



THE FRONT ROW  
at Scripps Research

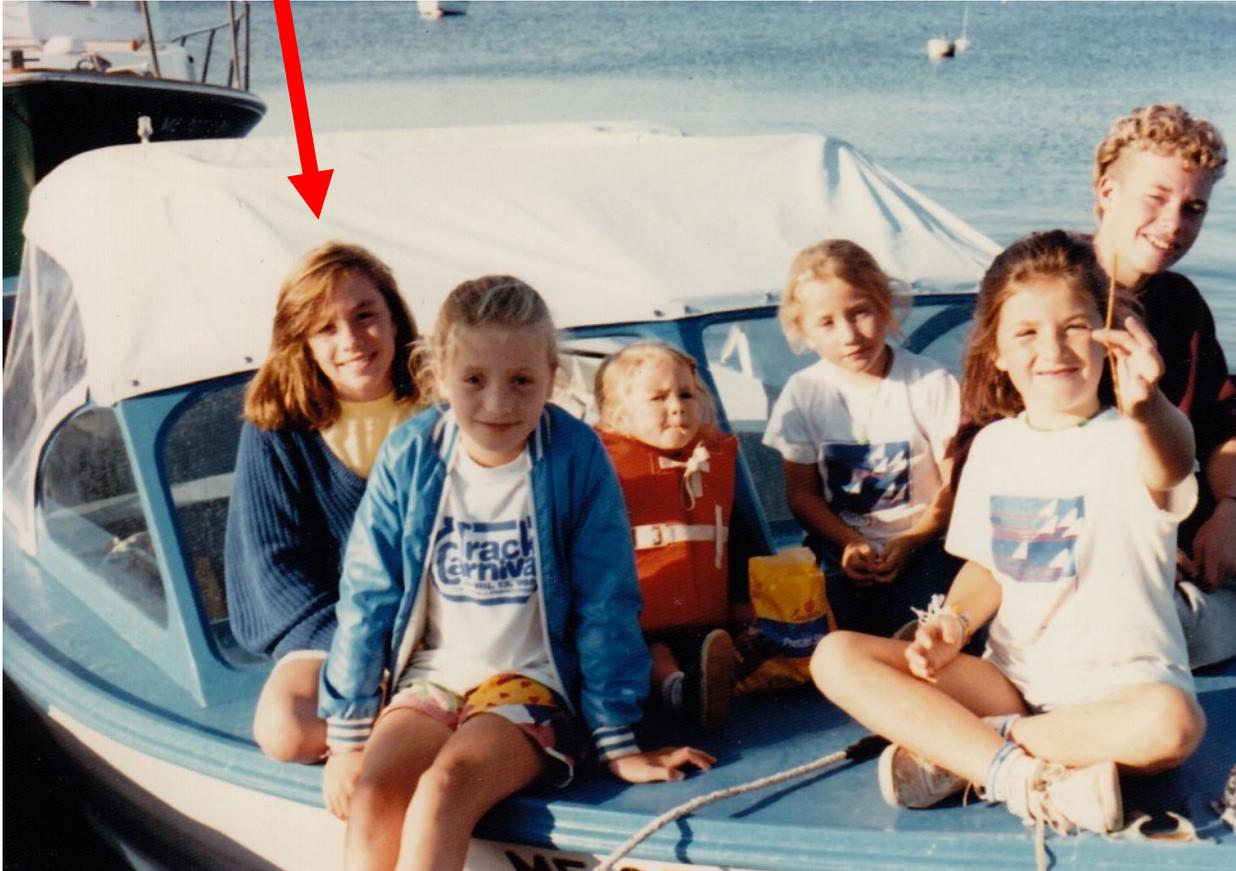
# Hacking our body clocks to optimize health

**Katja A. Lamia, PhD**

**Associate Professor of Molecular Medicine**



# Who is Katja Lamia?



# I grew up in:



- **Los Angeles, CA**



- **Washington, DC**



- **South Bristol, ME**

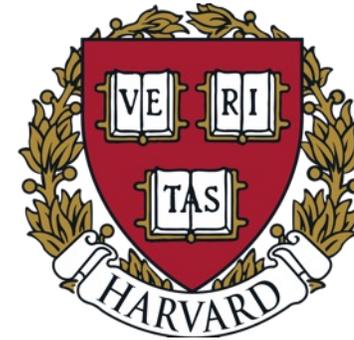
# Who is Katja Lamia?



# I was educated at:



- UC Berkeley
- BA, Physics



- Harvard
- PhD, Biophysics



- Salk Institute
- Postdoctoral with Ron Evans



# Take Home Messages

*Circadian clocks promote health*

*Clock disruption elevates risks*

*We are investigating why,  
...to reduce risks for shift workers*



# Outline

**History of circadian clocks research**

My early work in circadian biology

Recent work in my lab at Scripps

Q & A with YOU!





light  
warmth  
dryness



dark  
cold  
moisture



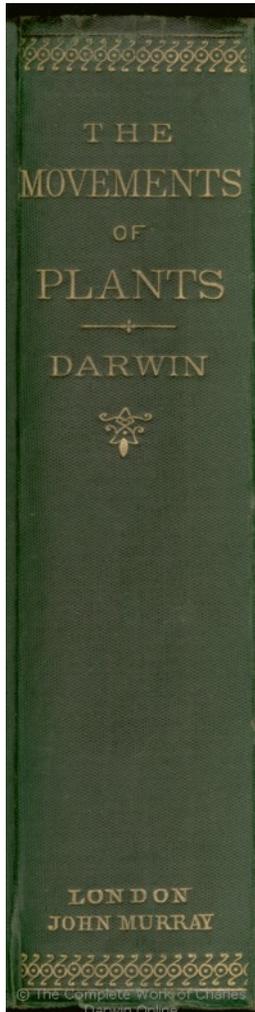


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# A (Very) Short History of Circadian Clocks



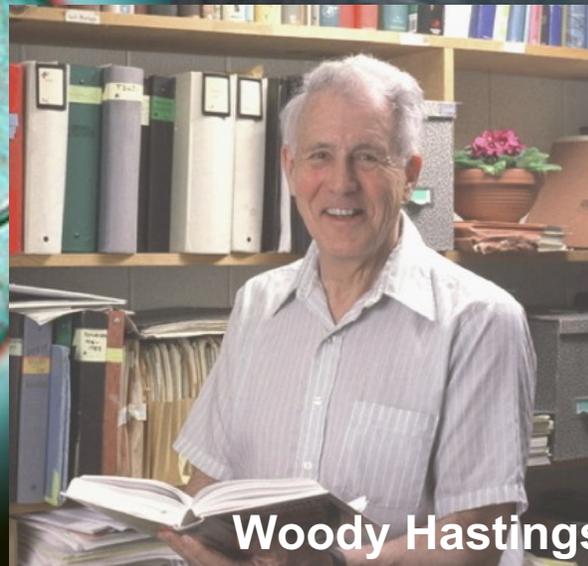
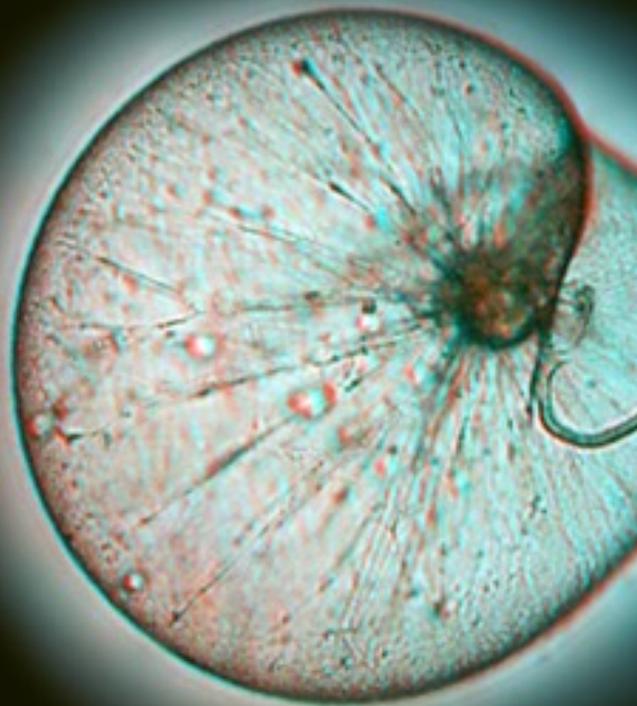
# Plant leaves exhibit daily movements



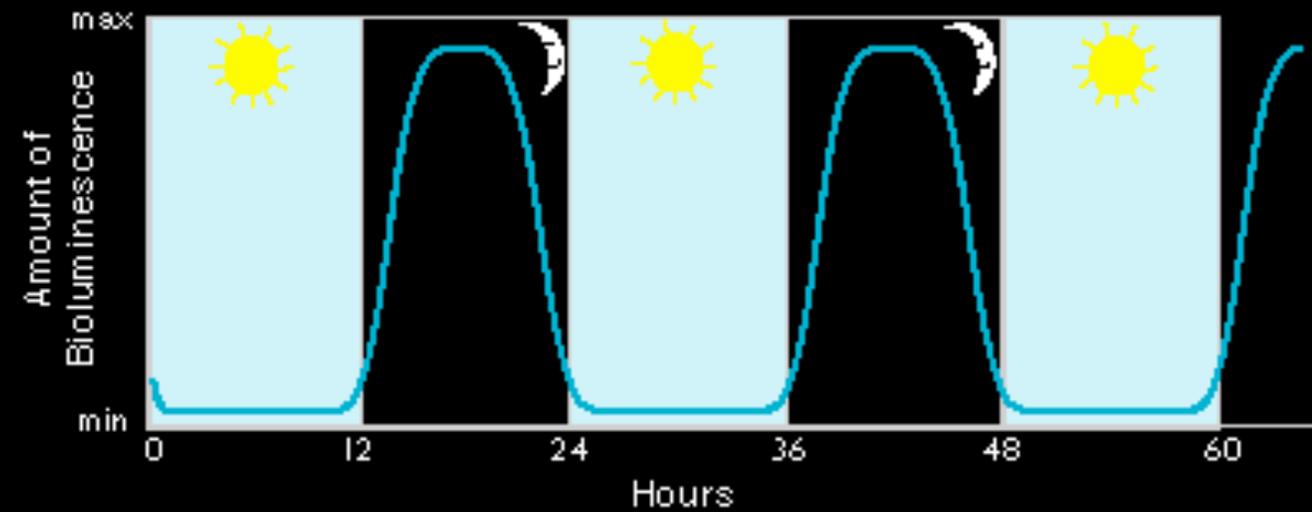
**1880:**  
**“The Movements of Plants”**  
**by Charles Darwin**

**Plant leaves move to  
maximize sun exposure  
...and they anticipate sunrise**





Woody Hastings





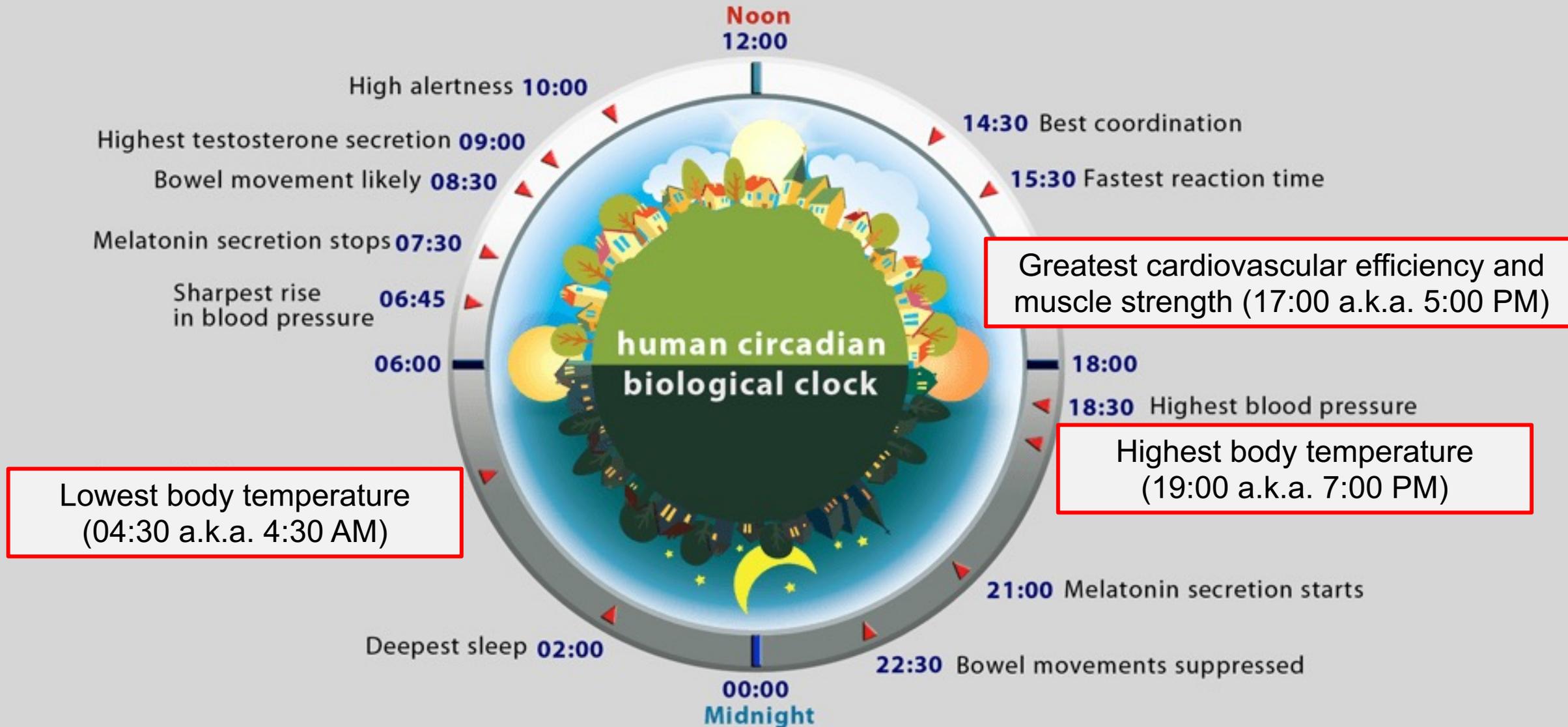
California grunion anticipate high tide  
to lay eggs above the water line



California Department of Fish  
and Wildlife

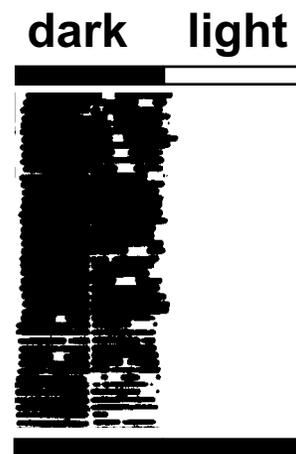
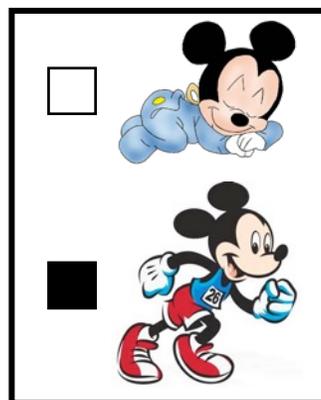
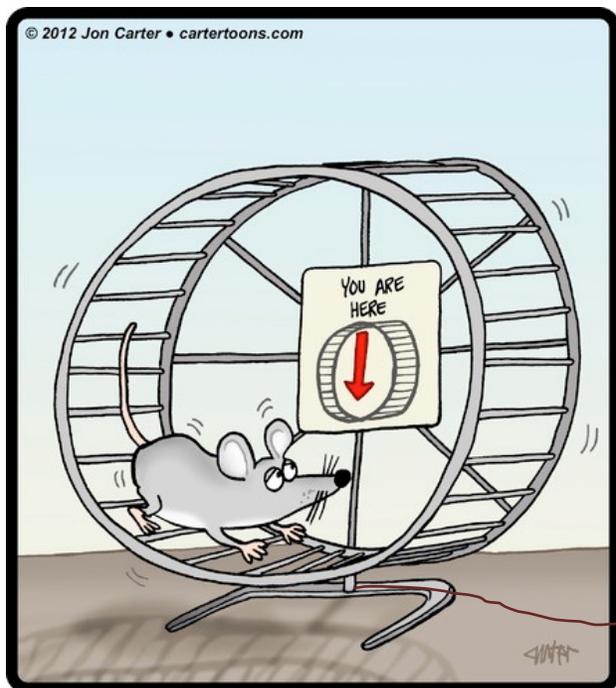
**California Grunion  
Information**







Seminal experiments led by Colin Pittendrigh at Princeton in the 1960s described behavioral rhythms in rodents and provided strong evidence for internal clocks



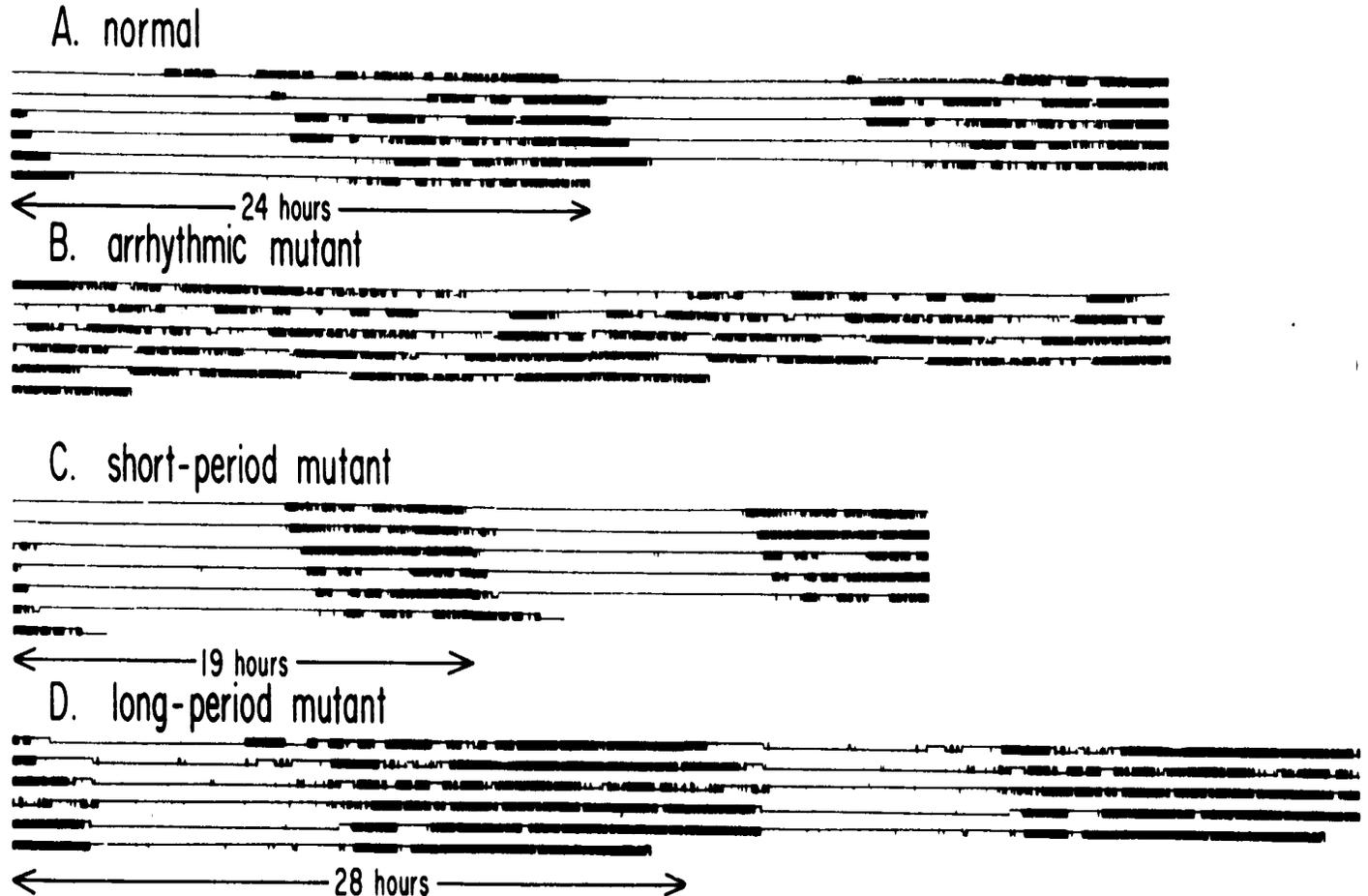
“Circadian” (circa = about, -dian = daily) is used to describe biological phenomena that exhibit ~24 hour oscillations independent of external timing cues



1971: Ron Konopka & Seymour Benzer identify flies with altered circadian rhythms due to genetic changes



Seymour Benzer



*This was the first demonstration that behavior can be controlled by a single gene!*



## The Nobel Prize in Physiology or Medicine 2017



Jeffrey Hall

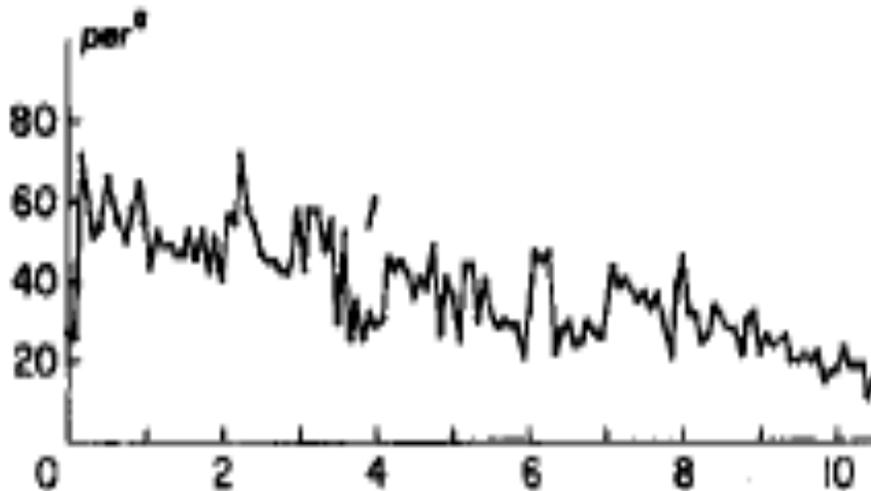


Michael Rosbash

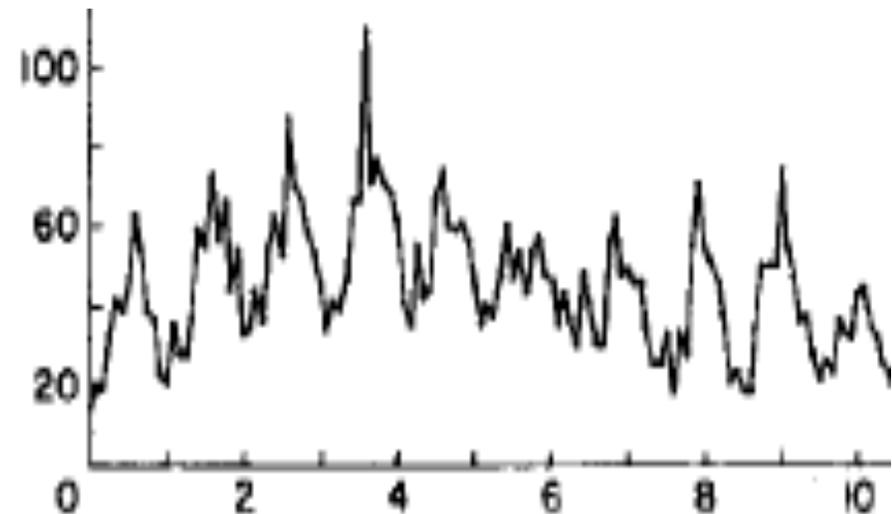


Michael Young

Benzer's arrhythmic mutant "*per*<sup>0</sup>"

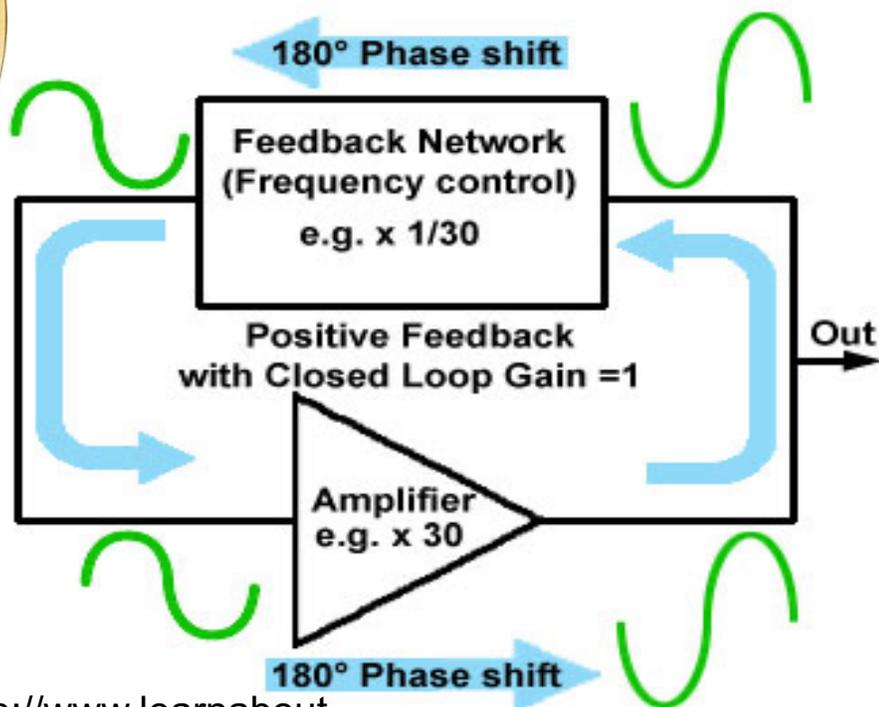


Behavior restored by fixing the "*period*" gene





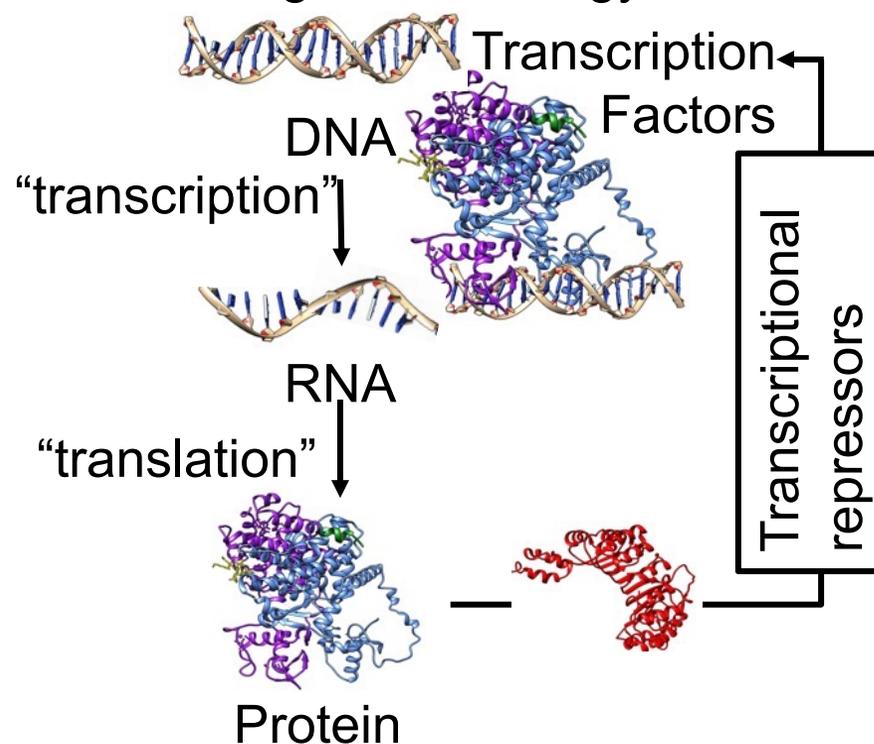
## Electrical Circuit



(<http://www.learnabout-electronics.org/Oscillators/osc11.php>)

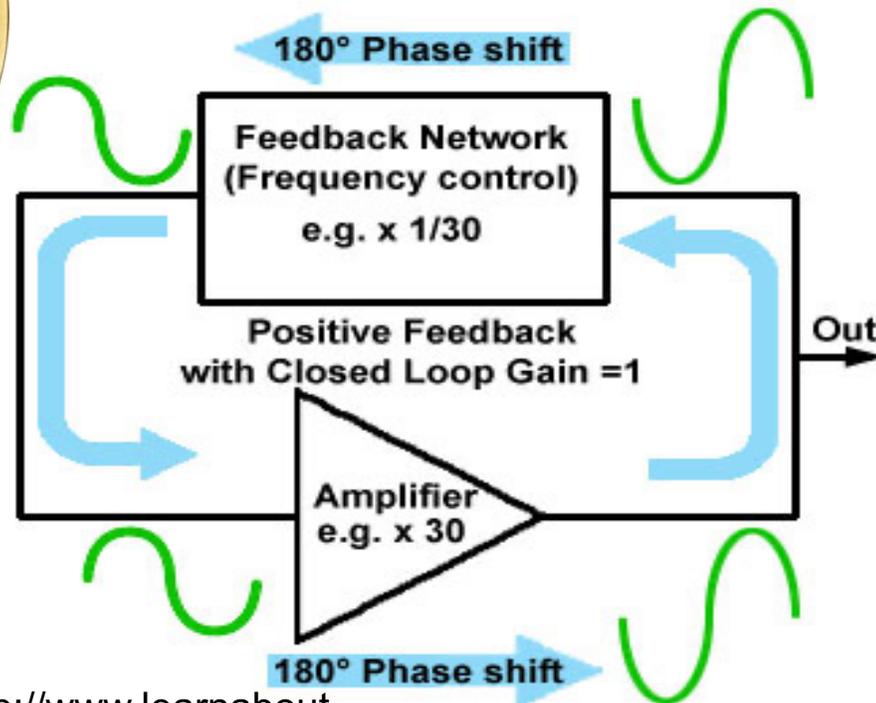
## Genetic Circuit

“central dogma” of biology:





## Electrical Circuit



(<http://www.learnabout-electronics.org/Oscillators/osc11.php>)

## Genetic Circuit

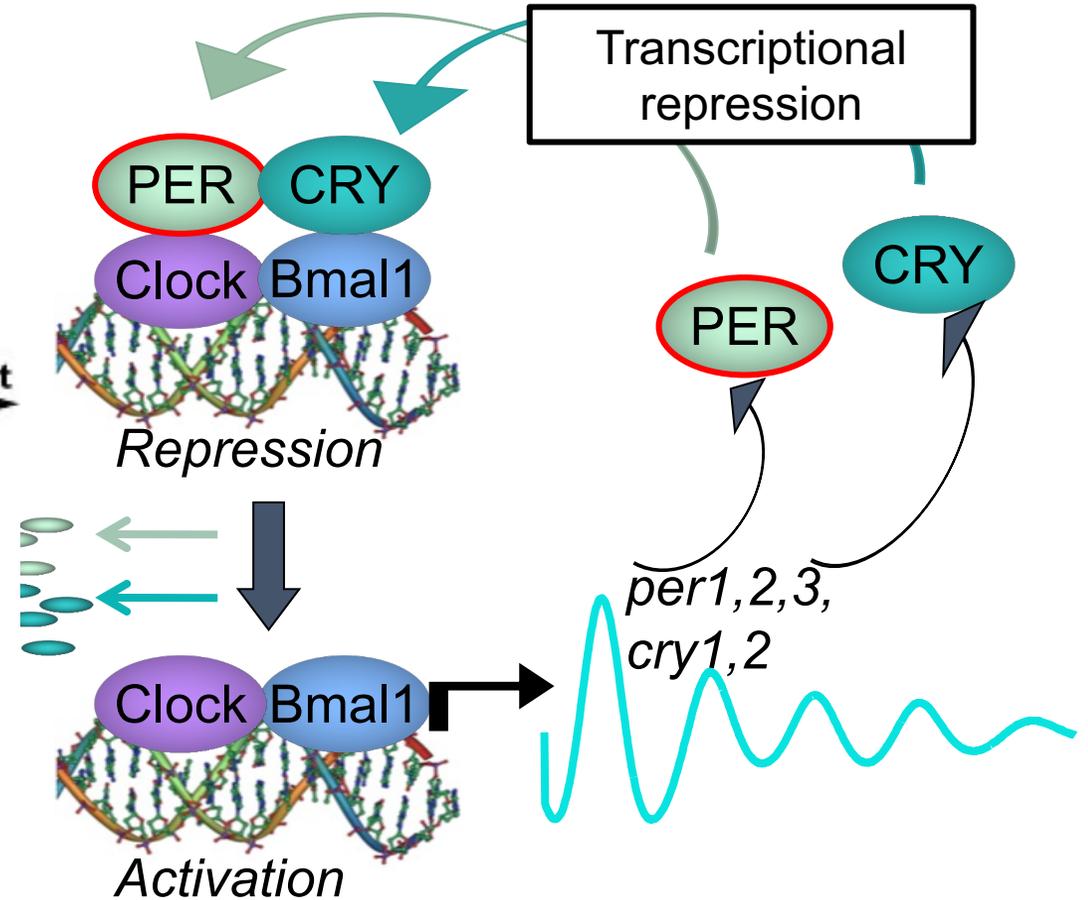
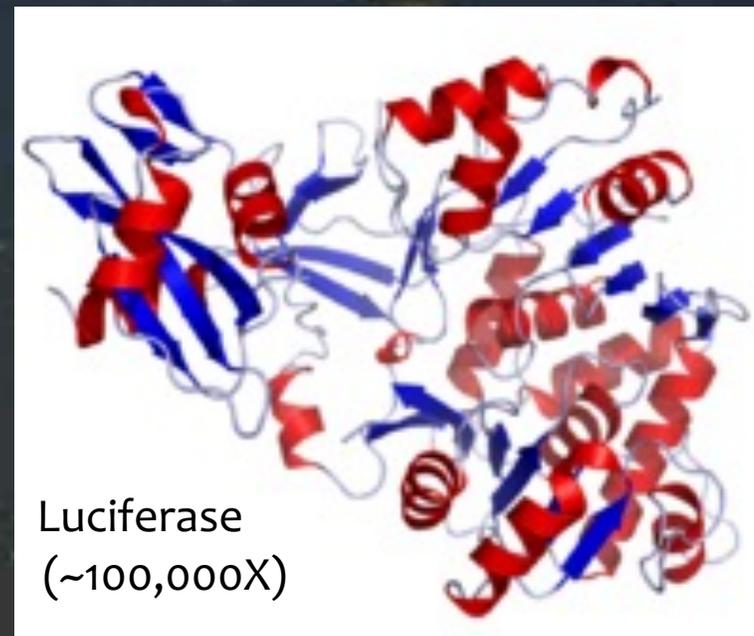




Photo by Radim Schreiber



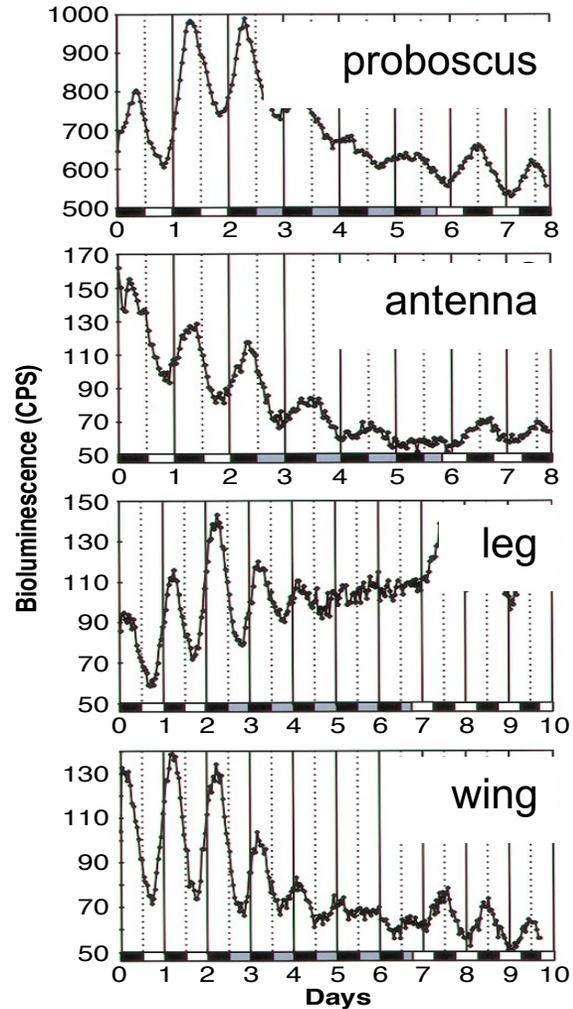


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# Light-emitting proteins let us watch biology

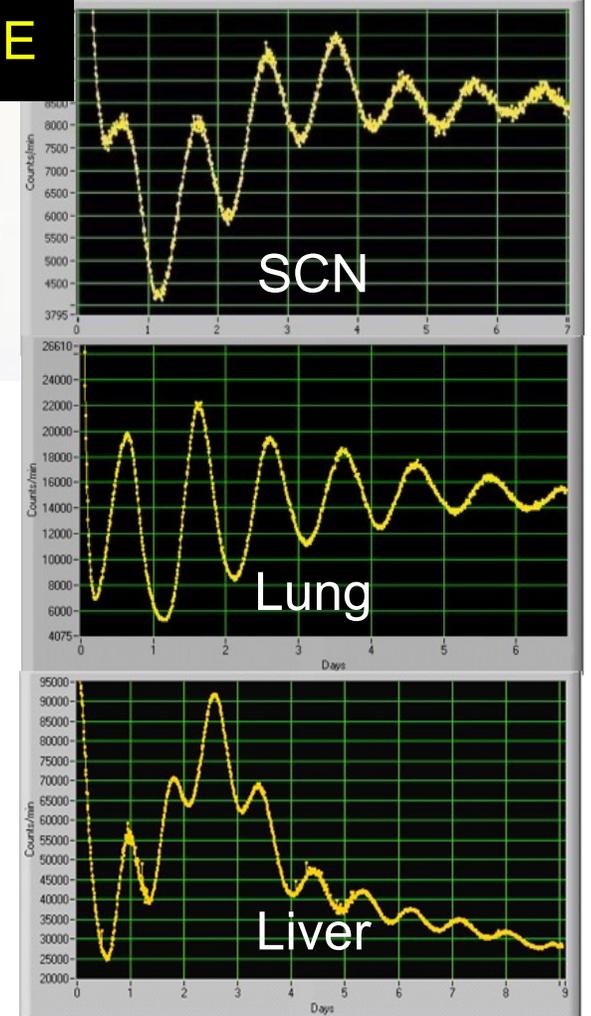


Green Fluorescent Protein, "GFP"



Plautz et al., *Science* 1997

## PER2-LUCIFERASE



Yoo, Yamazaki, et al., *PNAS* 2004

# Outline

History of circadian clocks research

**My early work in circadian biology**

Recent work in my lab at Scripps

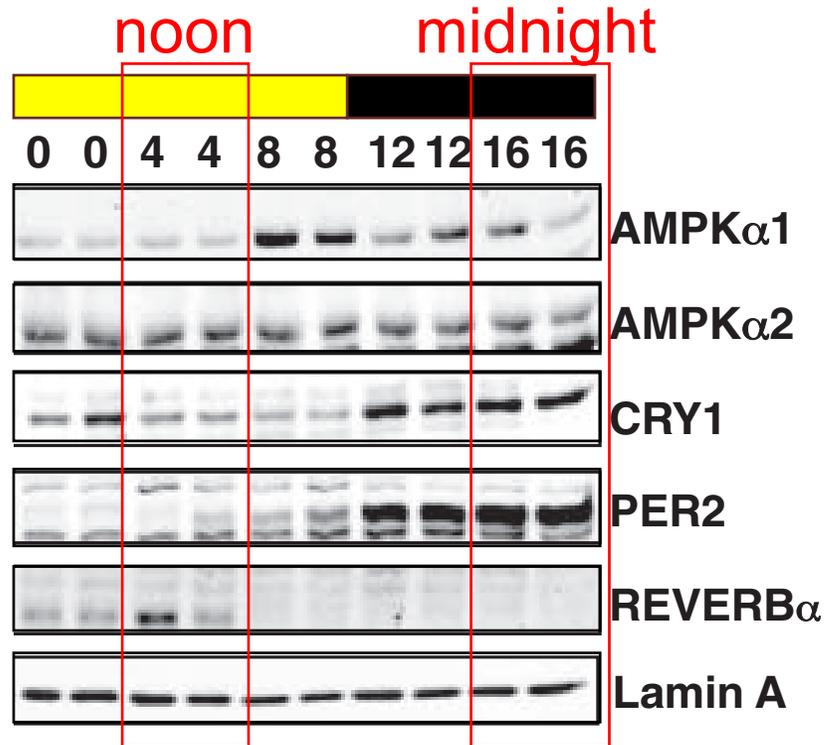
Q & A with YOU!





## Proteins in mouse liver nuclei:

Time of Day  
(hours after lights on)



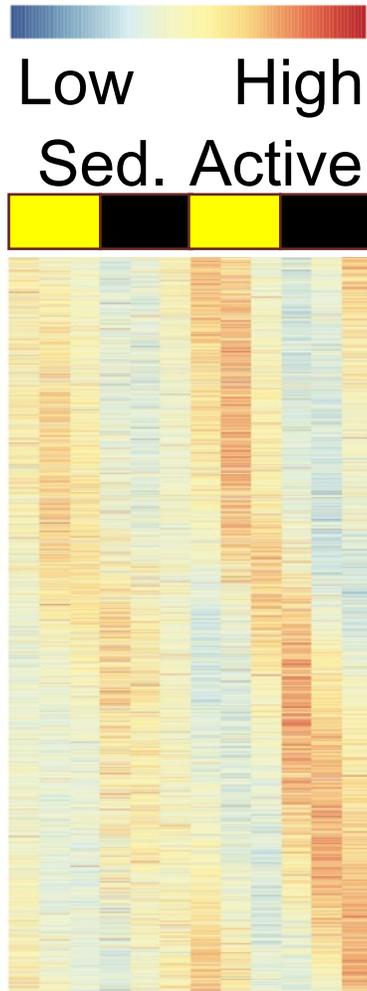
Data from Lamia et al., *Science* 2009

*“A rose is not necessarily and unqualifiedly a rose; that is to say, it is a very different biochemical system at noon and at midnight.”*

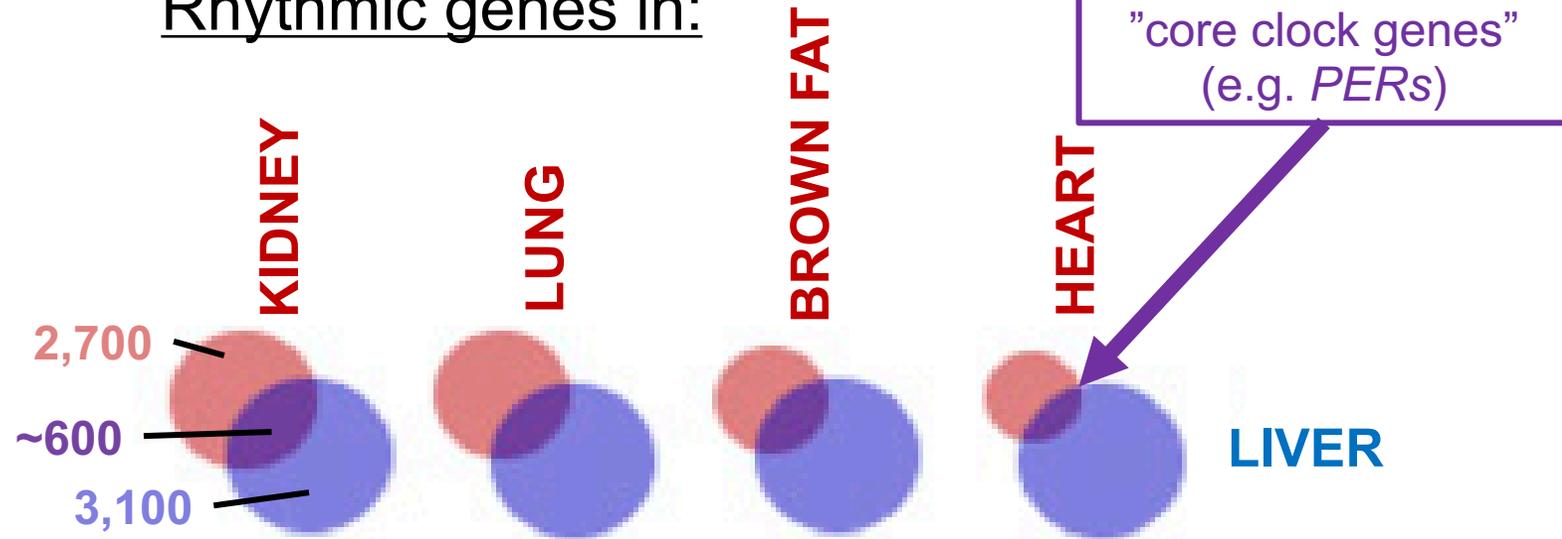
*~ Colin S.  
Pittendrigh*



3,995 Rhythmic genes  
in skeletal muscle



Rhythmic genes in:



Data from Zhang et al., *PNAS* 2014

*>50% of all genes are rhythmically expressed  
somewhere in the body*

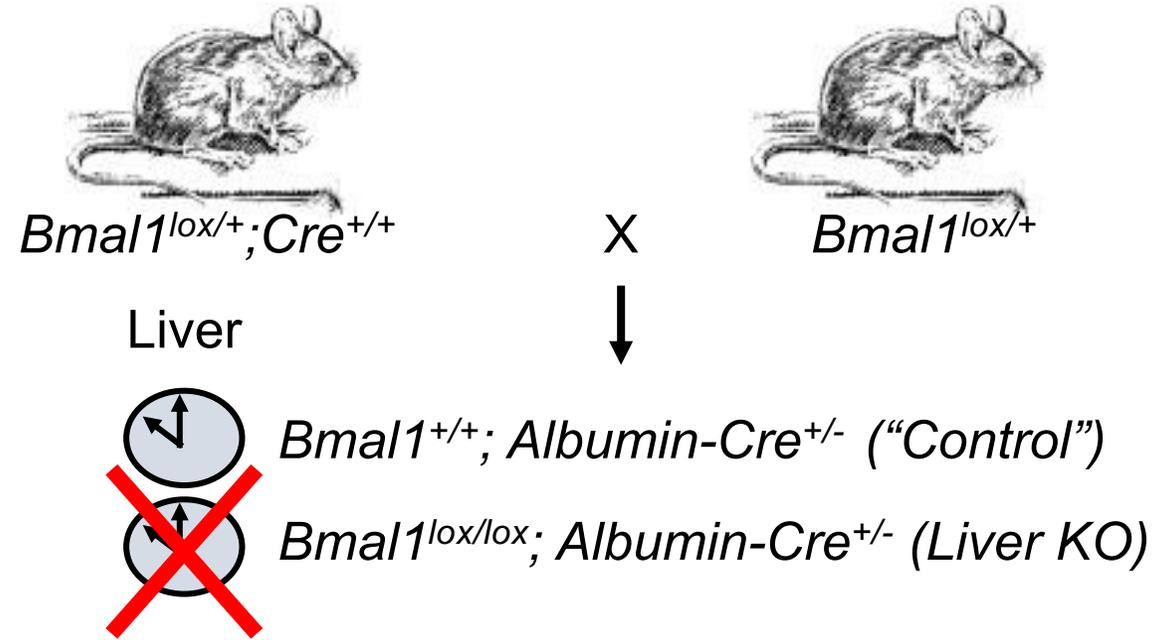
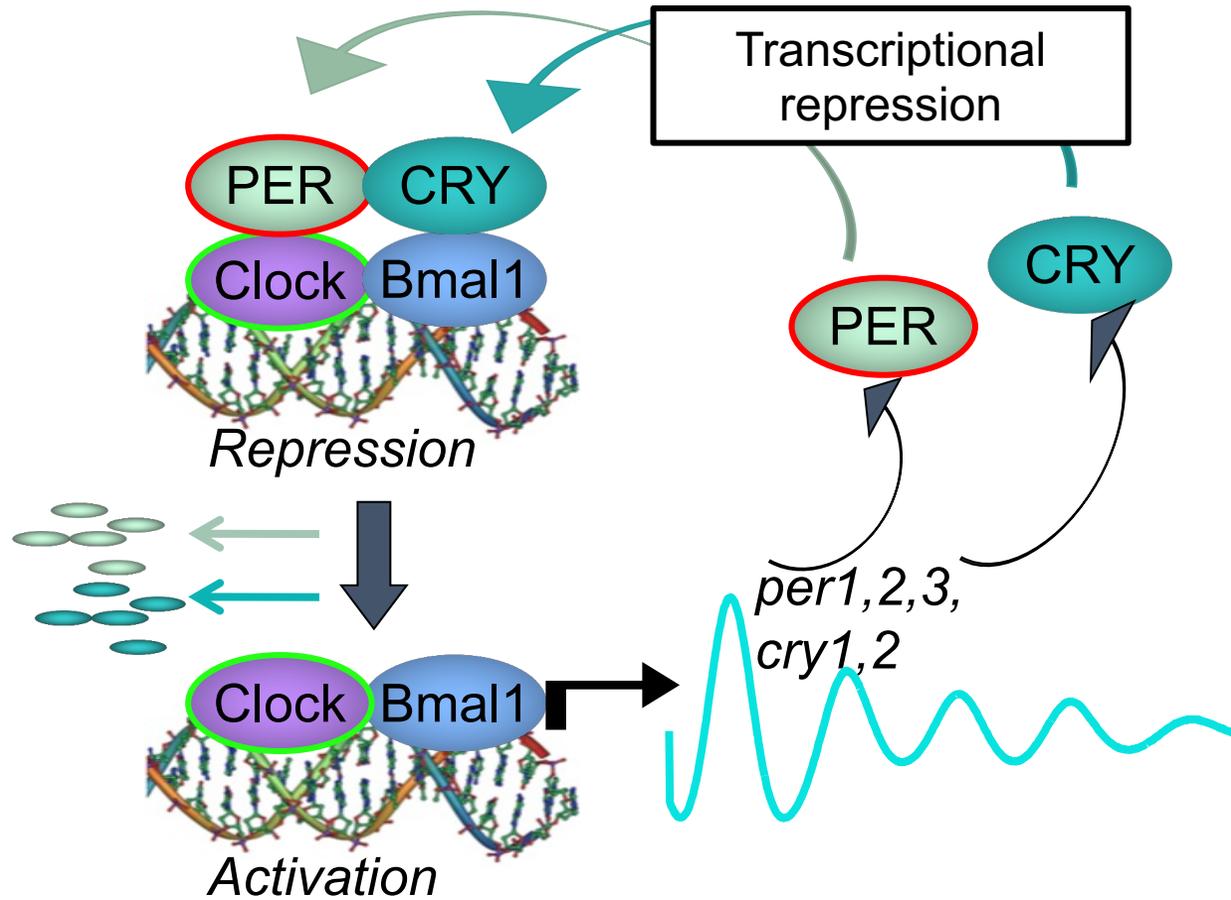


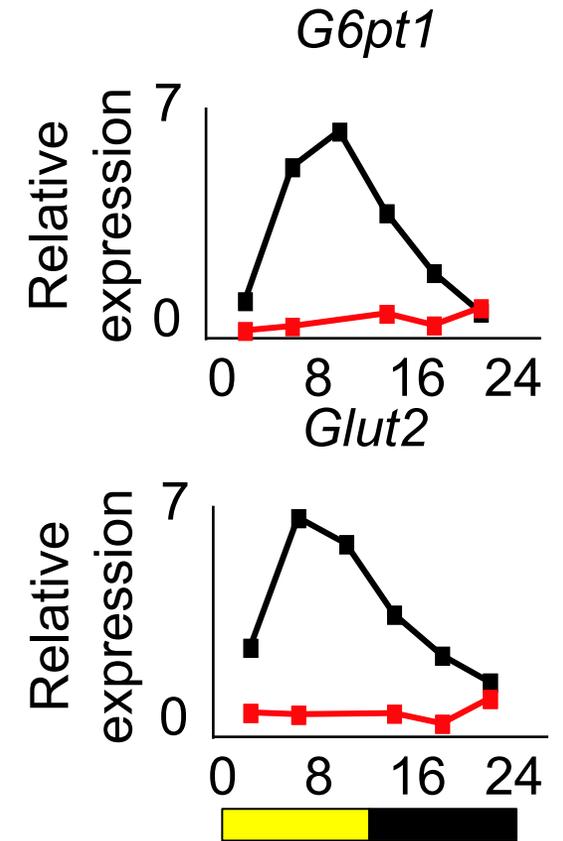
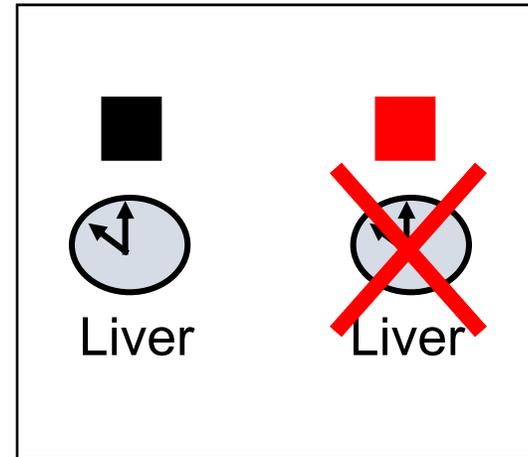
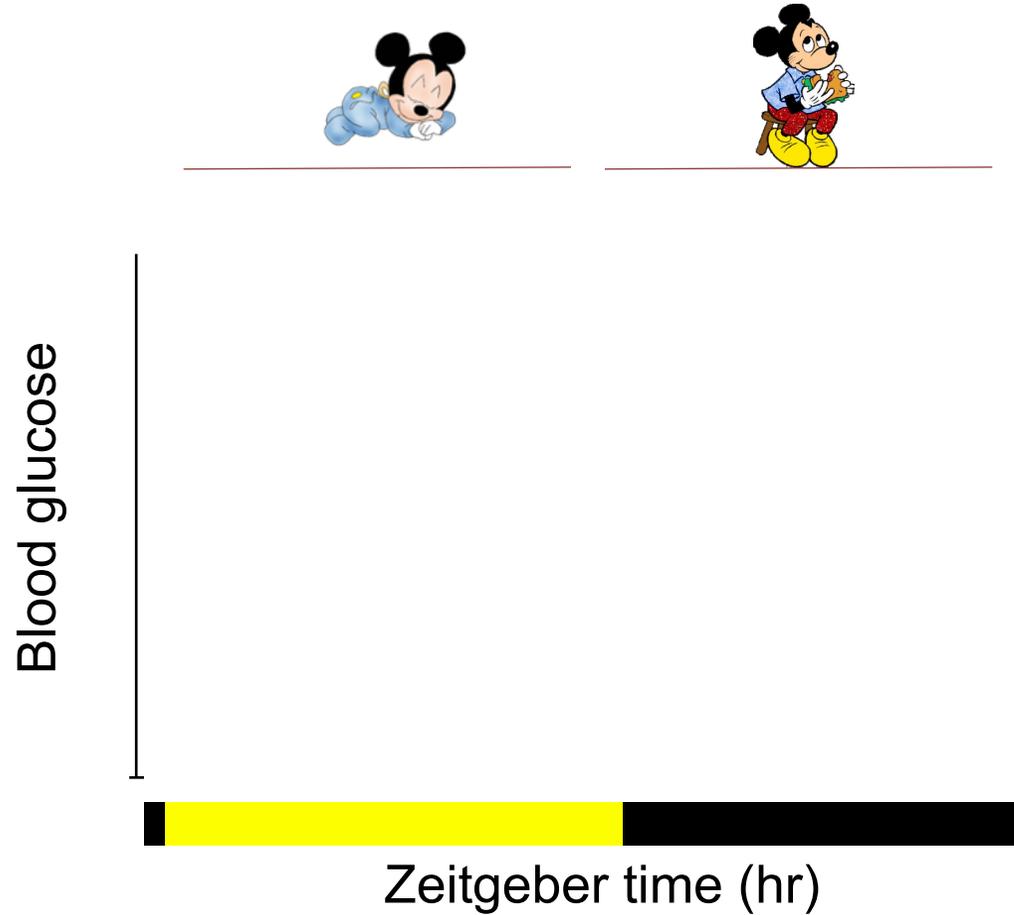
*"La fixité du milieu intérieur est la condition d'une vie libre et indépendante"*

*("The constancy of the internal environment is the condition for a free and independent life")*

~Claude Bernard (1813-1878)







# Outline

History of circadian clocks research

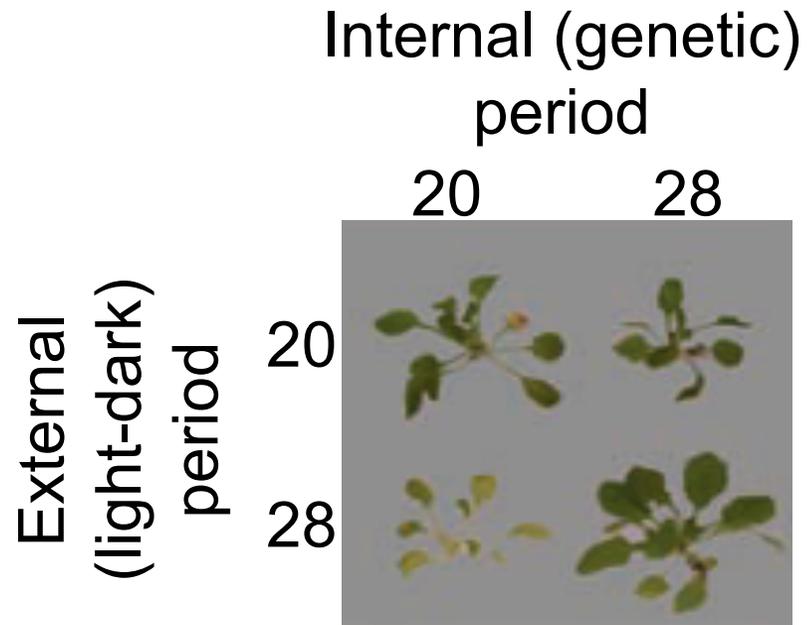
My early work in circadian biology

Recent work in my lab at Scripps

Q & A with YOU!



# Mismatch with natural cycles is detrimental



## Plant Circadian Clocks Increase Photosynthesis, Growth, Survival, and Competitive Advantage

Antony N. Dodd,<sup>1</sup> Neeraj Salathia,<sup>2\*</sup> Anthony Hall,<sup>2†</sup> Eva Kévei,<sup>3</sup>  
Réka Tóth,<sup>3</sup> Ferenc Nagy,<sup>3</sup> Julian M. Hibberd,<sup>1</sup> Andrew J. Millar,<sup>2‡</sup>  
Alex A. R. Webb<sup>1§</sup>



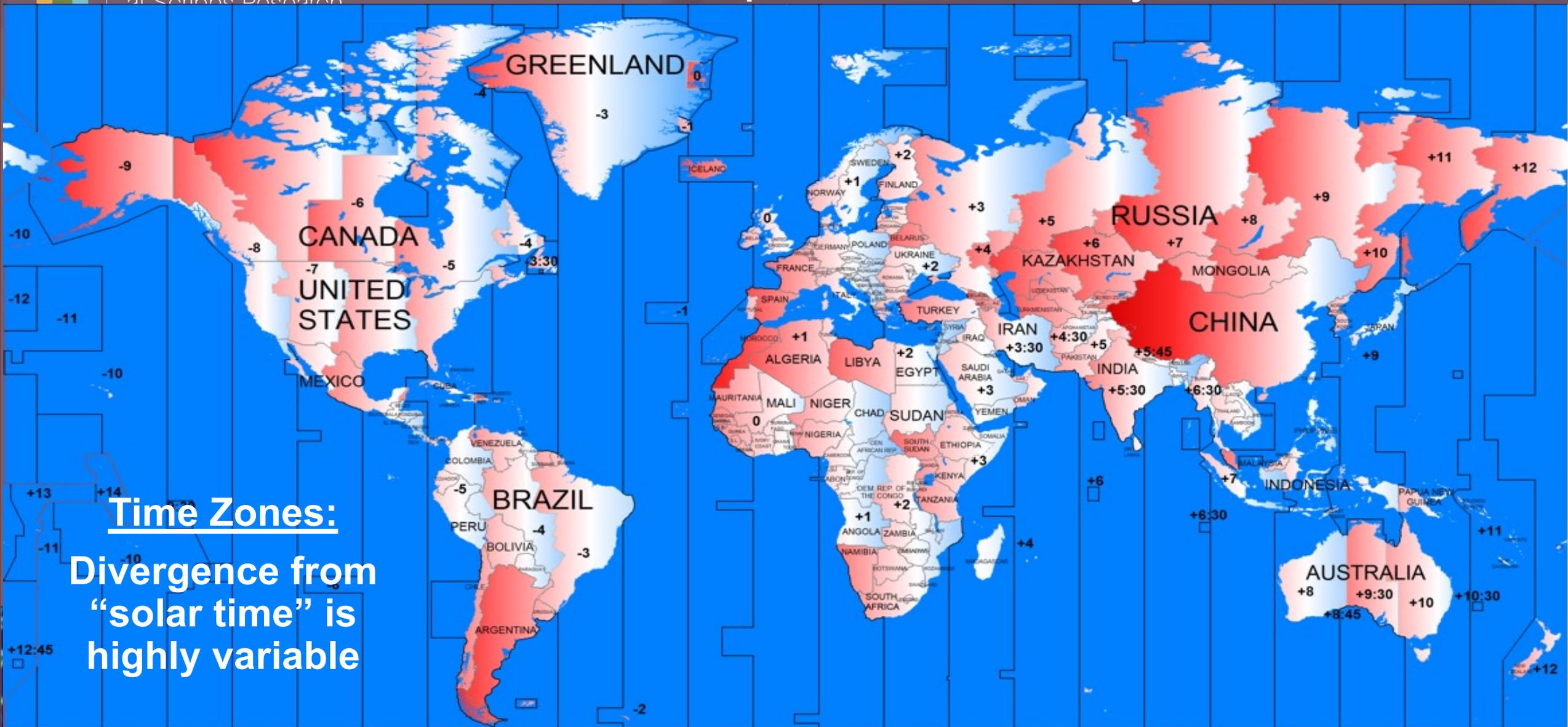


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# Disruption of natural cycles elevates risk

**Light at Night**

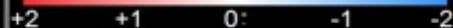




## Time Zones:

Divergence from  
“solar time” is  
highly variable

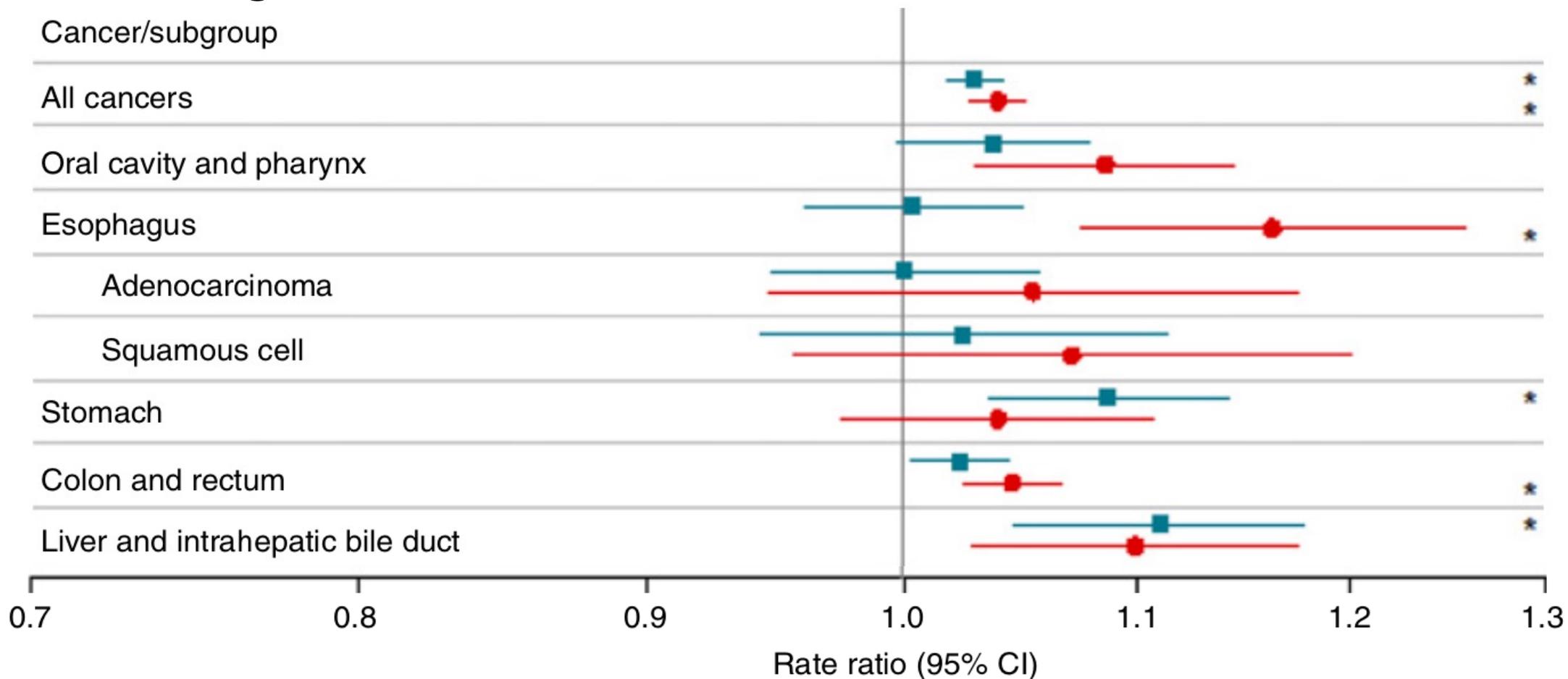
Difference between Solar Time and Standard Time (H)





## Time Zones:

**Westward divergence from “solar time” is associated with increased cancer risk**





## Shift Work





## RE: Night Shift Work and Breast Cancer Incidence: Three Prospective Studies and Meta-analysis of Published Studies

Eva S. Schernhammer



## **A meta-analysis including dose-response relationship between night shift work and the risk of colorectal cancer**

Xiao Wang<sup>1</sup>, Alin Ji<sup>1</sup>, Yi Zhu<sup>1</sup>, Zhen Liang<sup>1</sup>, Jian Wu<sup>1</sup>, Shiqi Li<sup>1</sup>, Shuai Meng<sup>1</sup>,  
Xiangyi Zheng<sup>1</sup>, Liping Xie<sup>1</sup>

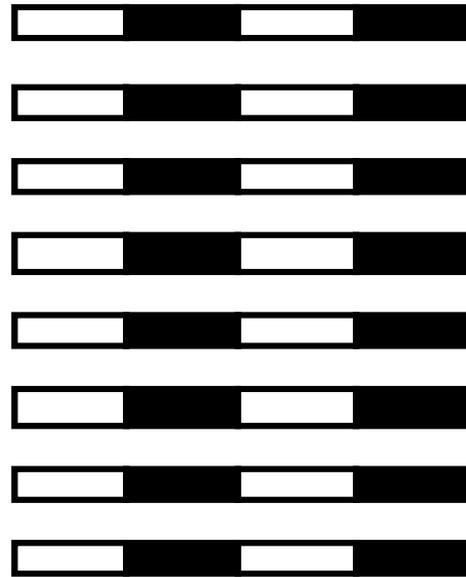


## Does night-shift work increase the risk of prostate cancer? a systematic review and meta-analysis

Dapang Rao, Haifeng Yu, Yu Bai, Xiangyi Zheng, Liping Xie

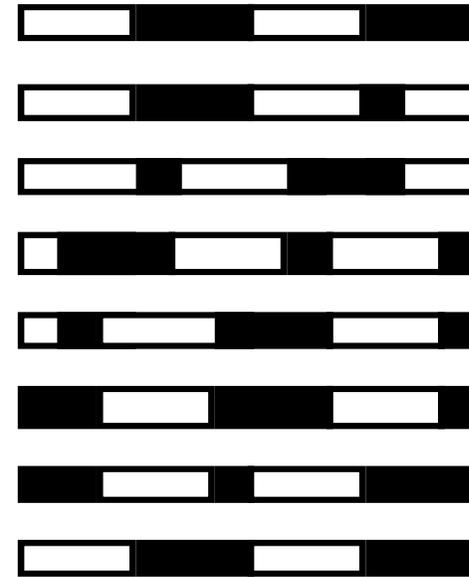


## Control (12:12LD)



⋮

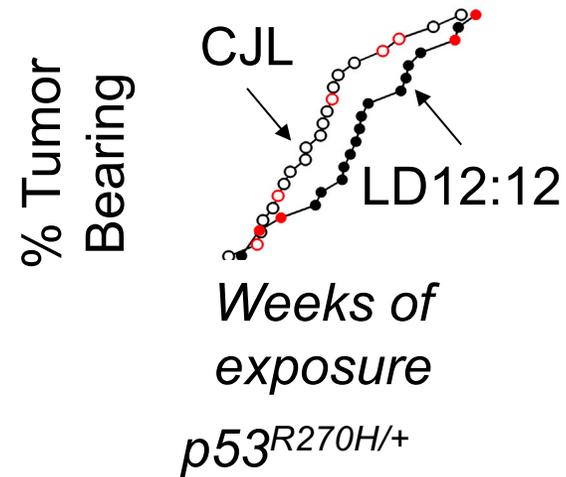
## Chronic Jetlag (CJL)



⋮

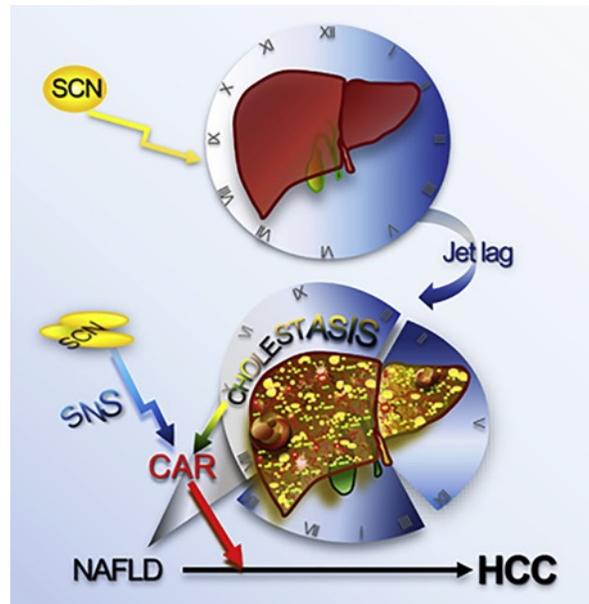


## Breast Cancer



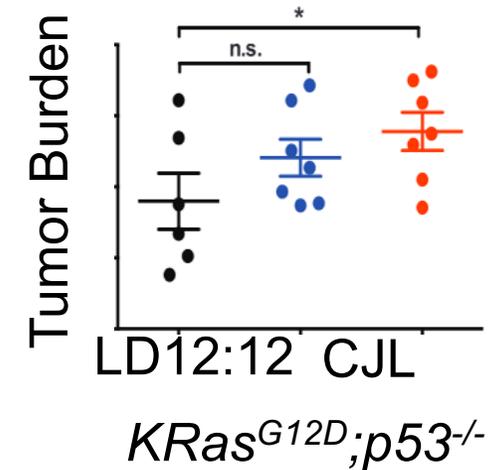
Van Dycke et al., 2011

## Liver Cancer



Kettner et al., 2016

## Lung Cancer

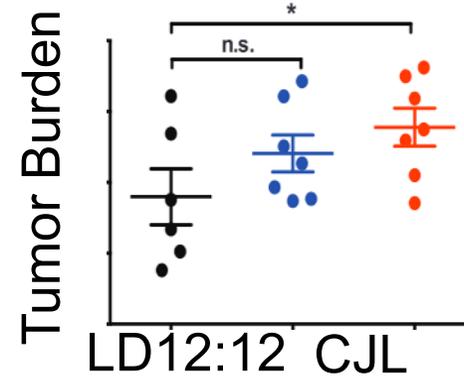


Papagiannakopoulos et al., 2016



**Marie  
Pariollaud**

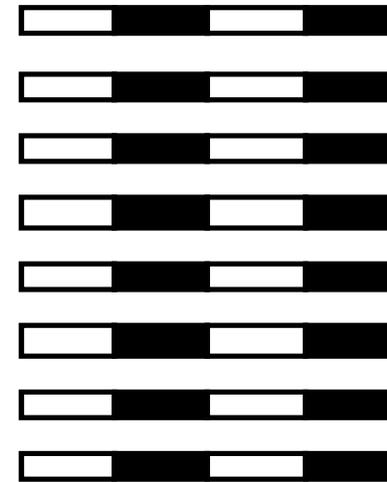
## Lung Cancer



*KRas*<sup>G12D</sup>

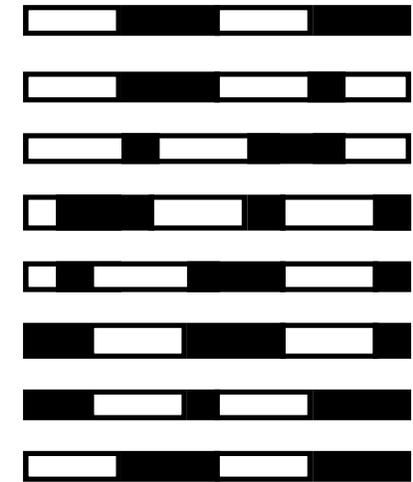
Papagiannakopoulos  
et al., 2016

## Control (12:12LD)

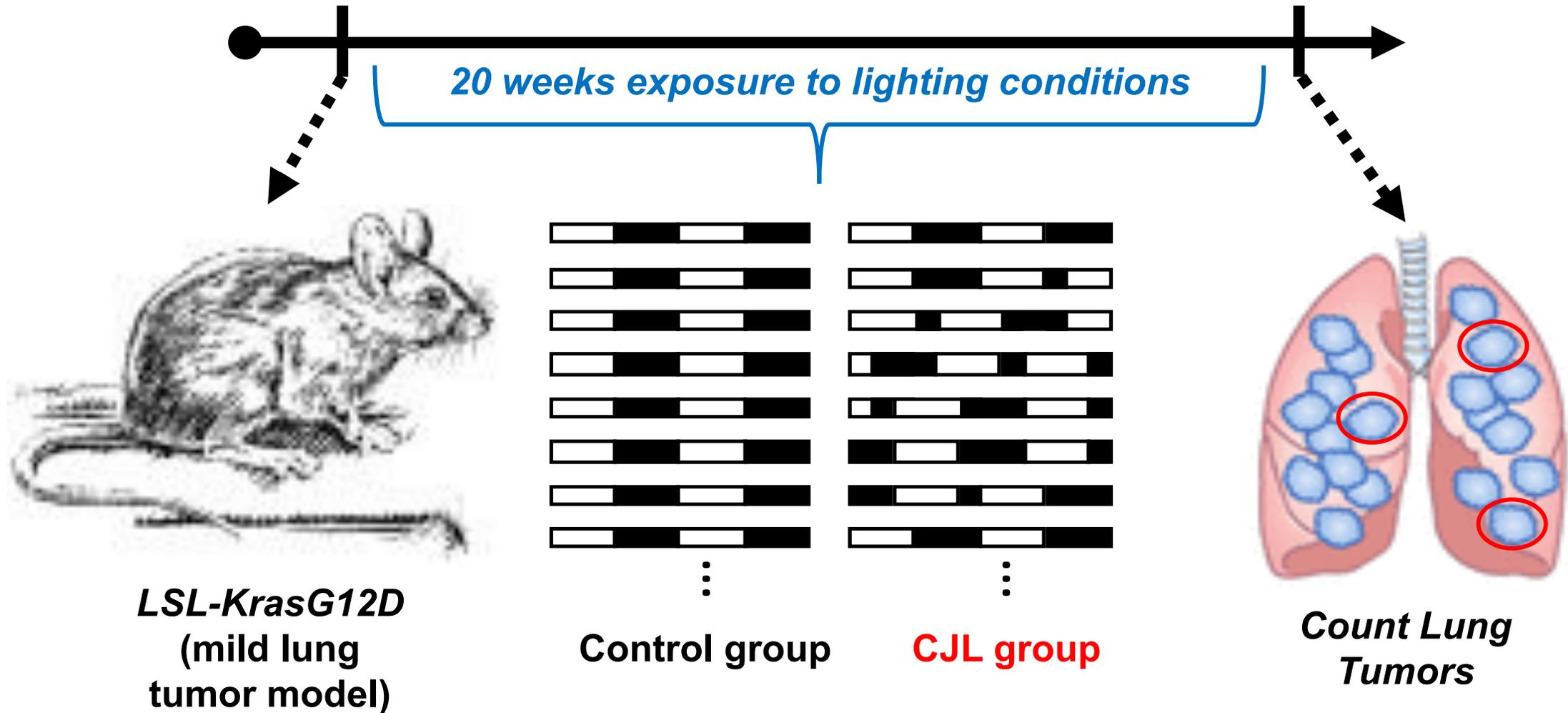


⋮

## Chronic Jetlag (CJD)

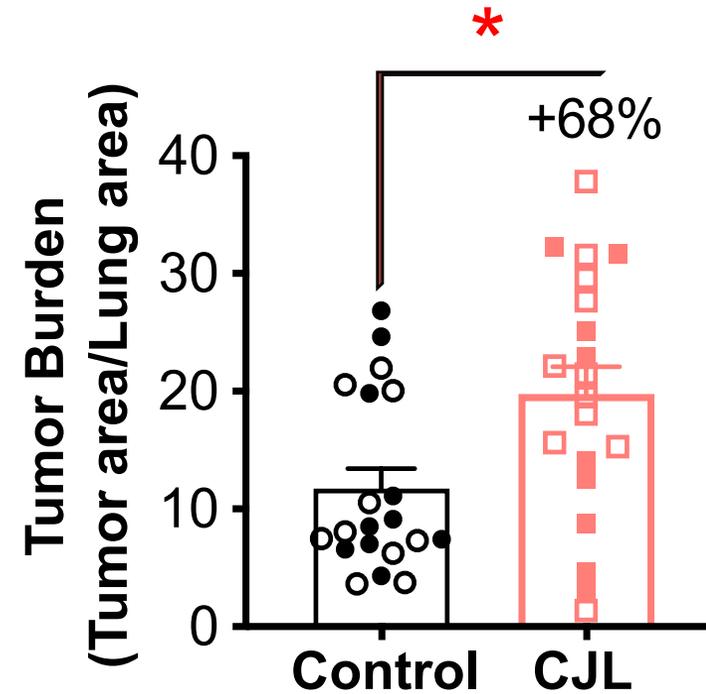


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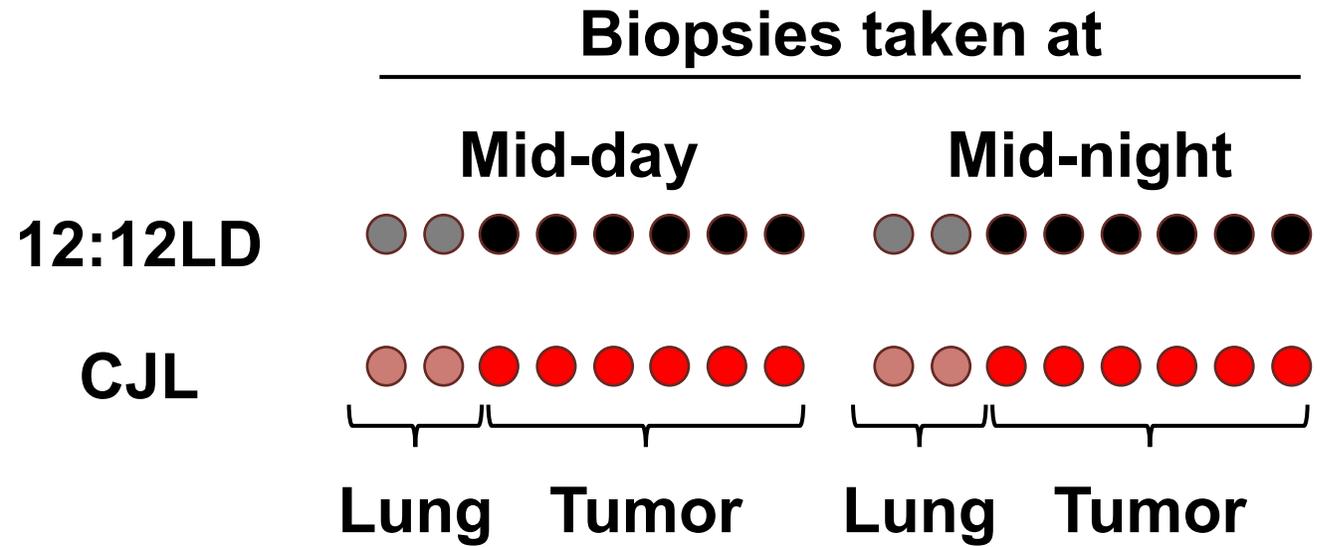
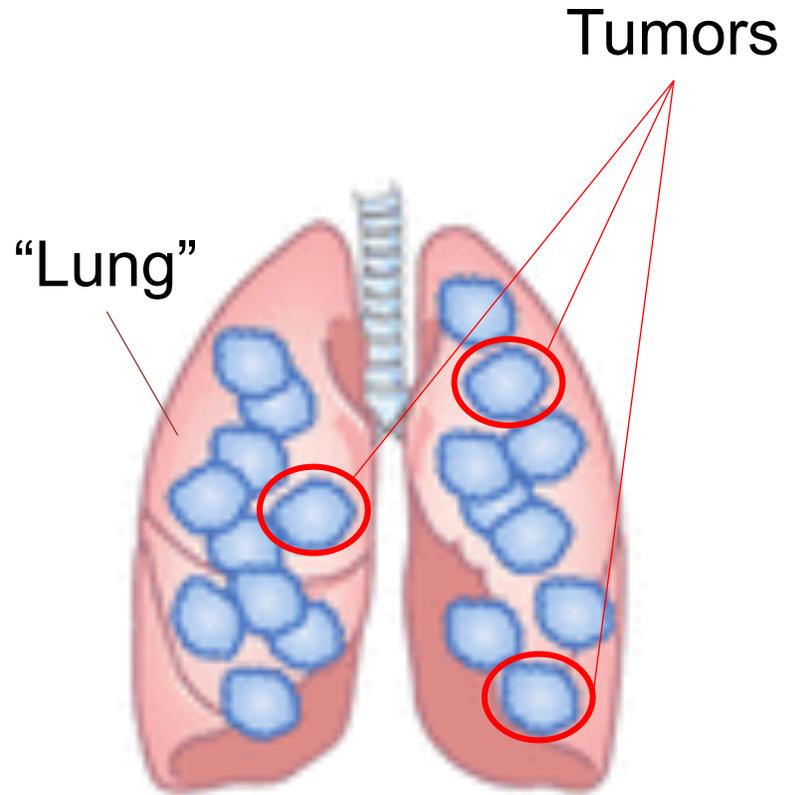


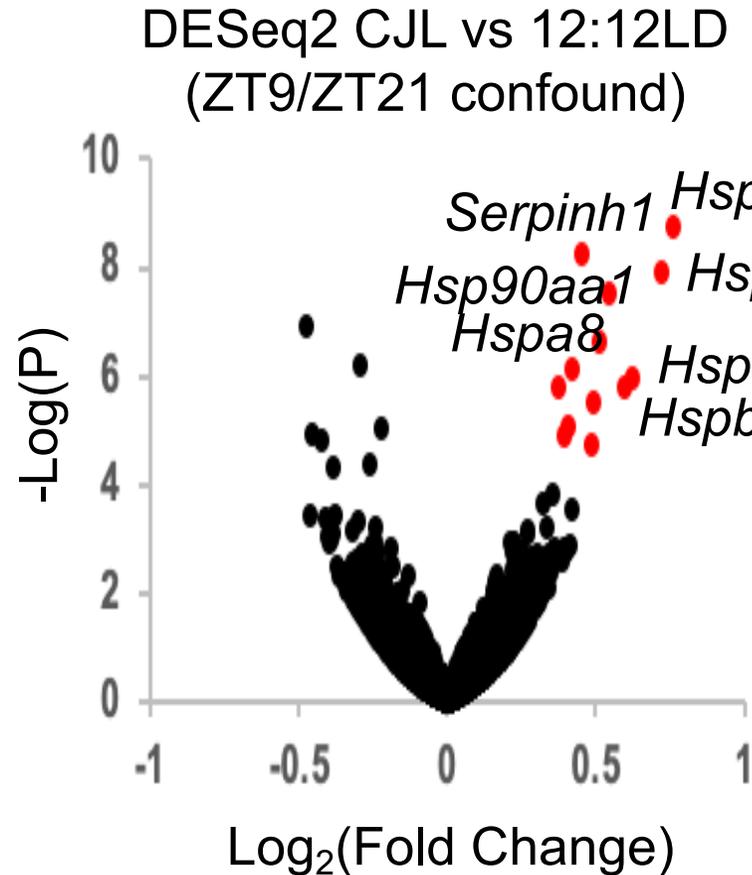


Circadian disruption  
increased lung tumors  
by 68%



Marie Pariollaud et al., (2022) *Science Advances*



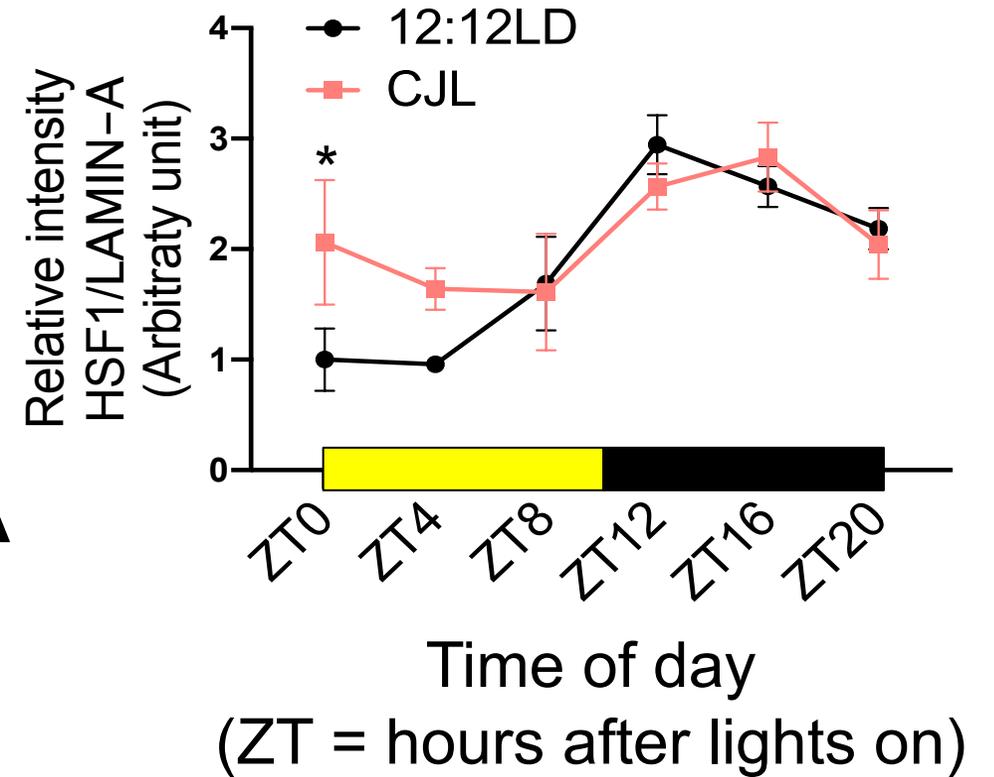
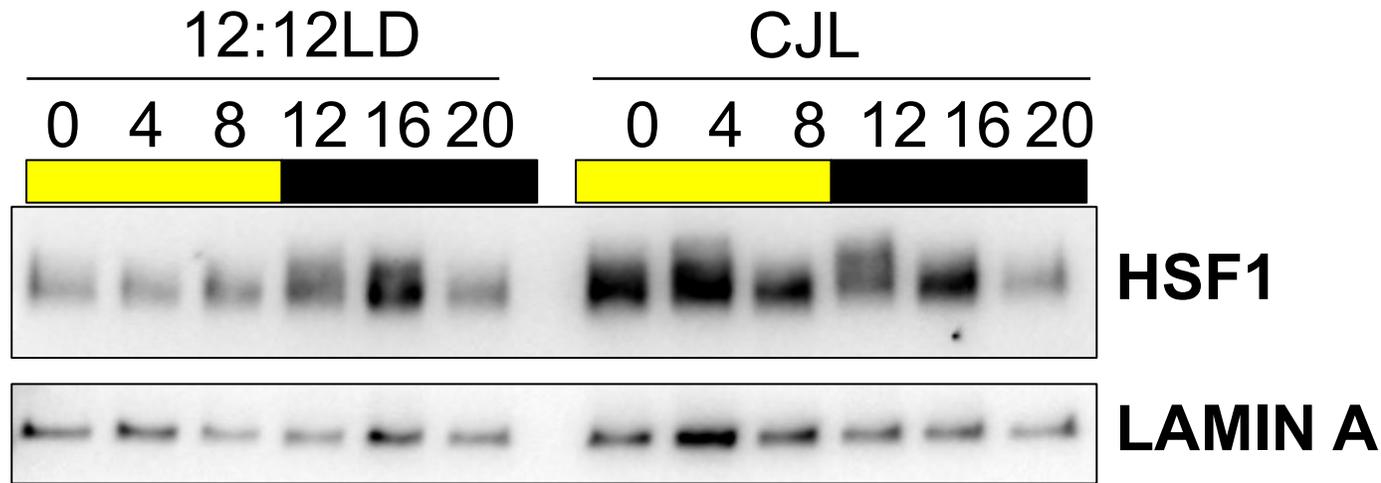


*Hsp* = "Heat shock protein"

CJL activates genes that are turned on by heat

These genes are controlled by a transcription factor called "Heat Shock Factor 1" (HSF1)







## Misaligned core body temperature rhythms impact cognitive performance of hospital shift work nurses

Hylton E. Molzof<sup>c</sup>, Aoyjai Prapanjaroensin<sup>a</sup>, Vivek H. Patel<sup>b</sup>, Mugdha V. Mokashi<sup>b</sup>,  
Karen L. Gamble<sup>b,\*</sup>, Patricia A. Patrician<sup>a,\*</sup>

## Characterizing the modern light environment and its influence on circadian rhythms

Dennis Khodasevich<sup>1</sup>, Susan Tsui<sup>2</sup>, Darwin Keung<sup>1</sup>, Debra J. Skene<sup>3</sup>,  
Victoria Revell<sup>4</sup> and Micaela E. Martinez<sup>5</sup>





The Lamia Lab:

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*Emanuel Irizarry*

Lamia Lab Alumni:

***Marie Pariollaud***

*Alanna Chan*

*Drew Duglan*

*Nuria Casanova-Vallve*

*Anne-Laure Huber*

*Sabine Jordan*

*Stephanie (Papp) Correia*

*Lara-Leonie Fetzer*

*Helena Althammer*

*Megan Vaughan*

*Julien Delezie*

*Emma Henriksson*

*Anna Kriebs*

*Erin (Dunn) Soto*

Key Collaborators:

*Luke Wiseman*

*Evan Powers*

*Michael Bollong*

*Lara Ibrahim*

*Reuben Shaw*

*Brian Altman*

*Ron Evans*

*Carrie Partch*

*Michael Downes*

*Ruth Yu*

*Chris Liddle*

*Pal Westermark*

*Christian Metallo*

*Kirk Lohmueller*





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National Cancer Institute  
National Institute For Environmental Health & Safety



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