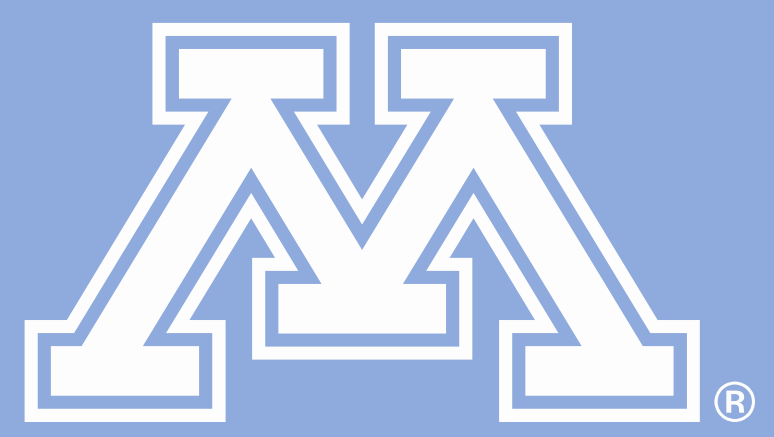
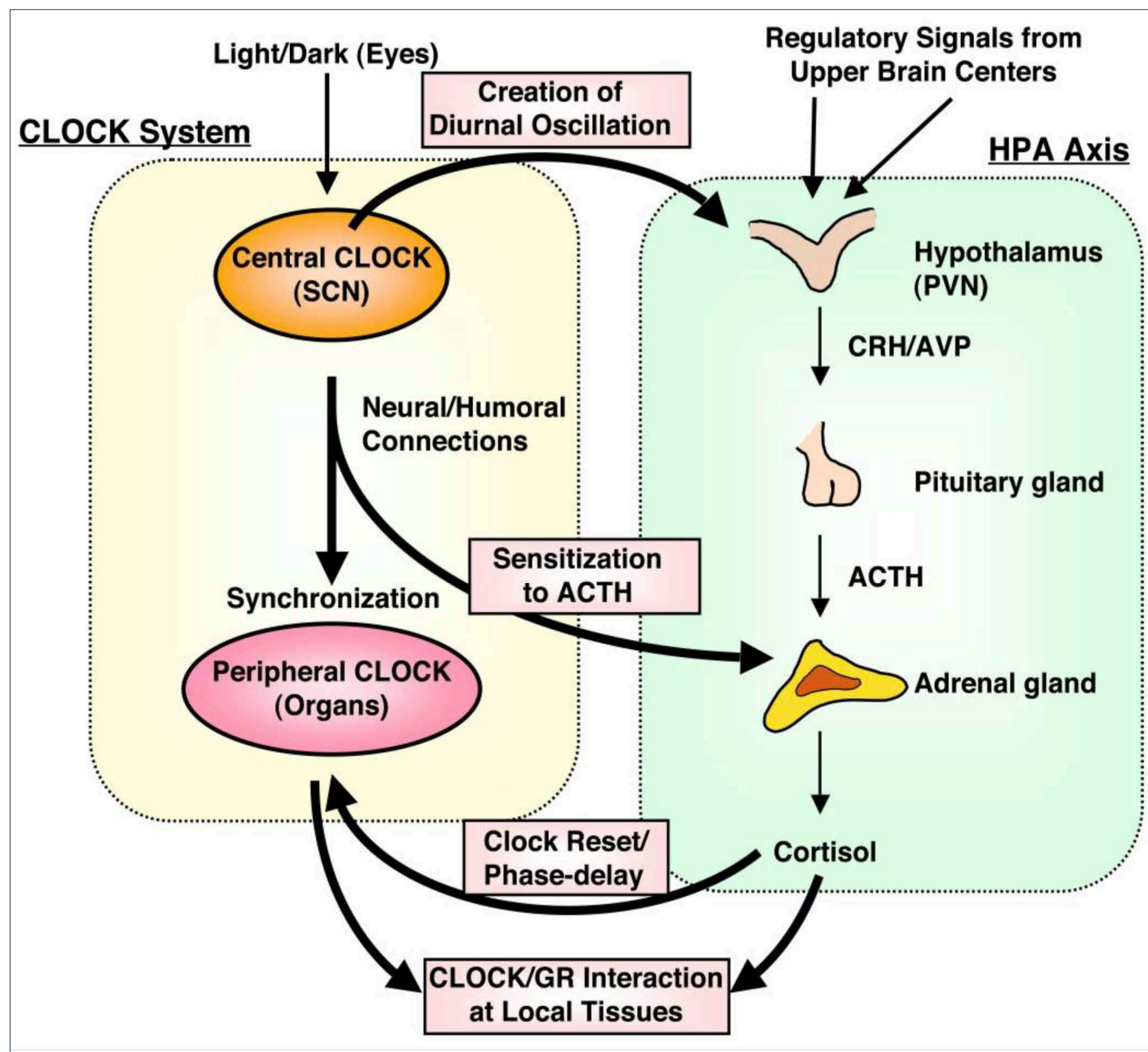


# Understanding the Role of the Adrenal Clock in the Stress Response

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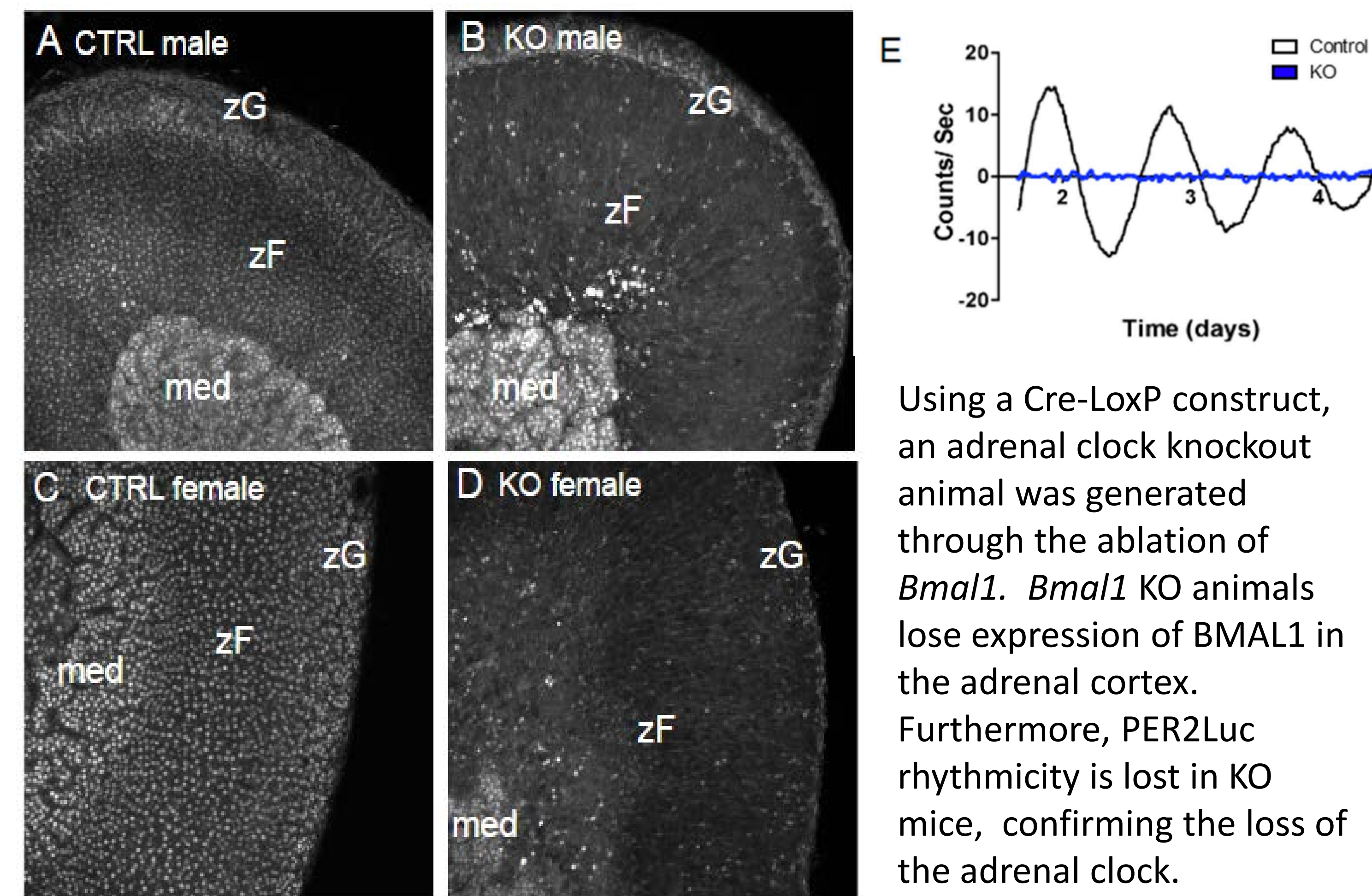


## The HPA Axis, Clock Genes, and Stress<sup>1</sup>

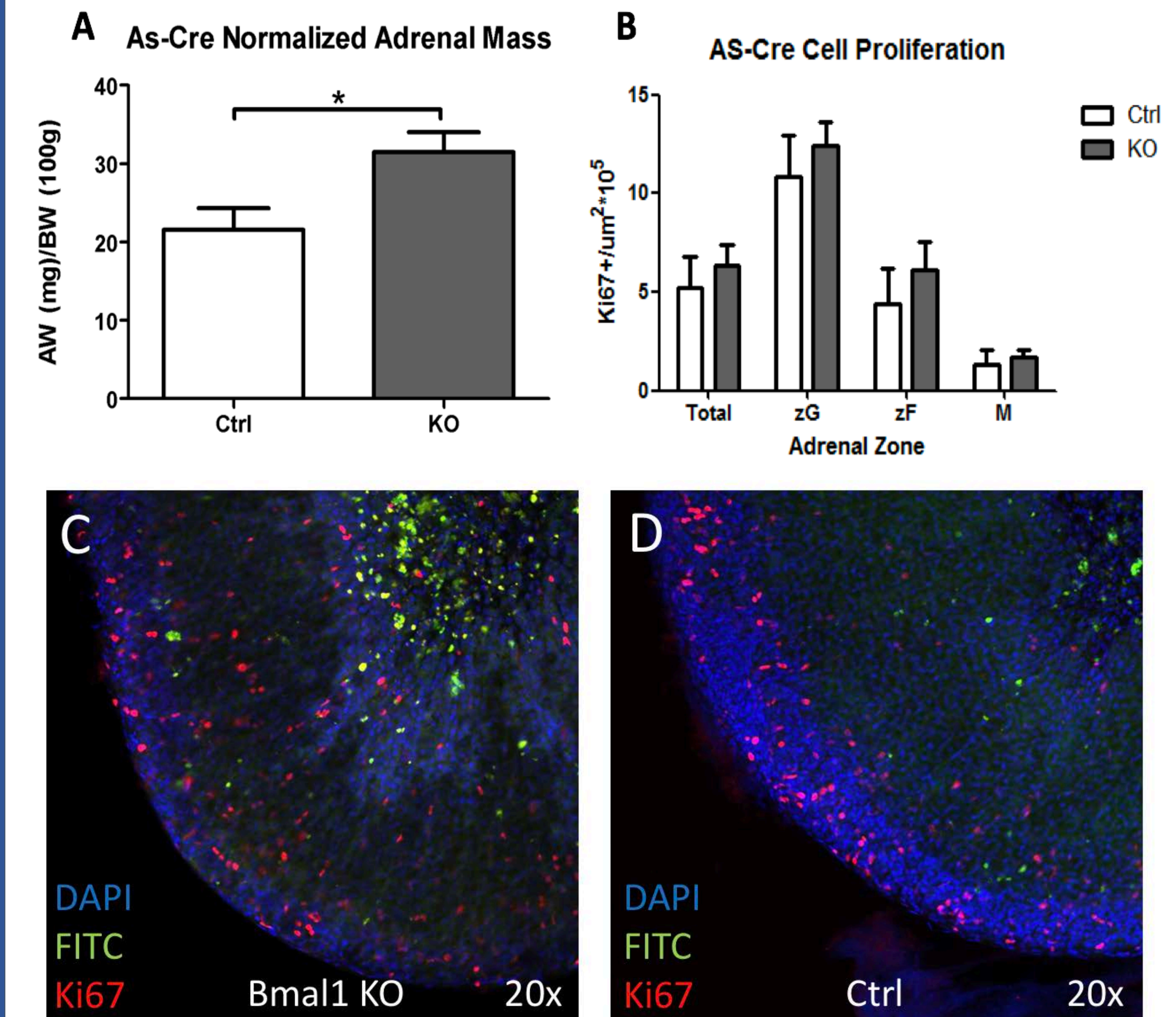


The primary goal of this research is to better understand the purpose of the adrenal clock in gating adrenal responsiveness to ACTH under conditions of acute stress.

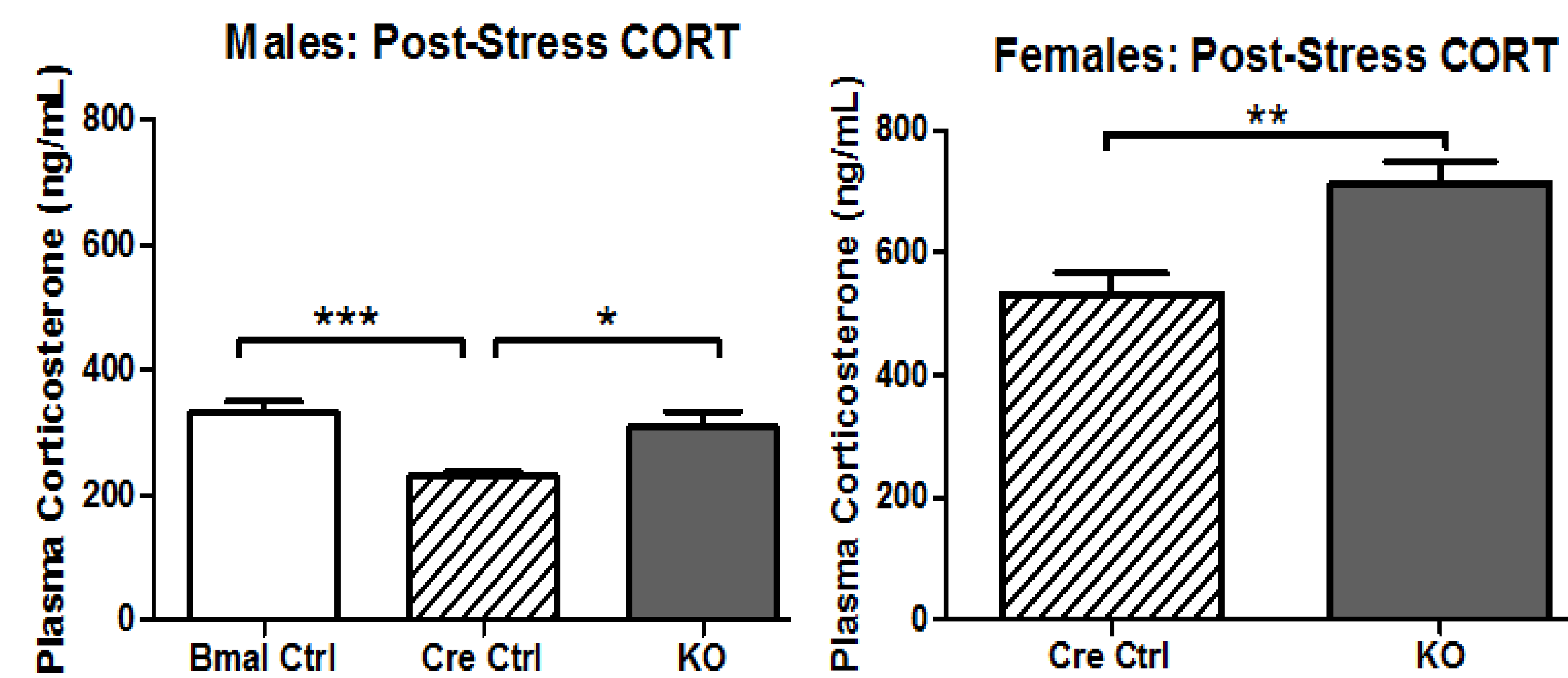
## Generating an Adrenal Clock KO Model



## Animals with and Ablated Adrenal Clock Exhibit an Increase in Adrenal Mass



## Adrenal Clock KO Animals Have a Heightened Glucocorticoid Response to Acute Stress



Animals were restrained for 15 minutes using a conical tube. Blood samples pre and post-stress were taken and analyzed using a radioimmunoassay (RIA) for plasma corticosterone and ACTH concentrations. Cre Controls (SCC<sup>cre/+</sup>::*Bmal1*<sup>+/+</sup>) in addition to *Bmal1* Controls (SCC<sup>+/+</sup>::*Bmal1*<sup>fl/fl</sup>) were used to account for presence of only one functional *p450scc* gene in the KO animal due to the Cre-Recombinase insertion. Contrary to previous studies<sup>2,3</sup>, both male and female *Bmal1* KO animals exhibited a *higher* plasma corticosterone response to stress relative to Cre Control animals, suggesting the adrenal clock is necessary for proper response to stress.

## Conclusions and Future Directions

- Contrary to previous findings, we have shown that adrenal clock knockout animals produce an *increased* response to acute stress
- The increase in adrenal mass seen in adrenal clock knockout animals is not due to an increase in cell proliferation
- Adrenal sensitivity with new control consideration warrants further investigation
- Continue to explore responsiveness to stress; vary stress intensity
- Examine alternative mechanisms for increase in adrenal mass and increase adrenal responsiveness to acute stress in *Bmal1* KO animals
  - *In vitro* adrenal sensitivity experiments
- Examine glucocorticoid response at different time points (AM vs PM)

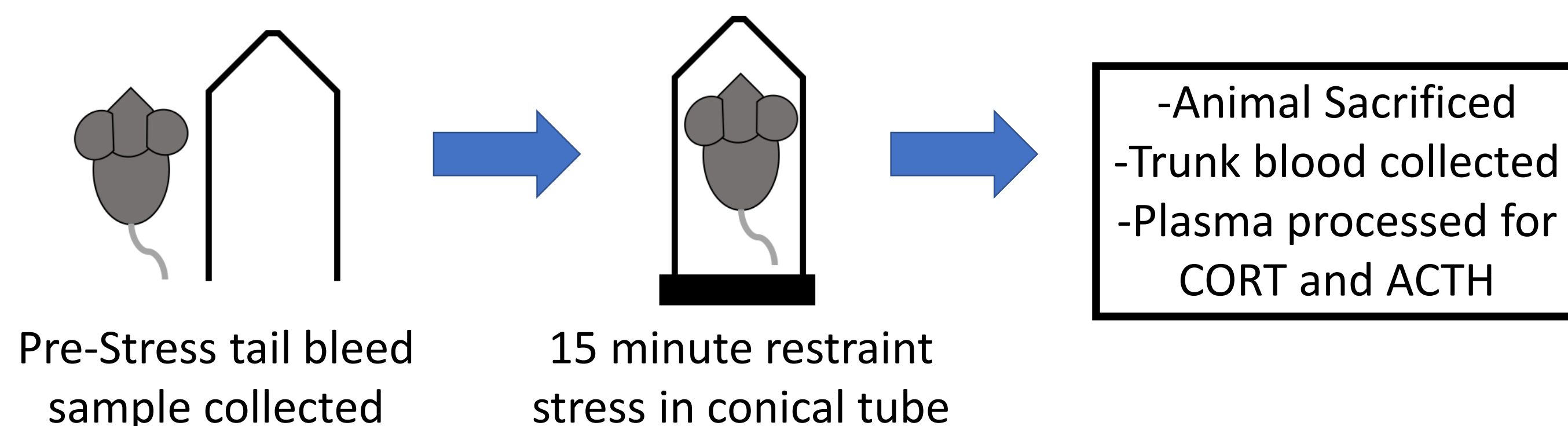
## References and Acknowledgements

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2.) Son, G.H., Chung, S., Cho, H.K., Kim, H.-D., Baik, S.-M., Lee, H., Lee, H.-W., Choi, S., Sun, W., Kim, H., et al. (2008). Adrenal peripheral clock controls the autonomous circadian rhythm of glucocorticoid by causing rhythmic steroid production. *Proc Natl Acad Sci U S A* 105, 20970-20975  
3.) Dumbell, R., Leliavski, A., Matveeva, O., Blaum, C., Tsang, A.H., and Oster, H. (2016). Dissociation of Molecular and Endocrine Circadian Rhythms in Male Mice Lacking *Bmal1* in the Adrenal Cortex. *Endocrinology* 157, 4222-4233.

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## Materials and Methods

### Restraint Stress



### Immunohistochemistry and Cell Quantification

