

# *Circadian Control of Nucleotide Excision Repair*

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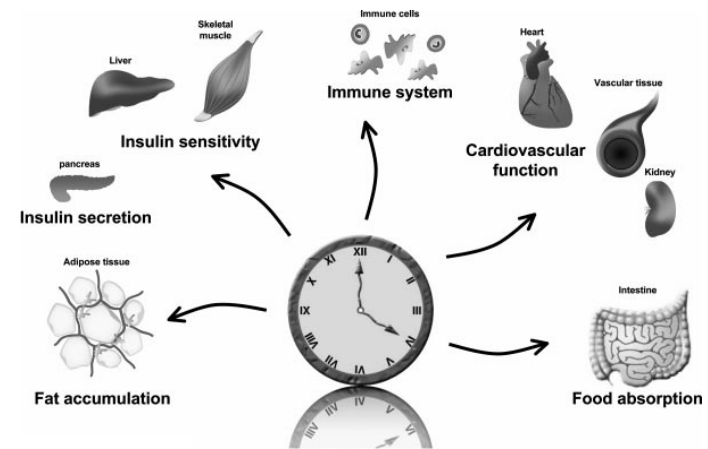
Aziz Sancar Lab

# Circadian (Daily) Oscillation of Biological Processes

*circa*, "around," and *diem* or *dies*, "a day"

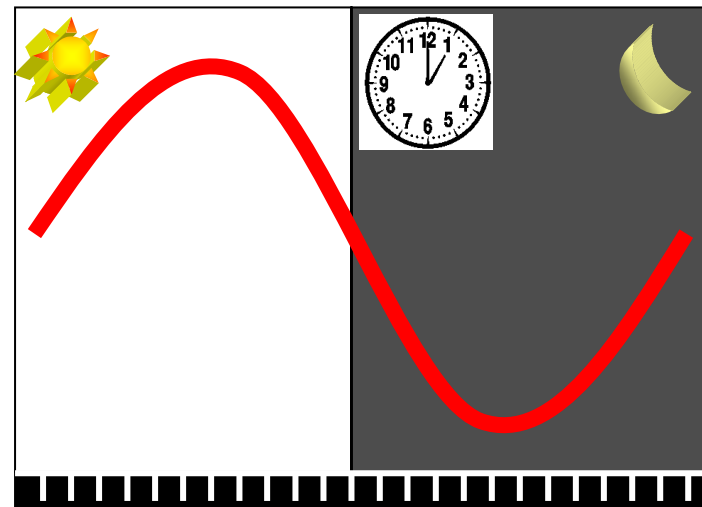


[www.learner.org/jnorth/images](http://www.learner.org/jnorth/images)

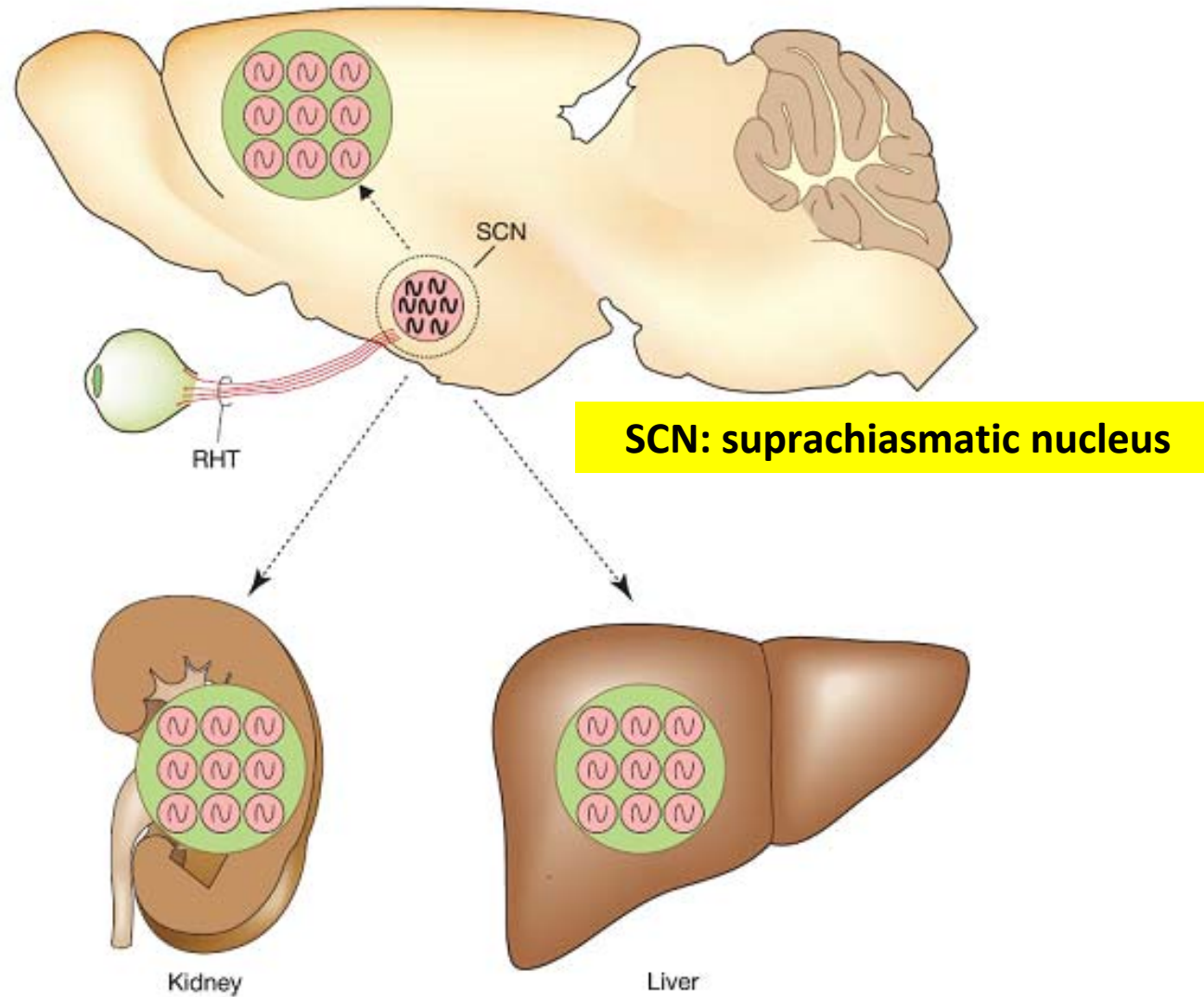


Maury et al. *Circ Res* (2010) 106, 447-462

## Circadian (Daily) Rhythm

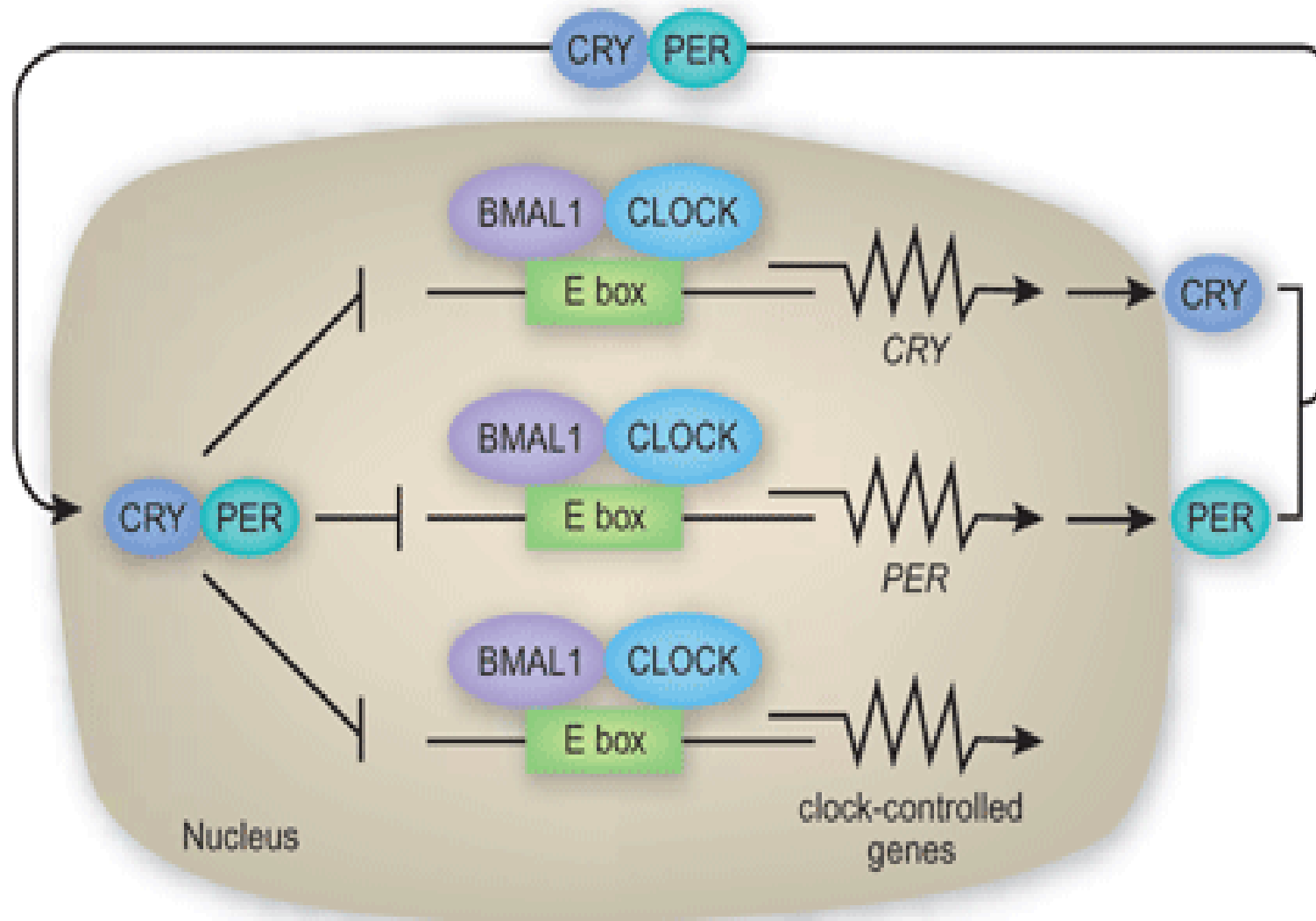


# Hierarchy of Mammalian Circadian Timing System



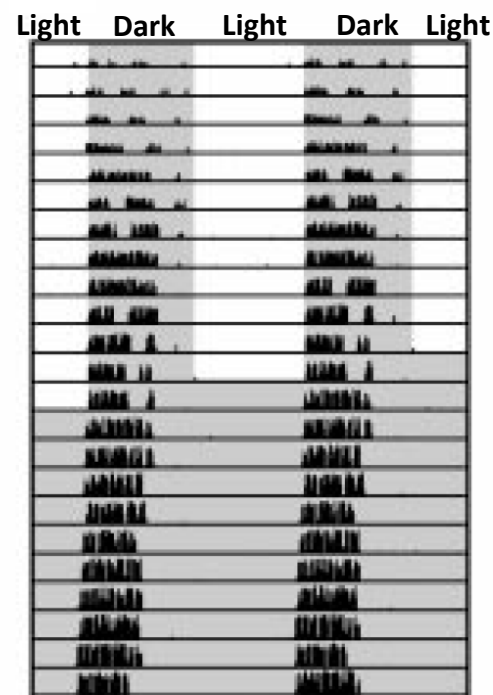
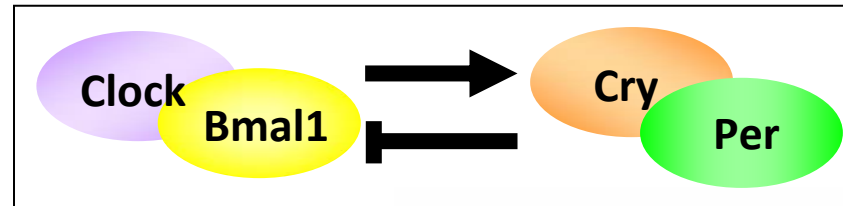
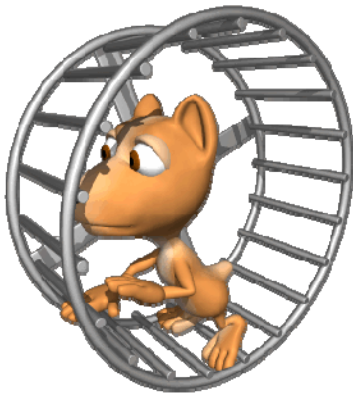
**Nature** (2002) 418, 935-941

# Molecular Clock

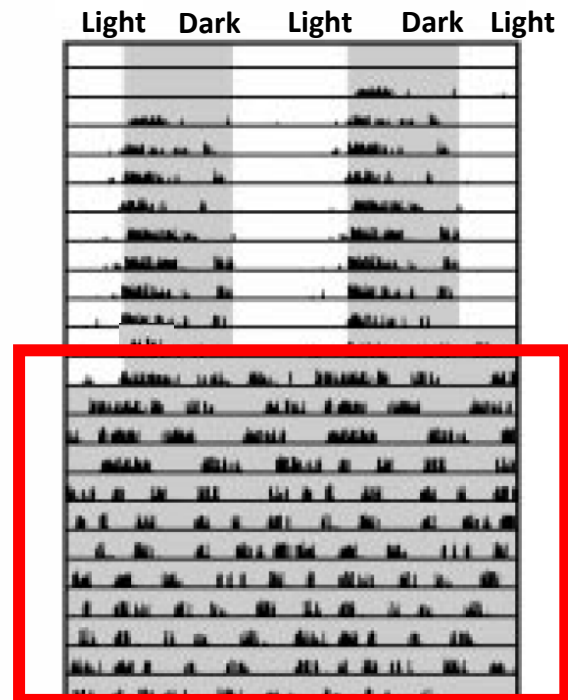


# Loss of Rhythmic Behavior in Clock-deficient Mice

Actogram: Wheel running activity

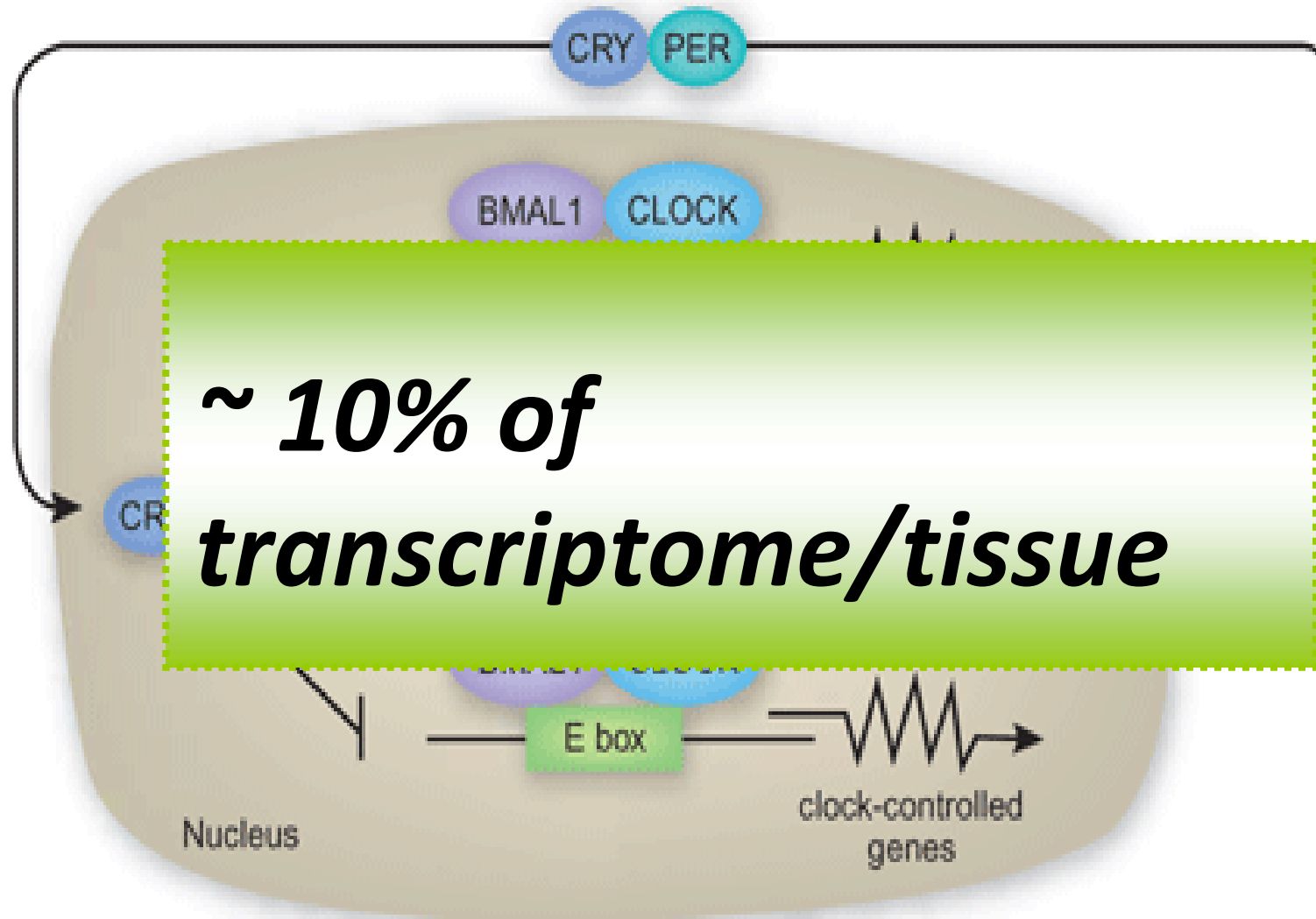


Wild type  
 $\tau = 23.77 \pm 0.07$  h

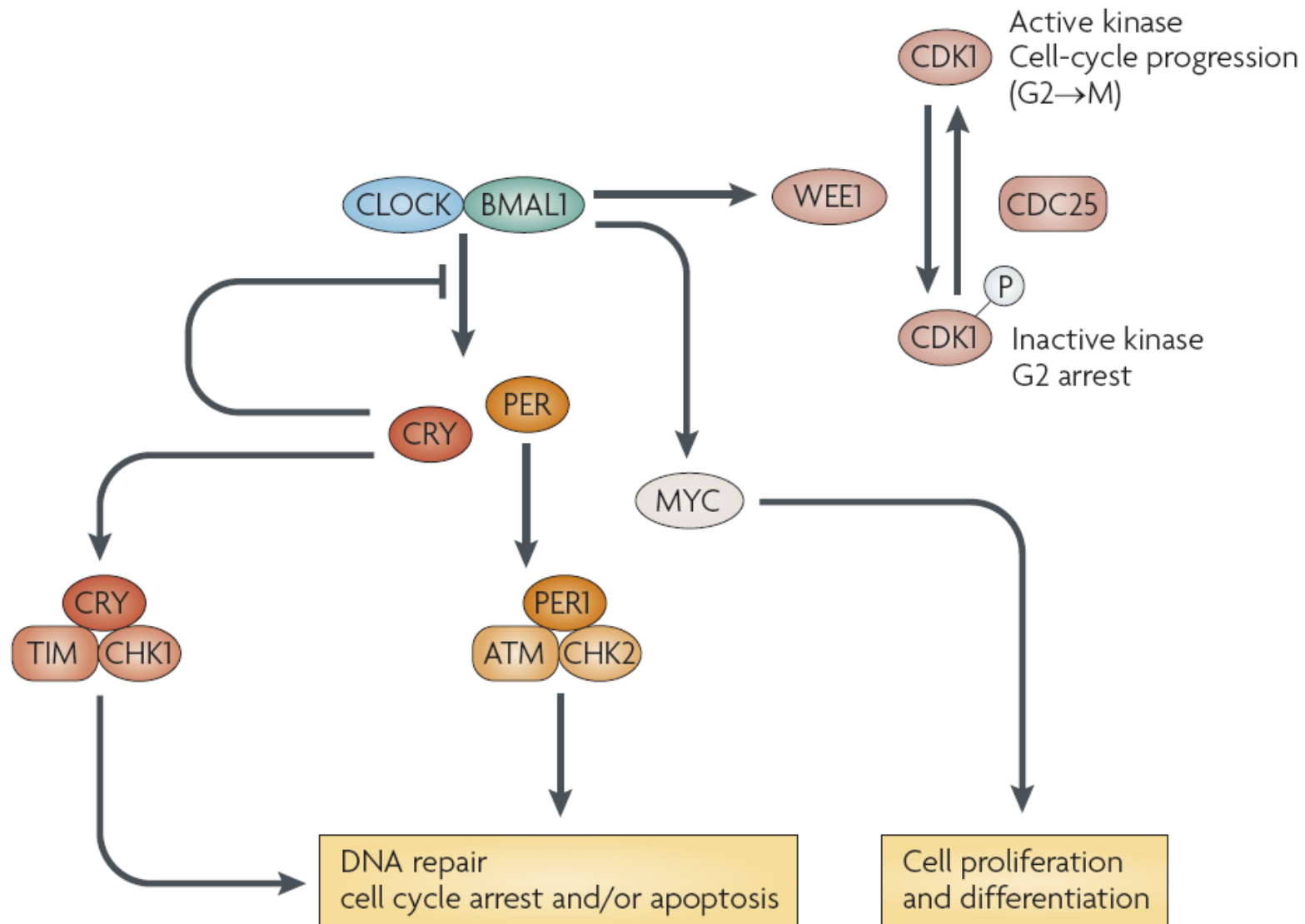


*cry1<sup>-/-</sup>cry2<sup>-/-</sup>*  
 Immediate arrhythmicity

# Capacity of Molecular Clock



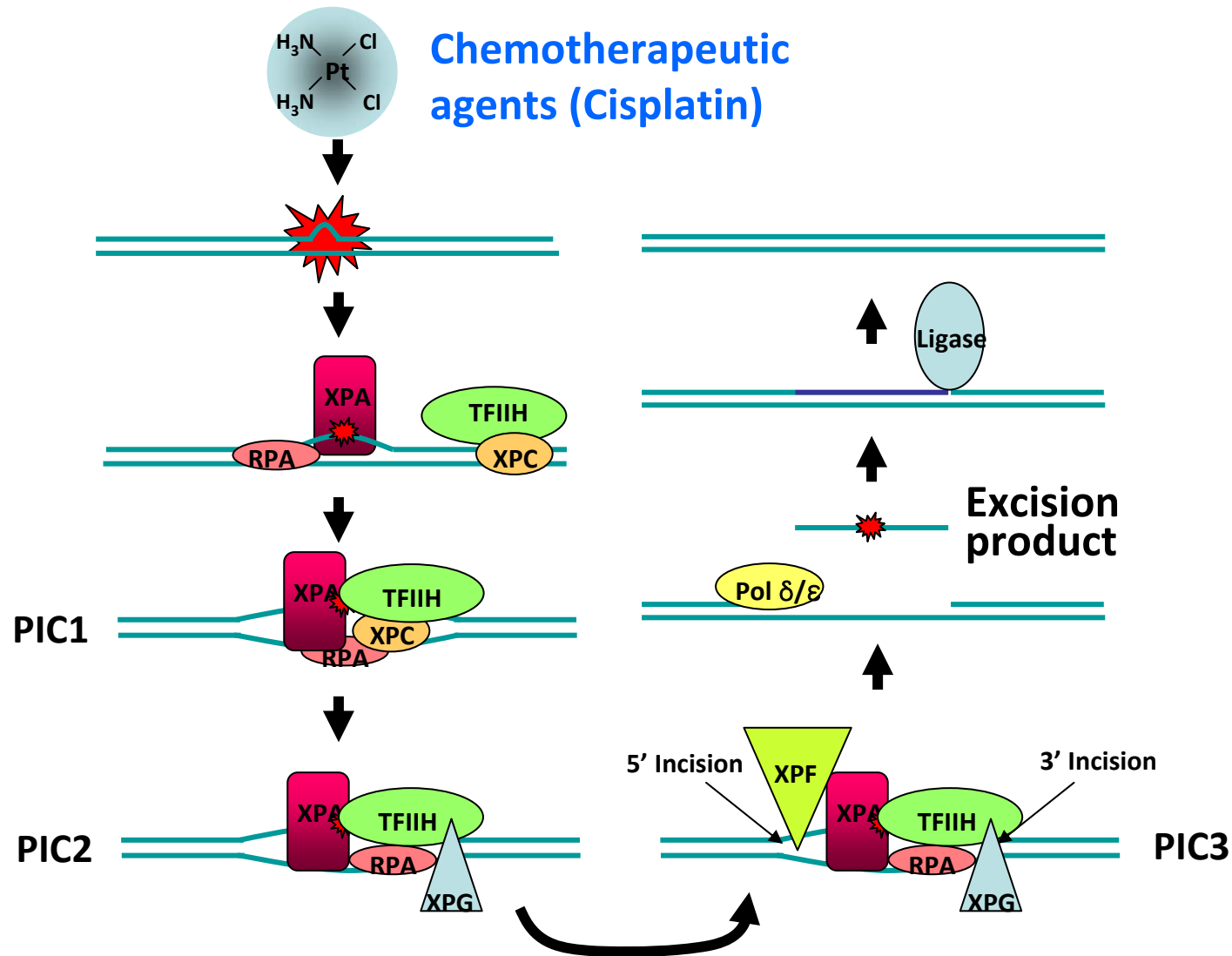
# Circadian Control of Cell-division Cycles



Nat Rev Genet (2008) 9, 764-75

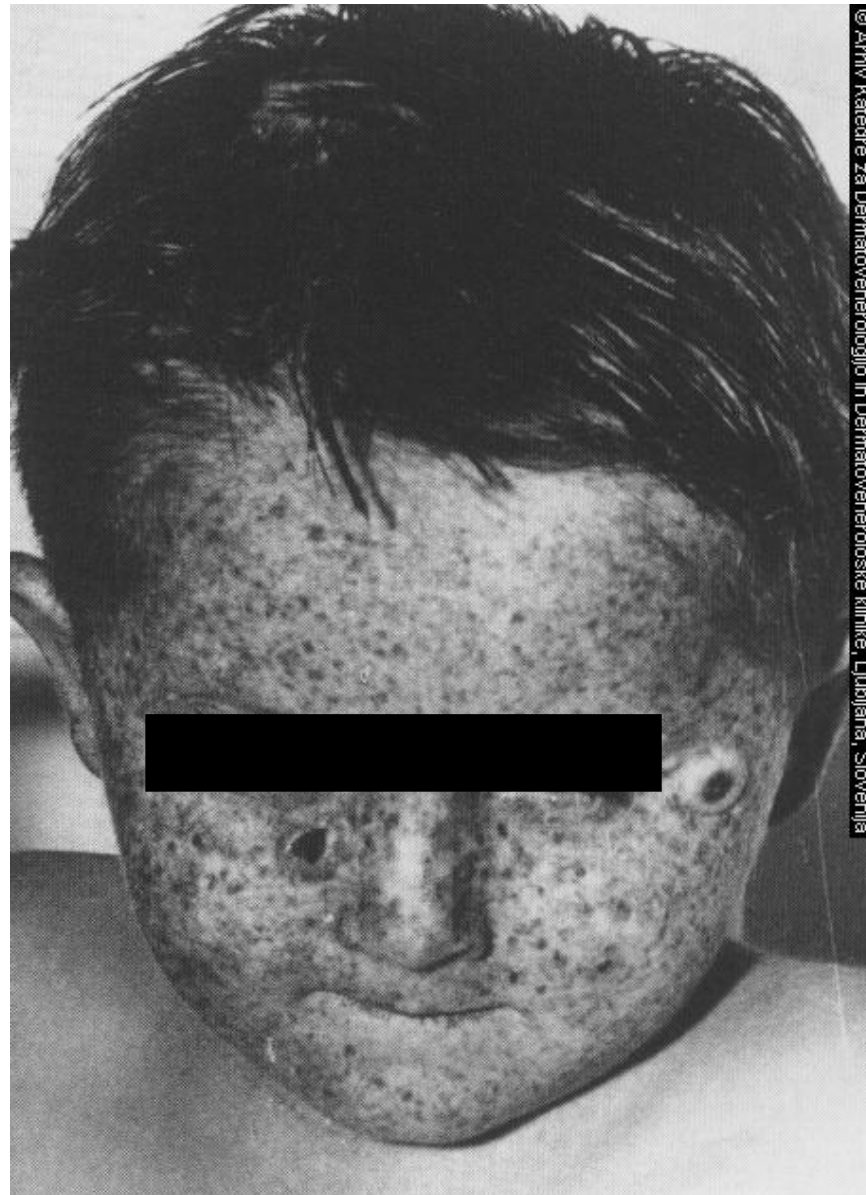


# Nucleotide Excision Repair



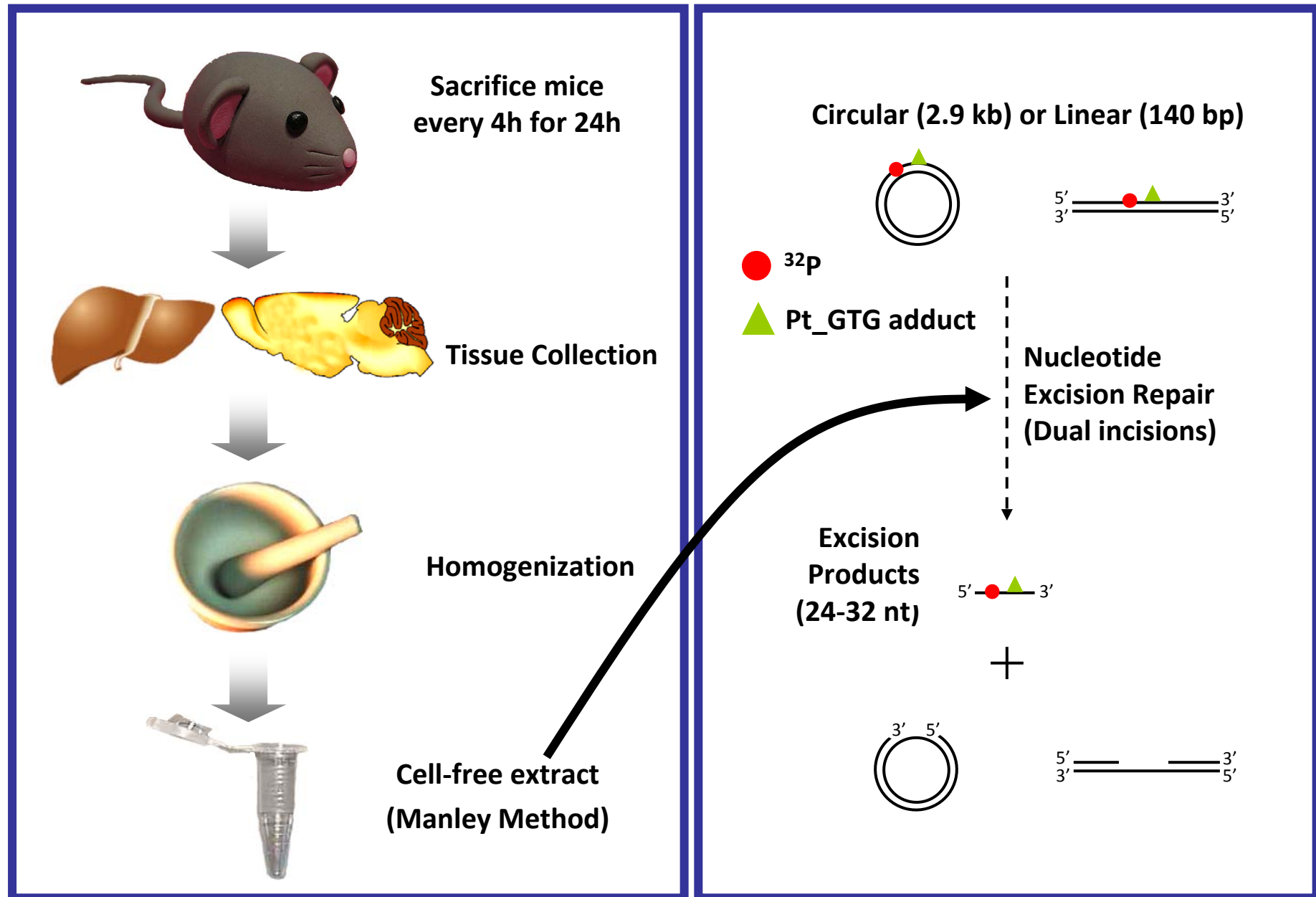


# Xeroderma pigmentosum (XP)

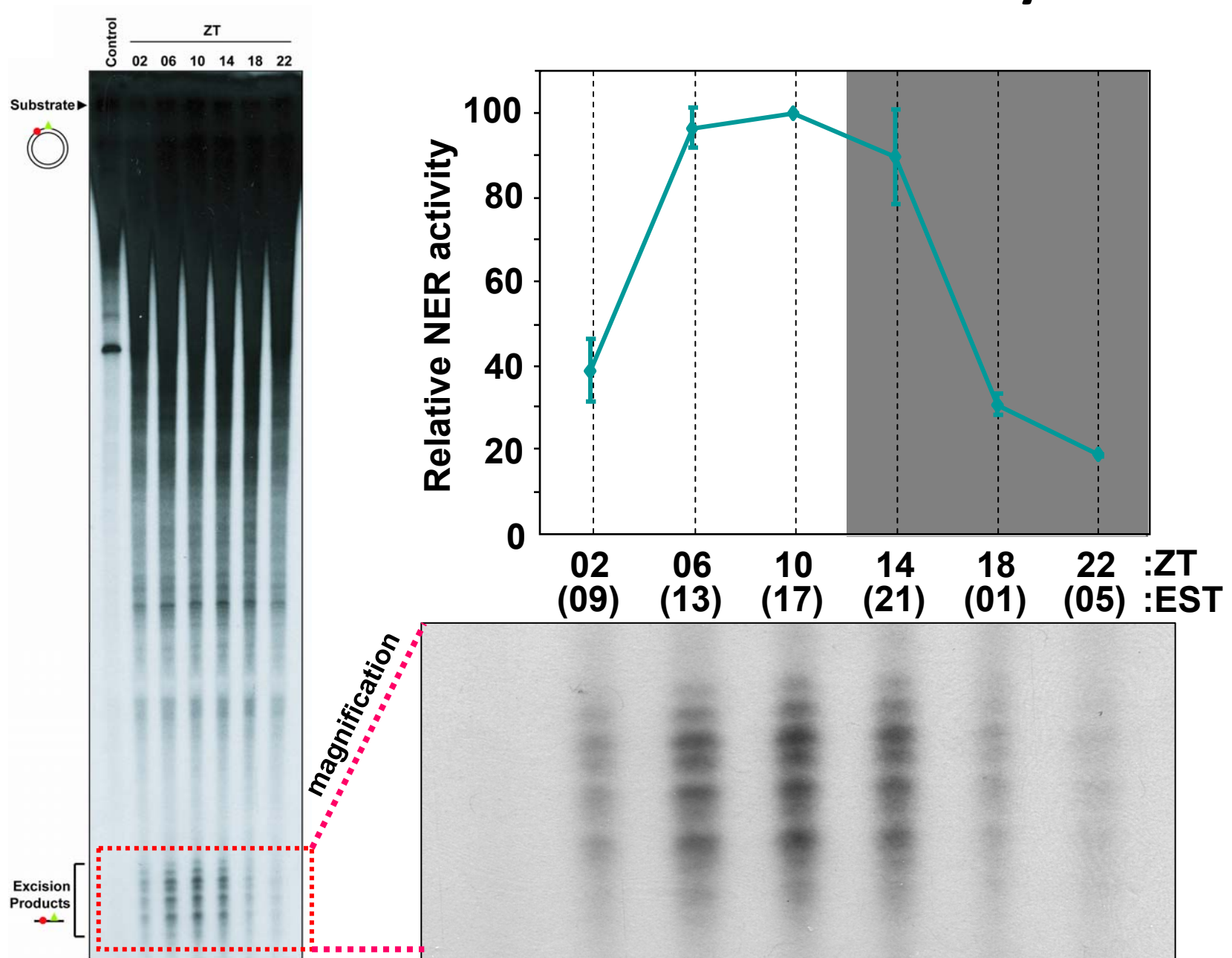


Google Image

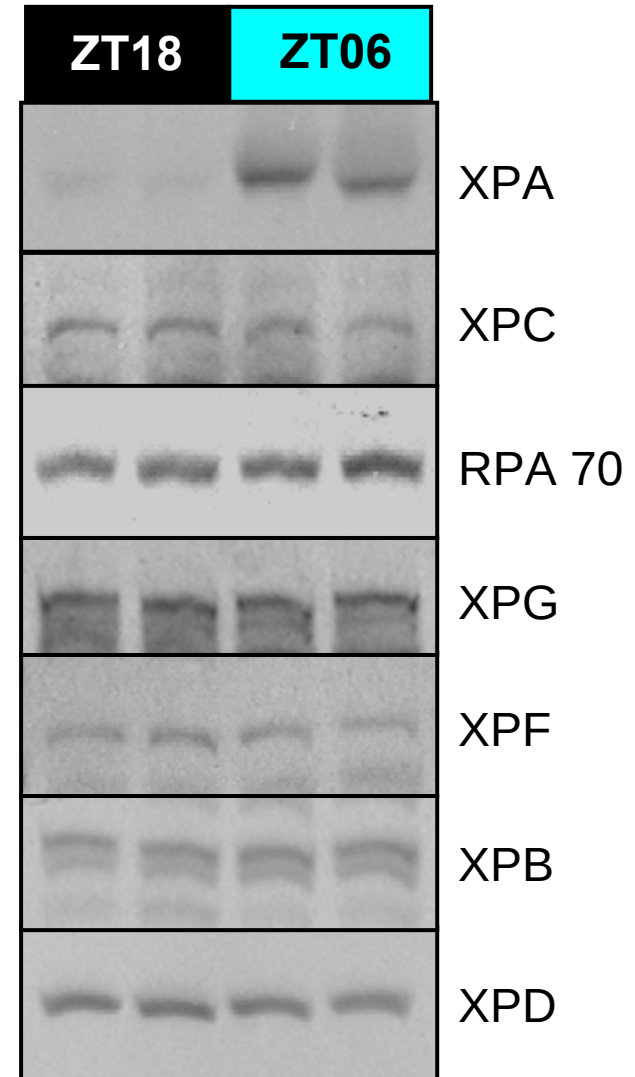
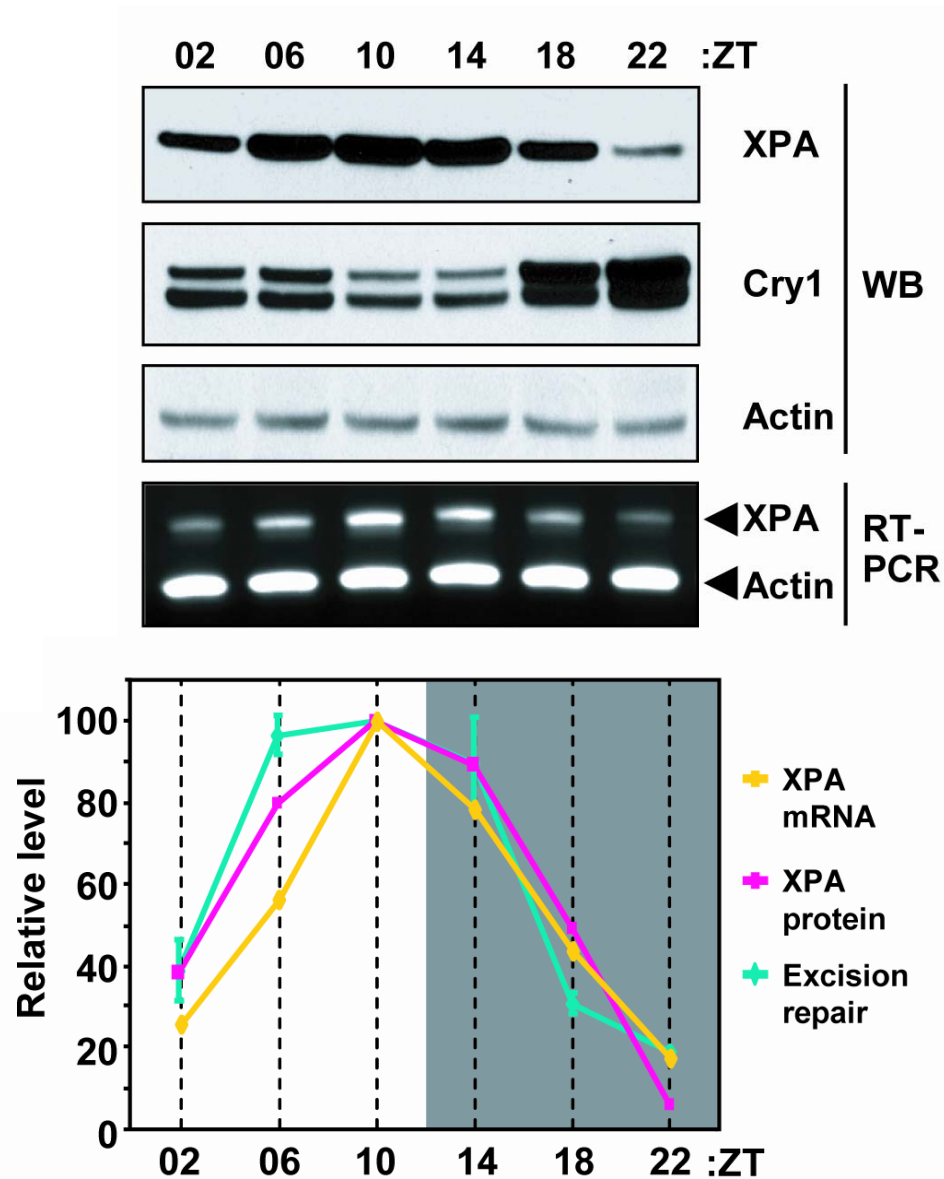
# DNA Excision Repair Activity Assay

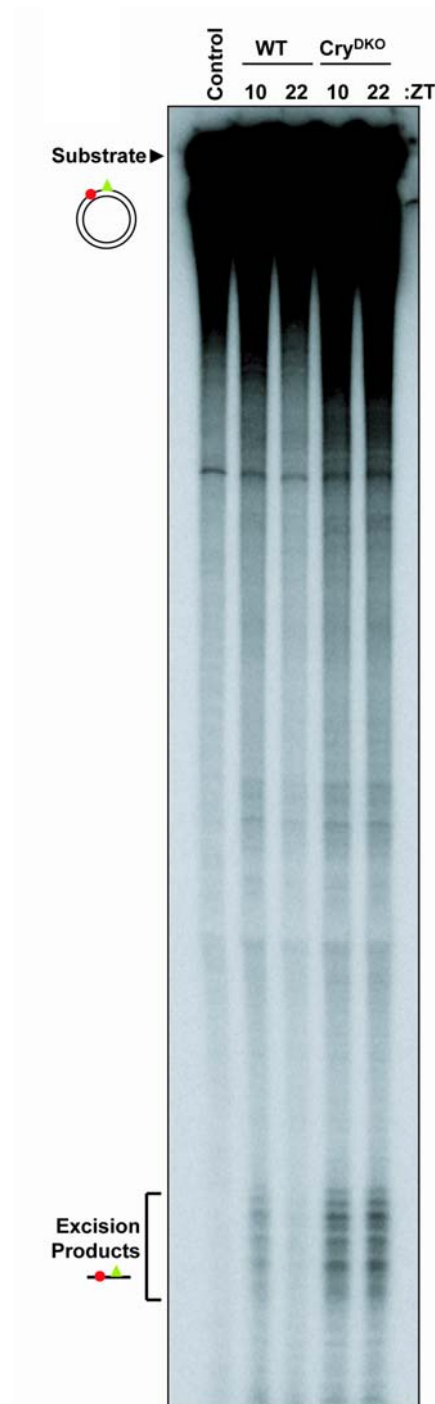


# Circadian Oscillation of NER Activity

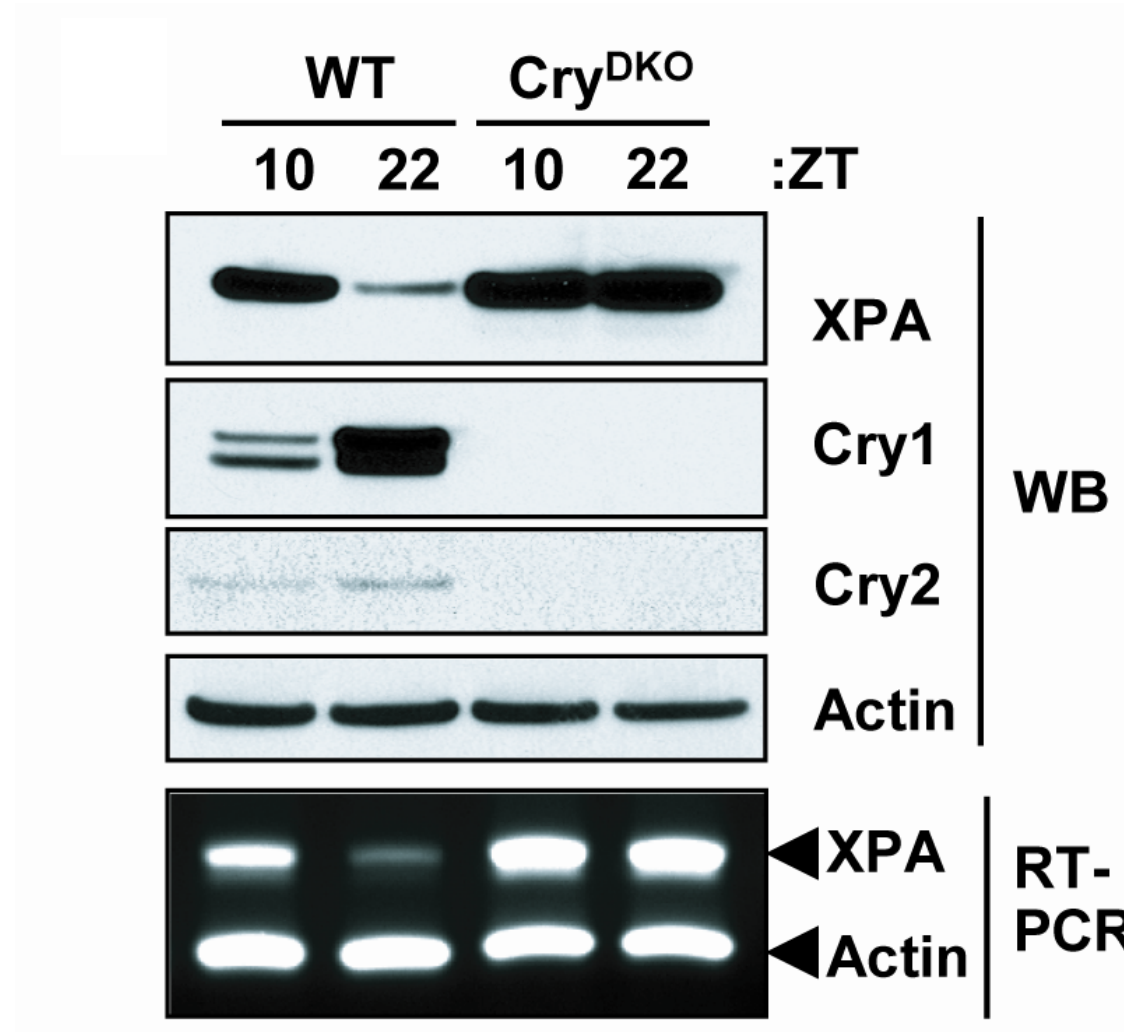


# Circadian Oscillation of XPA

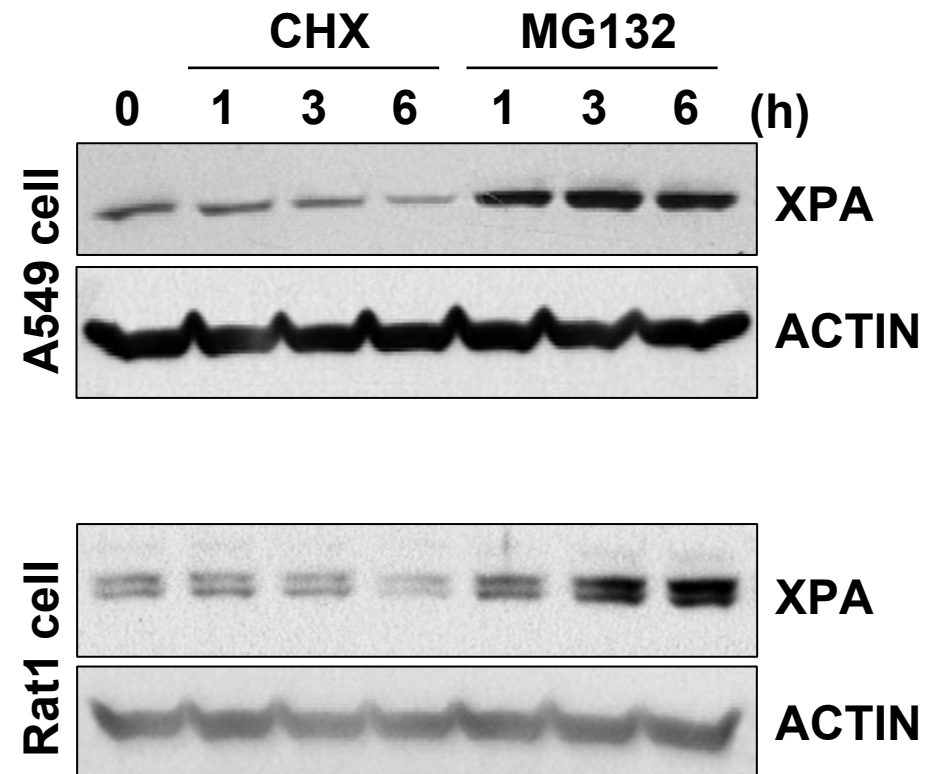
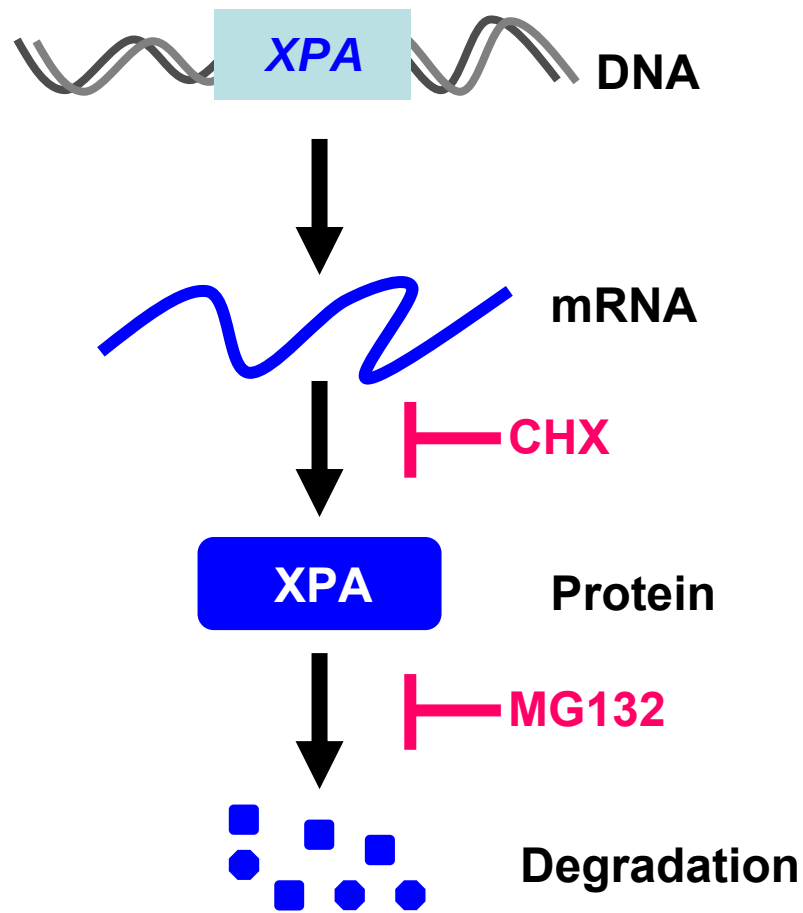




## Loss of Circadian Oscillation of XPA expression and NER Activity in Clock-deficient mouse

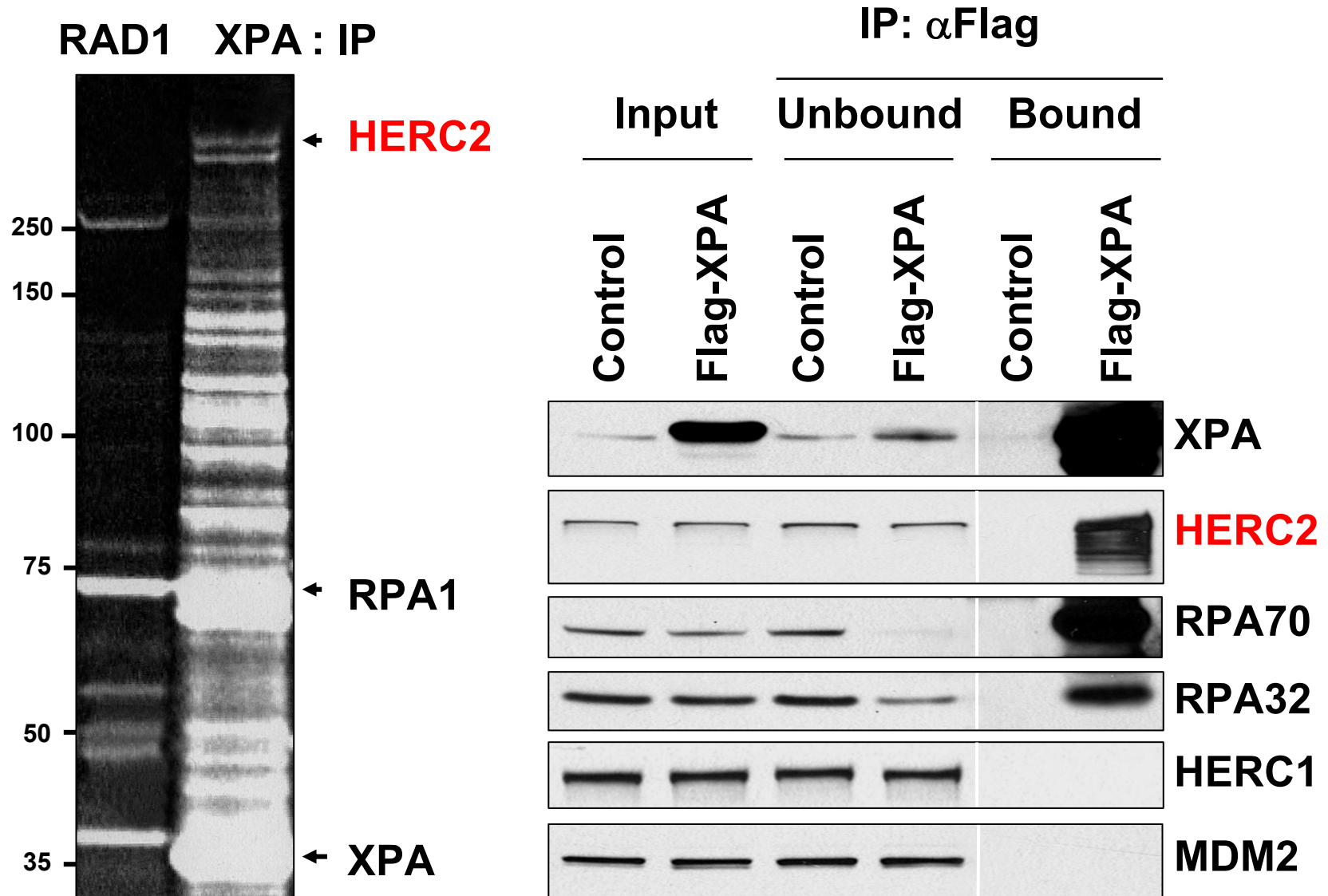


# Degradation of XPA by the proteasome



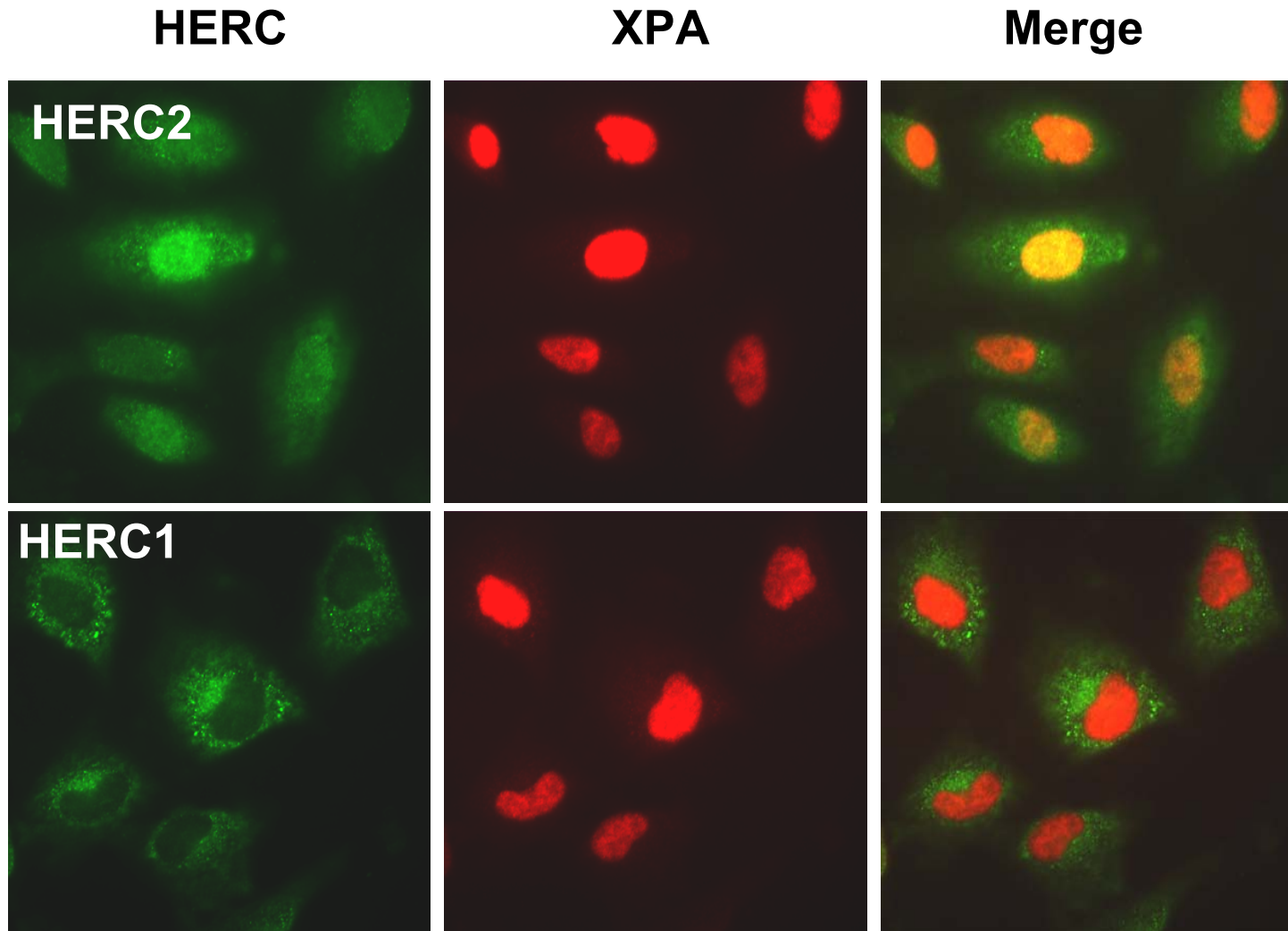


# Interaction of XPA and ubiquitin E3 ligase HERC2

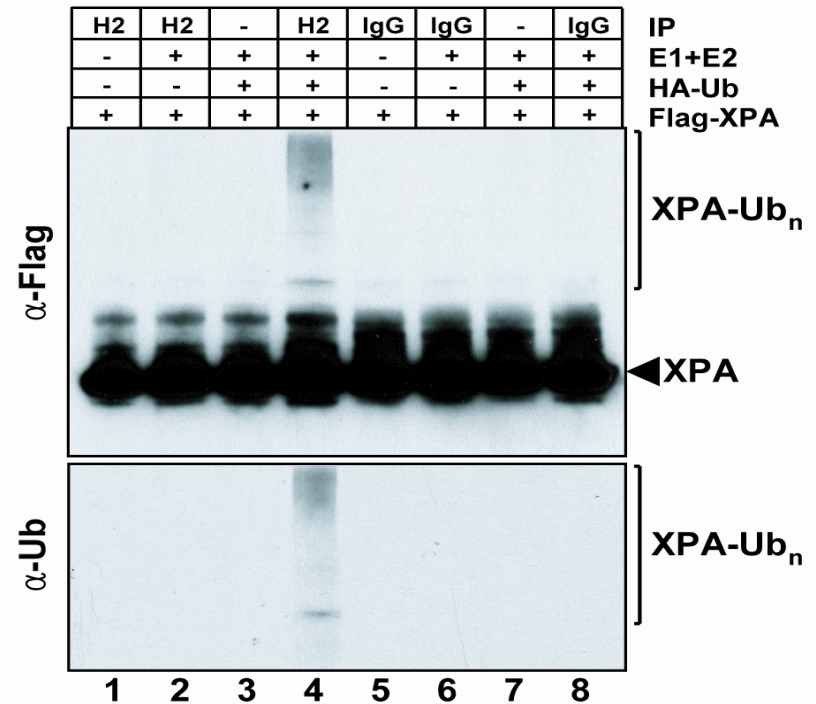
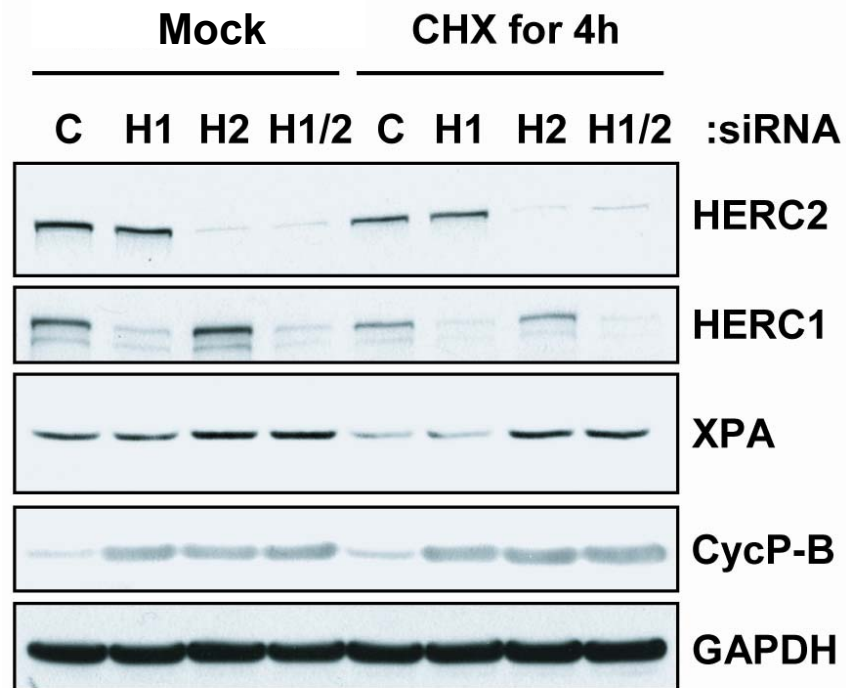




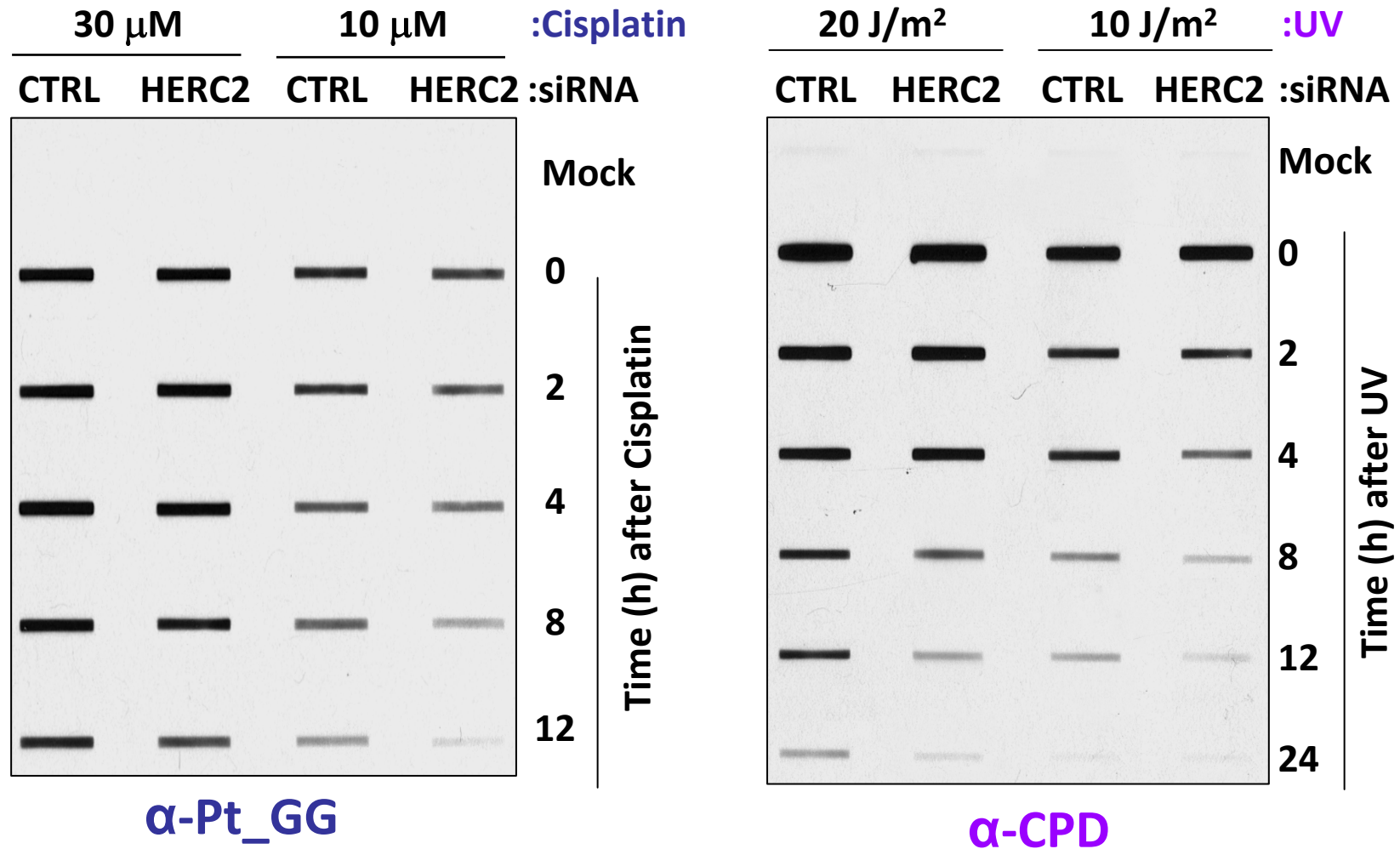
# Interaction of XPA and ubiquitin E3 ligase HERC2



# HERC2 is an E3 Ub-ligase for XPA

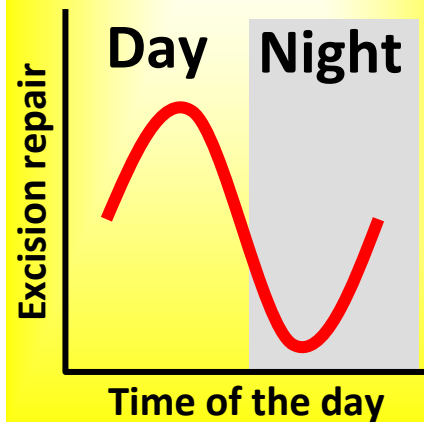
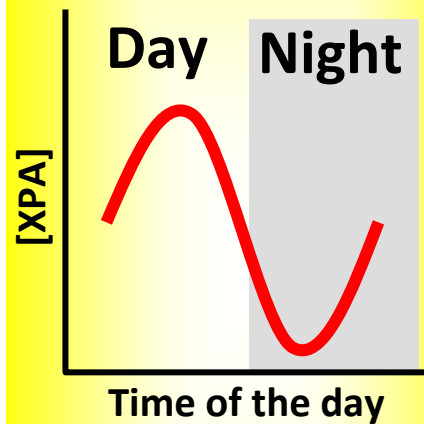


# Augmentation of NER activity by HERC2 down-regulation

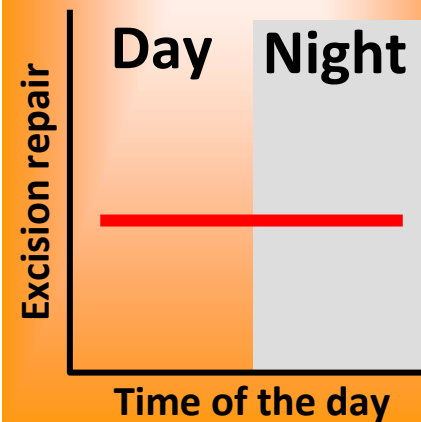
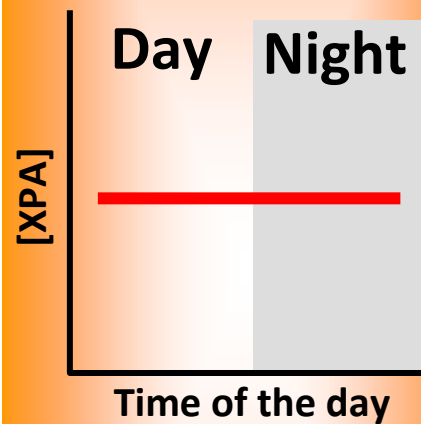


# Conclusion

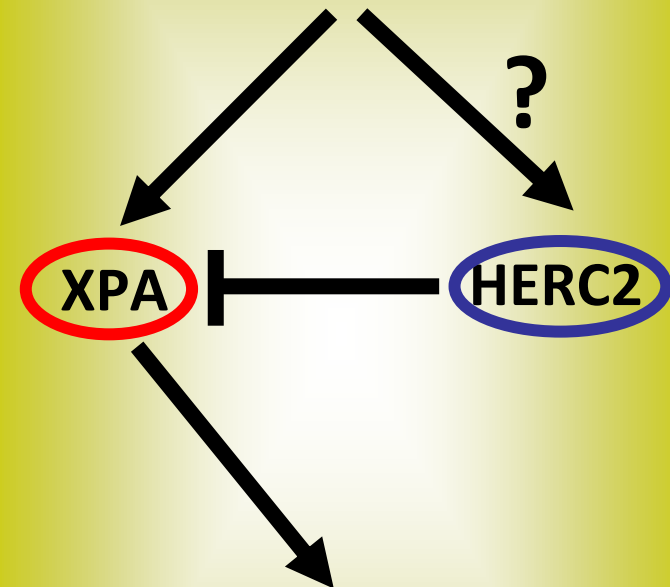
Liver,  
Brain,  
Kidney ...



Testis,  
 $Cry^{DKO}$



## Circadian Clock



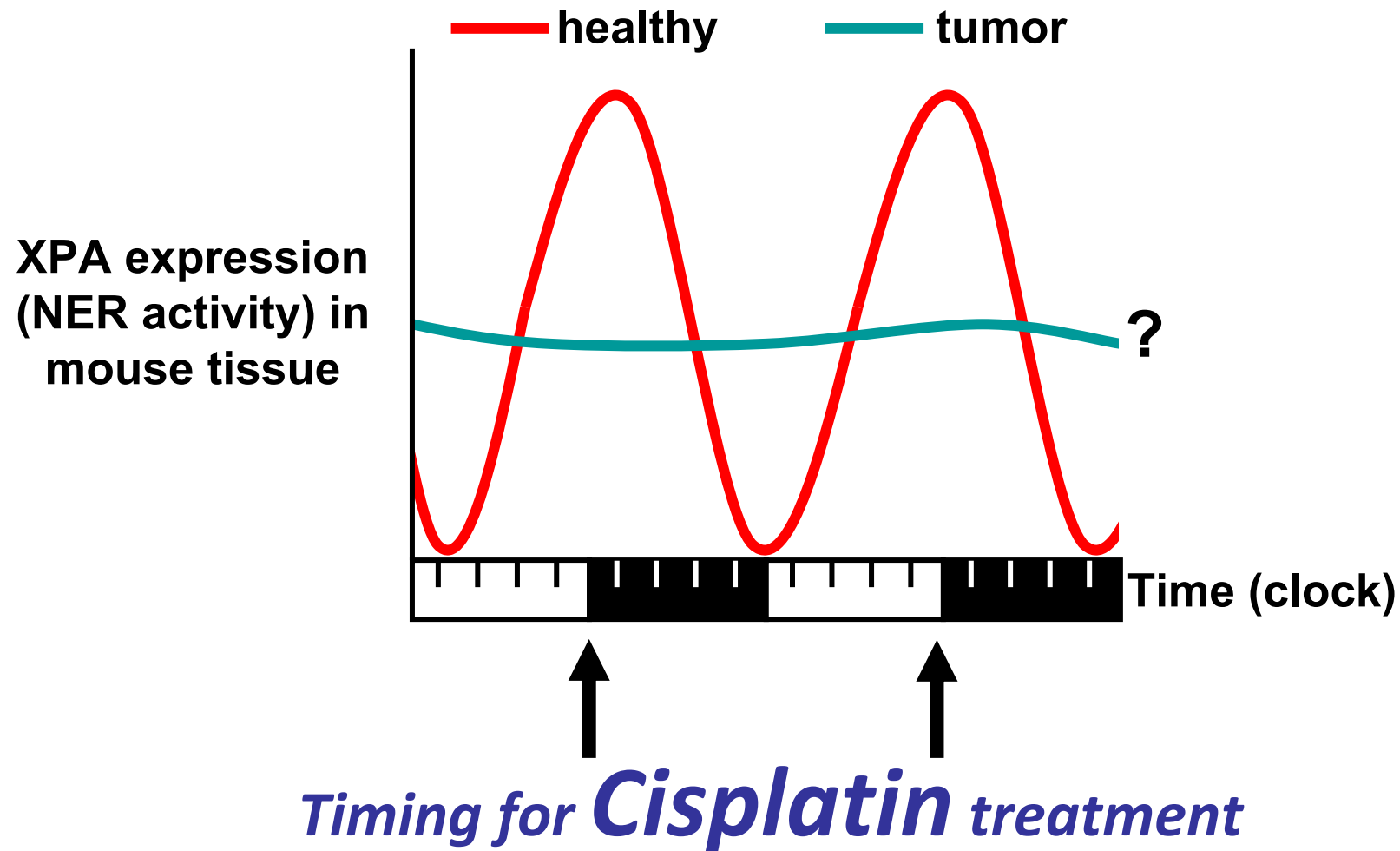
## Nucleotide excision repair

Kang et al. **PNAS** (2009) 106, 2864-2867

Kang et al. **PNAS** (2010) 107, 4890-4895

# Chrono-Chemotherapy

## : Circadian Timing for Cancer Chemotherapy



# Acknowledgements

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***Aziz  
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***Circadian Control of DNA Repair***

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