**INTRODUCTION**

The physiology of both vertebrates and invertebrates follows internal rhythms coordinated in phase with the 24-hour daily light cycle. This circadian clock is governed by a central pacemaker, the suprachiasmatic nucleus (SCN) in the brain. However, peripheral circadian clocks or oscillators have been identified in most tissues. How the central and peripheral oscillators are synchronized is still being elucidated.

Light is the main environmental cue that entrains the circadian clock. Under the absence of a light stimulus, the clock continues its oscillation in a free-running condition. In general, three functional compartments of the circadian clock are defined:

1. **Molecular clock (SCN)**: This is the central circadian oscillator located in the suprachiasmatic nucleus (SCN) of the hypothalamus.
2. **Peripheral oscillators**: These are distributed throughout the body and entrain to the central clock through the release of hormones like melatonin.
3. **Output**: The circadian clock regulates various physiological processes, including sleep-wake cycles, metabolism, and gene expression.

**RESULTS**

Our immunofluorescence results are in agreement with the description of the distribution of ipRGC. RGC positive for melanopsin were found uniformly distributed in the RGC layer throughout the retina, with occasional crowding along the periphery. Virtually no immunoreactive cells were found in retina samples from mice aboard STS133 after one day upon return; however, several positive cells were seen in samples from mice after flight on R+7. Likewise, both vivarium and AEM ground controls showed evidence of ipRGC.

Analysis of melanopsin mRNA levels by real time PCR revealed a drop in melanopsin gene expression in flight samples upon return to Earth, compared to ground controls, but control levels are recovered after 7 days after landing.

**CONCLUSIONS**

In addition, we investigated whether RGC loss by apoptosis, measured by activated caspase-3 immunoreactivity could be associated with the decrease in melanopsin expression. Conclusive quantification of apoptosis-positive cells is in progress, however, some differences were seen in the apparent distribution of apoptotic RGC in the different samples, being more prevalent in the ONL in vivarium samples and in the INL and RGC in flight samples. Therefore we infer that cell death may be one of the causes in the decrease of melanopsin expression, besides a downregulation in melanopsin expression itself. In vivarium samples, where cell death was observed in the photoreceptor layer, there is no decrease in melanopsin expression.

**MOLECULAR MECHANISMS OF CIRCADIAN REGULATION DURING SPACEFLIGHT**

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**BIBLIOGRAPHY**


**ACKNOWLEDGEMENTS**

This work was funded by NASA HRP/MTL070. We thank the assistance of Audrey Nguyen, JSC SLS Intern, Clear Lake High School, in the preparation of immunostained slides and image analysis, and James Fiedler, PhD, for help with graphing the gene expression data.