

## FORMAT FOR SLTBR ABSTRACTS

Abstracts must be single spaced in Times or Times New Roman with a font size of 10 pt. as a Word document (not pdf). All Abstracts must be in English and follow the format outlined below. Abbreviations are encouraged once defined, and references, if desired, should be kept to a minimum and cited as 1st author et al. abbreviated journal title, vol and pages, year. Ideally, abstracts should be no longer than 350 words.

**[Title]** Bold, All Caps

**[Author names]** First name initial(s) (separate by periods, no space between initials), Last name. Separate authors by comma only. Use superscript number after each name for corresponding affiliation.

**[Affiliation]** List affiliations preceded by superscript number if more than one affiliation. Run affiliations continuously, separated by a semicolon.

**[Abstract Body]** Use bold only for the headings of: **Objectives, Methods, Results,** and **Conclusions**. Do NOT enclose the abstract in a text box.

**[Figures/Tables]** Figures, if included, should be clean and made with dark lines. Do not use gray tones or colors. Tables, if included, must be clear and legible. Please have an original copy available if requested.

**[Keywords]** List keywords ( $\leq 5$ ) each separated by commas. Cap each new keyword.

**[Funding Support]** List if applicable.

### **SAMPLE ABSTRACT**

#### **CIRCADIAN DISRUPTION IN EXPERIMENTAL CANCER PROCESSES**

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**Objectives:** Circadian rhythm alterations independently predicted for poor survival outcome in cancer patients (Filipski et al., Chronobiol. Int. 23: 191-205, 2000). Frequent transmeridian flights or predominant work at night increase cancer risk, possibly as a result of disrupted coordination of circadian clocks. We investigated the consequence of severe circadian dysfunction caused by suprachiasmatic nuclei (SCN) destruction or experimental jet-lag on tumor growth in B6D2F1 mice and the prevention of circadian dysfunction with feeding schedules.

**Methods:** Three series of experiments were performed: 1) The SCN of mice were destroyed by electrocoagulation and then, 3 weeks later, they were inoculated s.c. with a transplantable Glasgow osteosarcoma (GOS) or pancreatic adenocarcinoma

(PO3), 2) Mice were randomly divided in 2 groups, one was kept in LD 12:12 and the other phase advanced by 8h by advancing the light-dark cycle every 2 days to produce chronic jet-lag (CJL). All mice were inoculated with GOS 10 days after jet-lag onset, 3) GOS-bearing mice were submitted to CJL or to CJL and meal timing (MT) to prevent circadian rhythm alterations. In all experiments locomotor activity and temperature were recorded by telemetry. Time series were analyzed by spectral and Cosinor analyses. Mice survival was checked daily and tumor growth was measured 3 times a week. Mice with tumor weight reaching 2 g were sacrificed for ethical reasons and considered as dead from tumor progression on this date. In all experiments plasma corticosterone concentrations and lymphocyte counts were assessed every 4h over a 24h span, and in jet-lag experiments the mRNA expression of clock genes (*Per2*, *Reverb-a* and *Bmall1*) and genes involved in cell cycle progression (*c-Myc*, and *p53*) was determined in liver and tumor with RT-PCR.

**Results:** The 24h rest-activity cycle was ablated and serum corticosterone and lymphocyte count markedly altered in lesioned mice as compared to sham-operated animals. The growth rate of either tumor was 2-3 times faster in lesioned than in sham mice. In GOS-bearing mice, mean tumor weight ( $\pm$  SEM) on day 12 (before the death of the first animal) was  $1443 \pm 203$  mg vs.  $490 \pm 93$  mg in lesioned and in sham mice, respectively (t-test;  $p = 0.002$ ). In P03-bearing mice mean tumor weight on day 22 was  $1447 \pm 342$  mg in lesioned and  $749 \pm 136$  mg in sham mice (t-test;  $p = 0.05$ ). CJL markedly altered the rest-activity, temperature and corticosterone rhythms in all the mice. Tumor grew faster in these animals as compared to those kept in LD 12:12 ( $p$  from ANOVA  $< 0.001$ ). On day 11, mean tumor weight was  $1330 \pm 151$  mg in jet-lagged mice and  $647 \pm 56$  mg in controls (t-test;  $p = 0.001$ ). Significant circadian rhythmicity in *per2*, *bmall1* and *reverb-a* mRNAs expression was observed in the liver and tumor of control mice; whereas, no obvious rhythm was detected in *p53* or *c-Myc*. CJL shifted clock gene rhythms in the liver and ablated them completely in the tumor. It also caused down regulation of *p53* expression ( $p = 0.002$ ), up regulation of *c-Myc* and induced a 12-fold circadian variation in *c-Myc* mRNA ( $p = 0.03$ ) in the liver of healthy mice; whereas, complex interactions were found in tumor-bearing animals. Subjecting the mice to the timed meal regimen restored circadian rhythmicity in clock gene expression in jet-lagged animals and retarded malignant progression.

**Conclusions:** These results suggest that environmental conditions such as altered light-dark or feeding schedules modify circadian clock coordination at the physiological and molecular levels and play a significant role in malignant progression. This finding warrants the development of therapeutic strategies aimed at treating or preventing circadian clock dysfunctions along the course of cancer processes.

**Key Words:** Cancer, Circadian Rhythms Desynchronization, Simulated shift work, Mice