Circadian modeling of core clock gene expression in four tissues of rats

Panteleimon D. Mavroudis\(^1\), Richard R. Almon\(^1,2\), Debra C. DuBois\(^1,2\), William J. Jusko\(^1\)

\(^1\) Department of Pharmaceutical Sciences; \(^2\) Department of Biological Sciences, State University of New York at Buffalo, NY

**Objectives:** To explore the circadian rhythmicity of core clock genes in rat liver, muscle, adipose, lung, using a mechanism-based model, and to assess the mechanistic underpinnings of inter-tissue variability.

**Methods:** Affymetrix gene chip measurements were made using tissues obtained from a light/dark controlled experiment involving 54 normal rats sacrificed within the 24-h cycle [1-4]. The core clock mechanism-based gene fluctuation model of Korencic [5] was applied using Matlab.

Figure 1 A) Schematic of the mechanistic model used with 5 clock genes. Red lines indicate inhibition, black induction, and the model includes turnover and translation delays. B) Core clock genes responses over two 24-hr periods for four tissues. Dots depict mean data for 3 rat replicates and lines are model fittings. C) Parameter values estimated for the four tissues. Red dots are mean values and error bars are 95% confidence interval.

**Results:** Our mechanism-based model of core clock genes (Figure 1A) well describes the available data for all tissues (Figure 1B). Model parameters indicated both similarities and differences in translational delays and degradation rates for various genes in the four tissues (Figure 1C).

**Conclusions:** This work advances understanding of the control of core clock gene expression across several tissues in rats and can serve as a basis for modeling corticosteroid disturbances of diverse endogenous biorhythms.