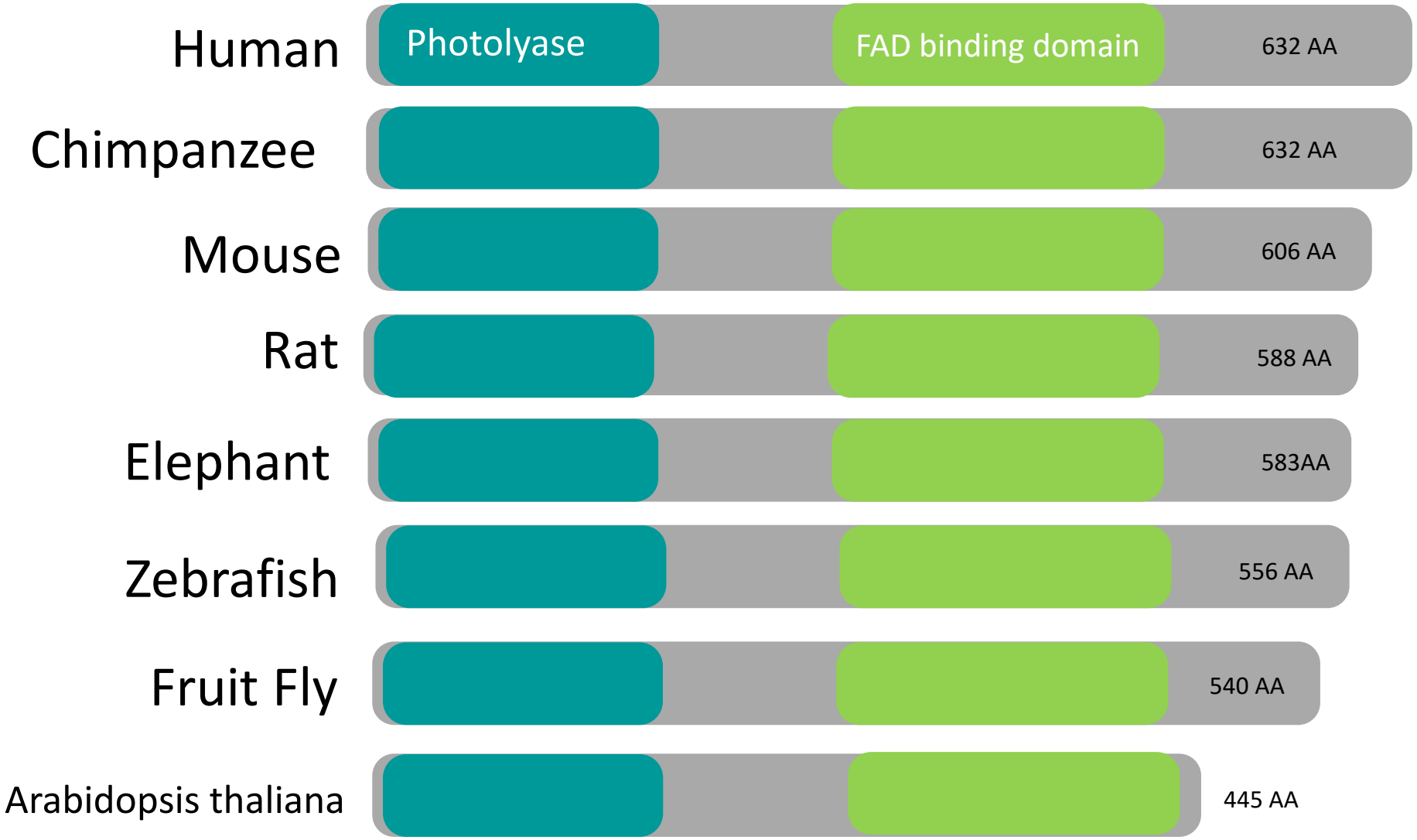
Transcriptional Repression

Biological Process

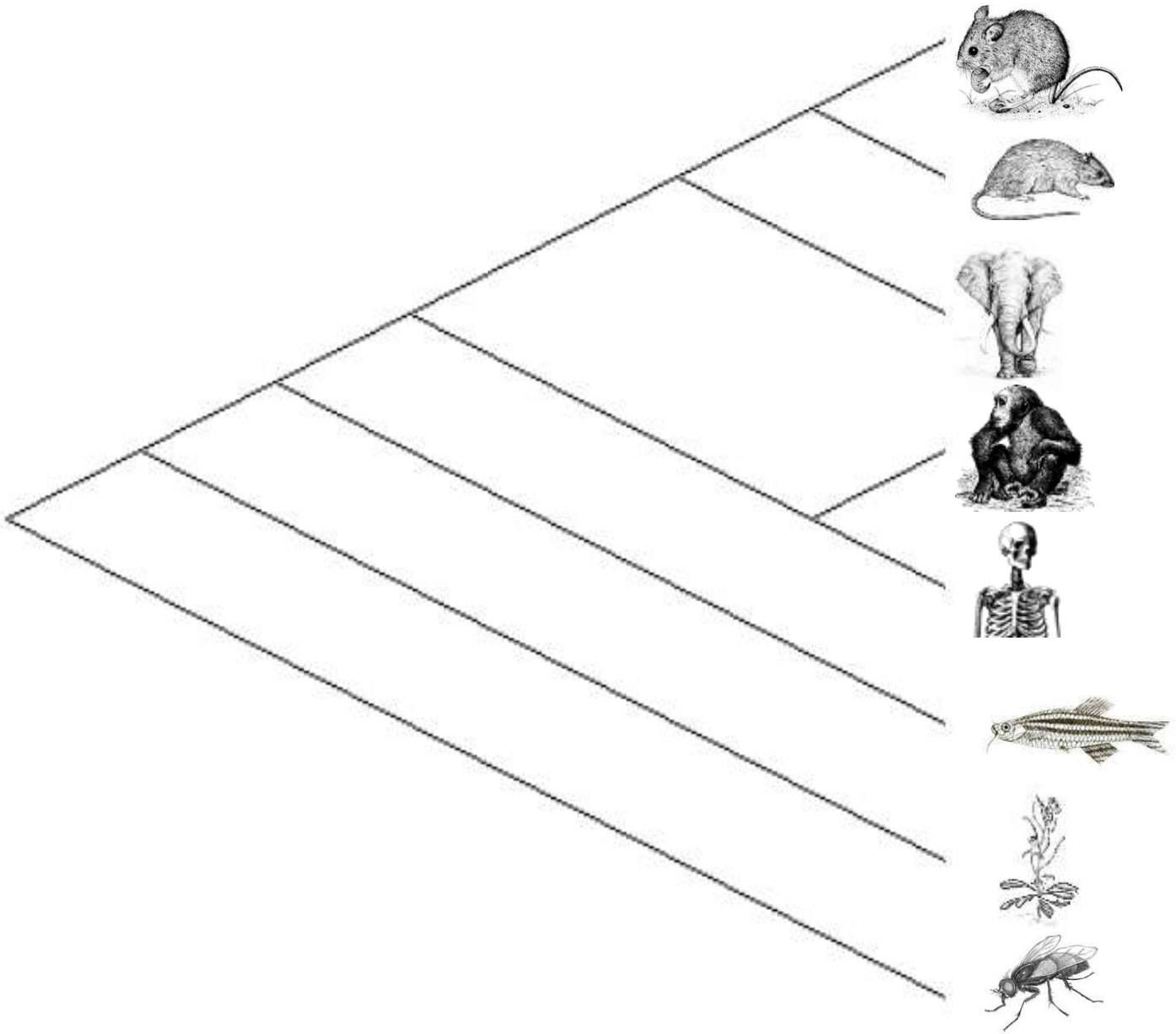


BMAL1-CLOCK

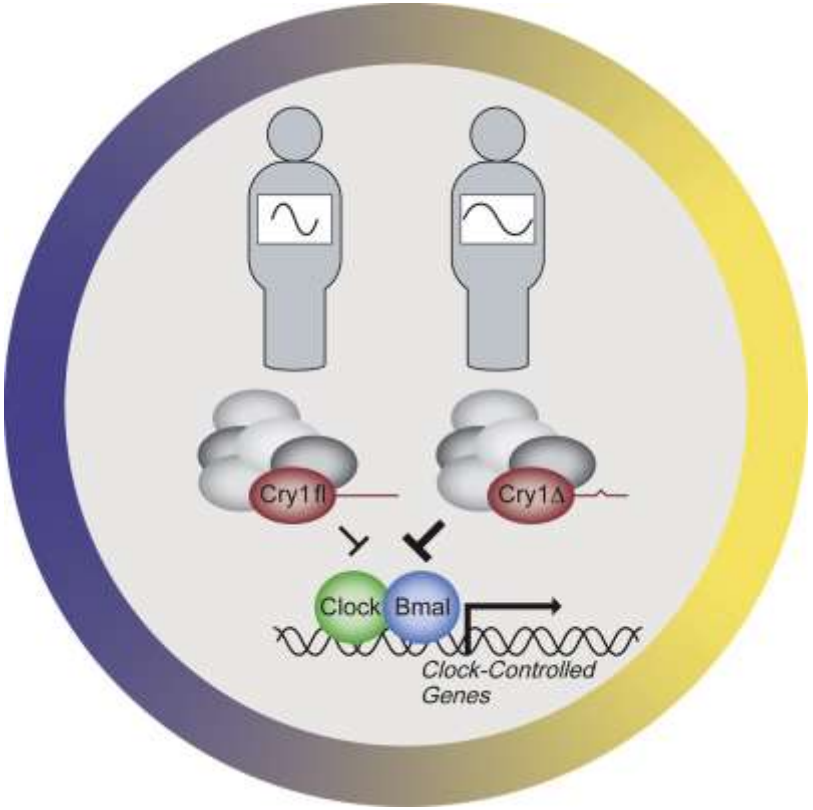
CRY1 is well conserved among species

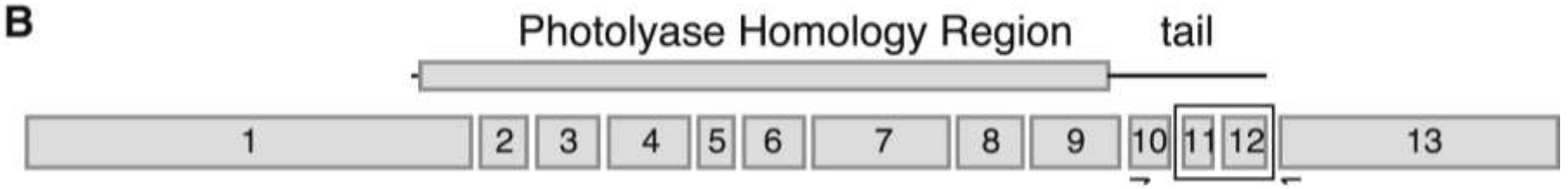


CRY1 is conserved in species



Gap in Knowledge

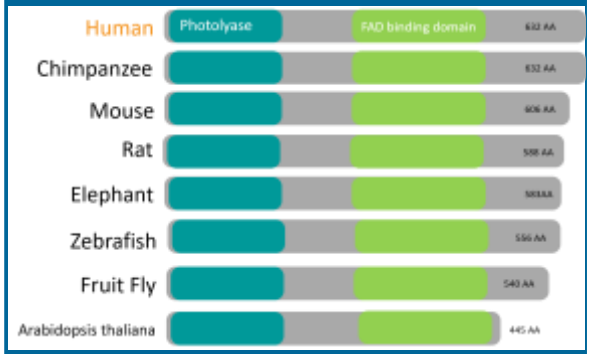




What is my primary goal?

To understand the role of phosphorylation of the Cry1 protein tail in the regulation of the circadian clock.

Aim 1

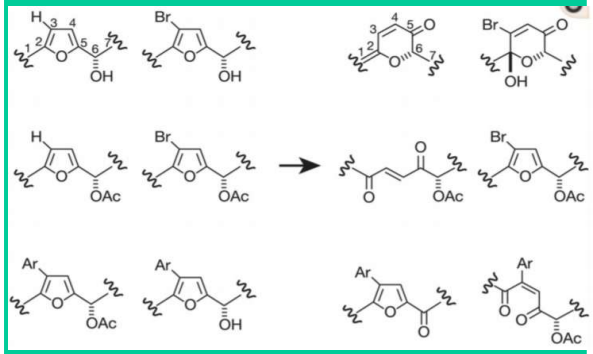


Determine amino acid conservation between normal and mutant lines

Aim 2

Establish protein interactions with mutant line

Aim 3

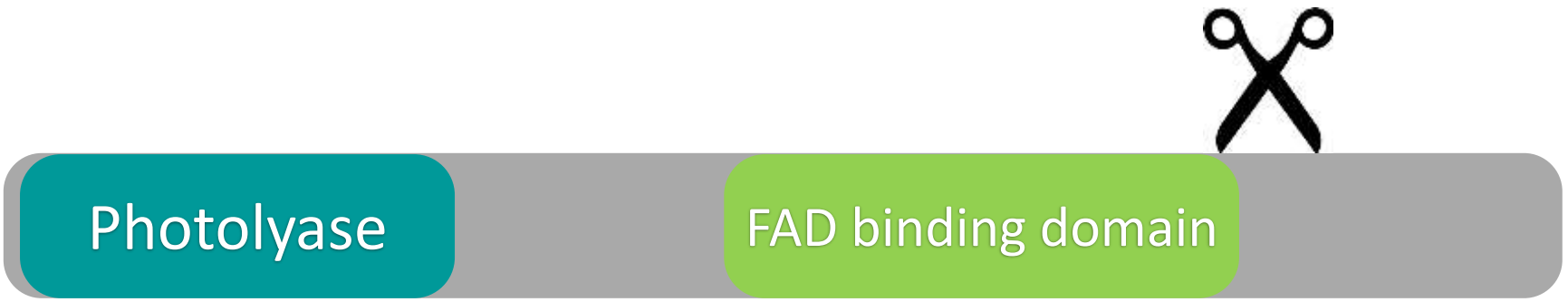


Identify interaction of mutant lines with chemical compounds

Aim 1

Determine conserved amino acids of CRY1 and mutant sequences to determine effects of deletion.

CRISPR/Cas9 → **Screen** → **Clustal Omega**



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WT

Mutagenic Cry1 Δ11

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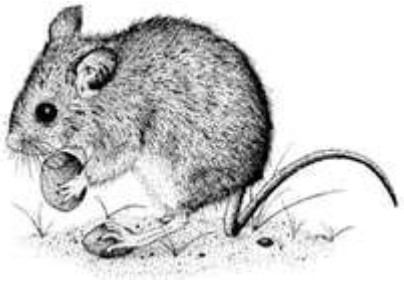

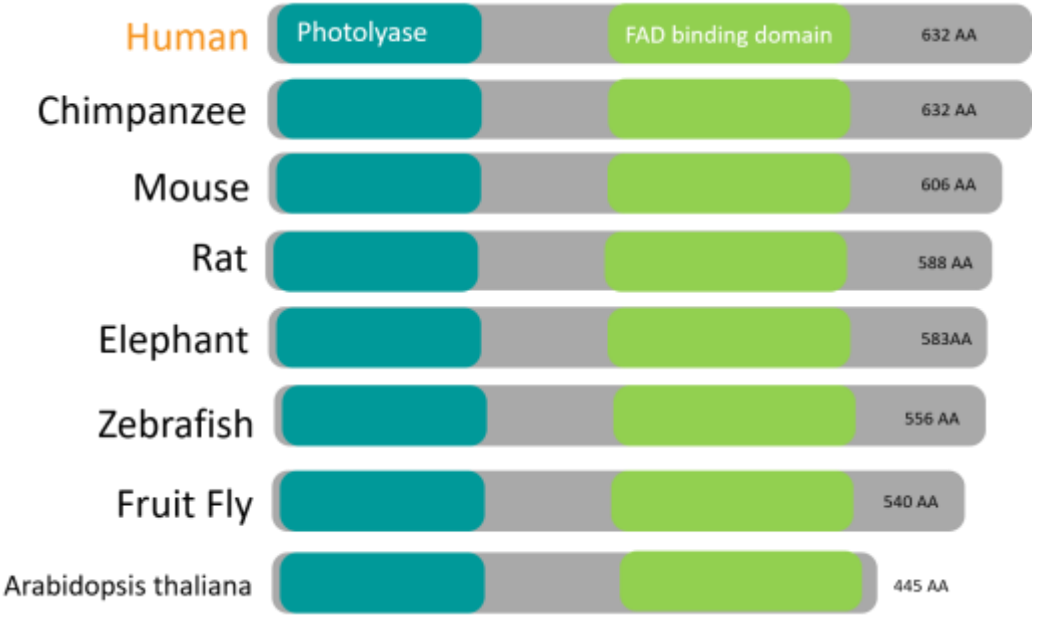

Aim 2

Establish protein interactions resulting from mutations in CRY1.

CRISPR/Cas9 → **TAP tag or Mass Spec** → **GO terms for interactions**

Creation of Mutagenic Cry1 Δ11 lines

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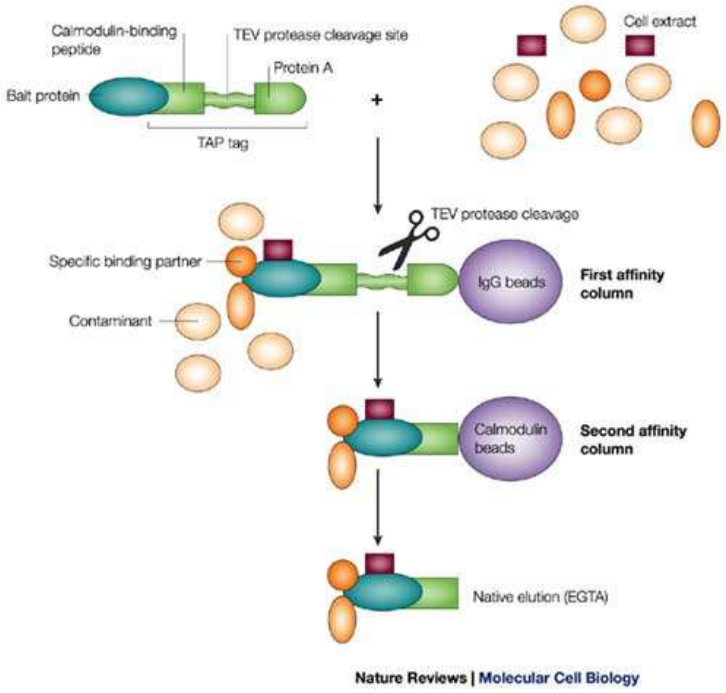

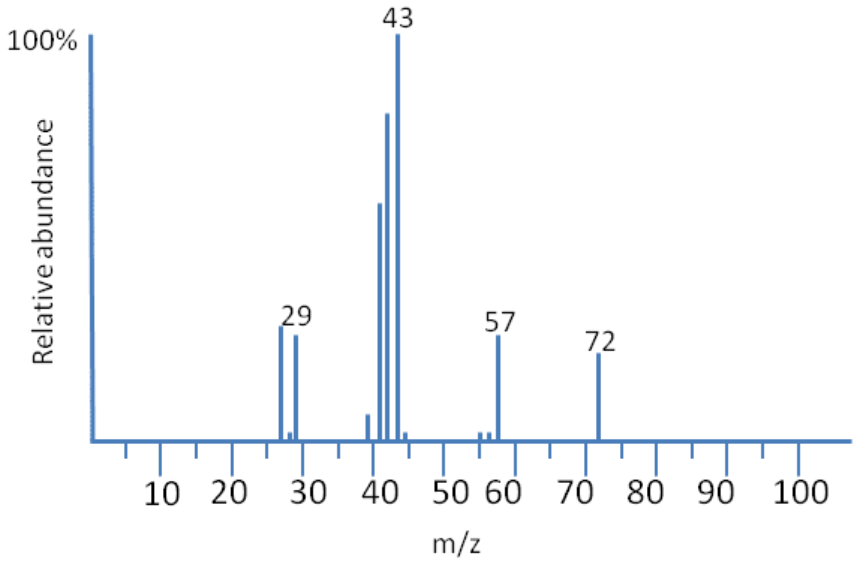

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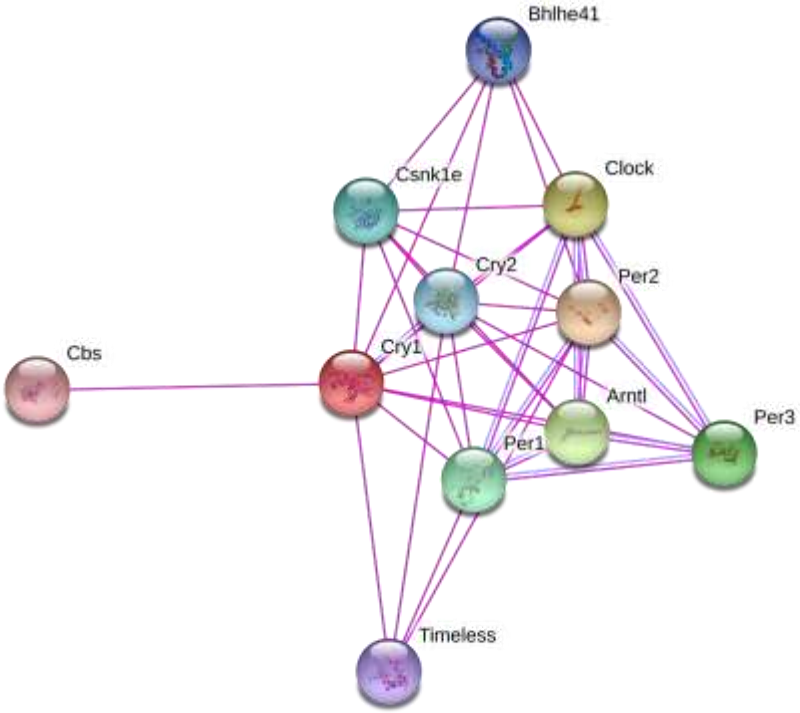

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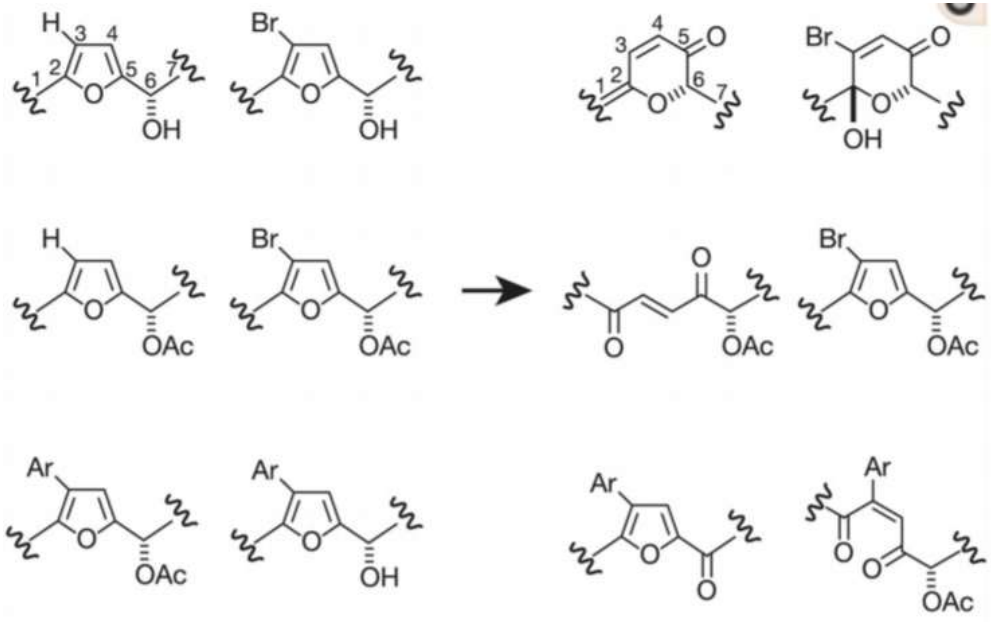
Aim 3

Identify chemical compounds that will interact with and potentially repress the effects of CRY1 tail deletion.

Assemble chemical library → **Protein binding assay** → **Phenotypic Screen**



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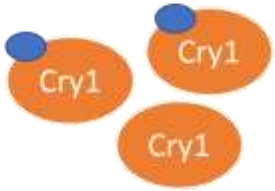
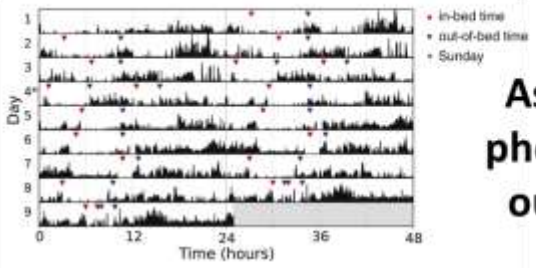
Overexpression of CRY1



Screen for binding compounds



Assay for phenotypic outcome

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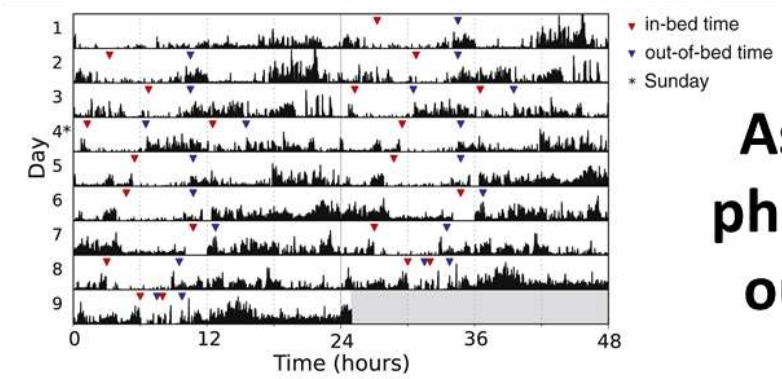
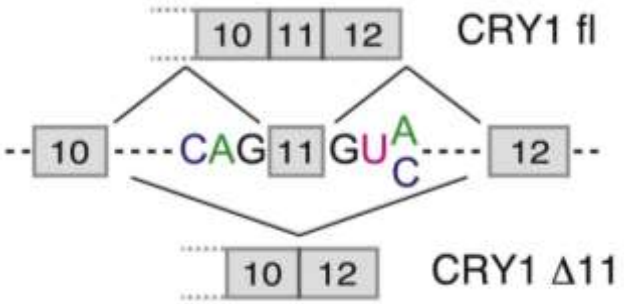


Assay for phenotypic outcome

Summary

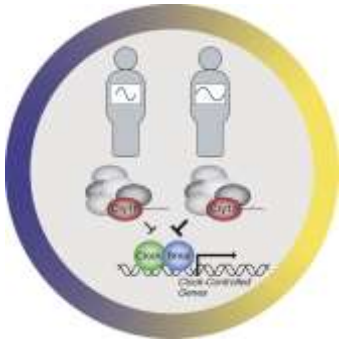


A deletion in CRY1 gene results in the overexpression of the protein and lengthening of the circadian cycle.

WT

Mutagenic Cry1 Δ11

The study of mutagenic lines allows for the study of protein interactions in diseased states.



Understanding the mechanisms behind the CRY1 protein tail will allow for the development of therapies and treatment for circadian rhythm disorders.