Supplementary Online Material

The Mammalian Circadian System is Resistant to Dioxin

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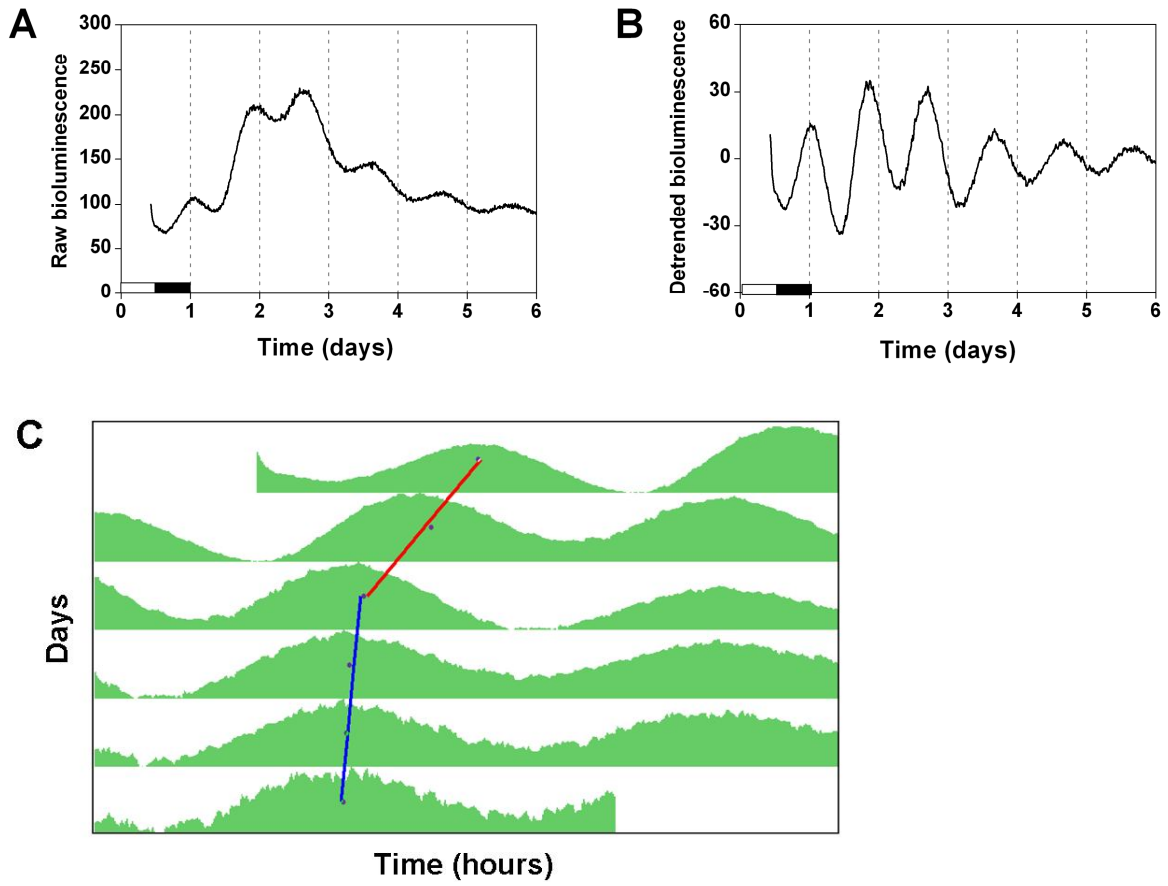
Table S1. Statistical analysis of *in vitro* experiments

Tissue	Parameter	*p*
Liver	Period 1	$F_{3, 32} = 1.01$, $p = 0.40$
	Period 2	$F_{3, 31} = 2.86$, $p = 0.06$
	Amplitude	Not determined
	Damping	Not determined
Lung	Period	$F_{3, 33} = 0.72$, $p = 0.55$
	Amplitude	$F_{3, 26} = 2.37$, $p = 0.10$
	Damping	$F_{3, 26} = 1.18$, $p = 0.34$
Pituitary	Period	$t_7 = -0.62$, $p = 0.56$
	Amplitude	$t_7 = -1.70$, $p = 0.13$
	Damping	$t_7 = 0.68$, $p = 0.52$
SCN	Period	$t_{10} = 1.50$, $p = 0.16$
	Amplitude	$t_7 = 0.87$, $p = 0.42$
	Damping	$t_7 = 0.66$, $p = 0.53$
Thymus	Period	$t_{13} = 0.78$, $p = 0.45$
	Amplitude	$p = 1.00$*
	Damping	$t_{10} = 0.94$, $p = 0.37$

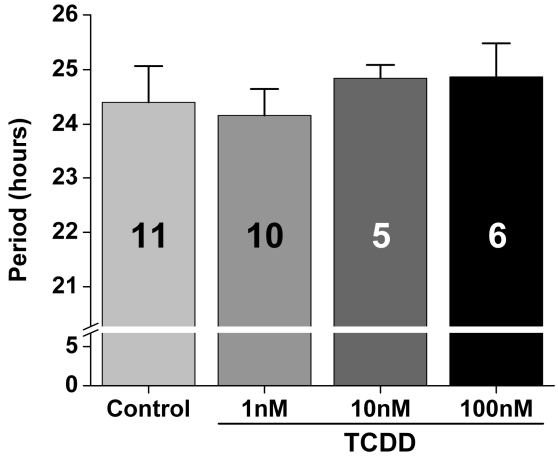
*Variance was not homogeneous; Mann-Whitney Rank Sum Test was used

***Ex vivo* liver rhythms are characterized by variability in baseline, amplitude, and period.** We used LumiCycle software, which employs a curve-fitting method, to analyze the amplitudes and damping rates of the PER2::LUC rhythms (Izumo et al. 2003). We were not able to successfully fit the liver rhythms (defined as a goodness-of-fit greater than 90%) and therefore could not analyze the amplitudes and damping rates of liver PER2::LUC rhythms. We found that PER2::LUC expression in liver explants was characterized by variability in baseline (Supplementary Fig. S1A) and amplitude (i.e. the damping rate is not constant) (Supplementary Fig. S1B). Nearly all liver explants showed a spontaneous change in period after 2 to 4 cycles *in vitro* (Supplementary Fig. S1C). These characteristics of liver rhythms *in vitro* were observed in

both DMSO- and TCDD-treated explants. The period analysis shown in Fig. 1 of the main text represents the first period measured *in vitro*. We also analyzed the second period of liver explants and found that there was no difference between control (DMSO)- and TCDD-treated explants (Table S1 and Supplementary Fig. S2).



Supplementary Figure S1. PER2::LUC rhythms in liver explants are characterized by variability in baseline, amplitude, and period. Representative traces of raw (A) and detrended (B) bioluminescence rhythms in a liver explant treated with DMSO. Detrended data was double-plotted in ClockLab (C) to show the spontaneous change in period. The first period in culture was determined by fitting a regression line to the acrophases of the first 3 cycles in culture (red line; period: 20.36h) and the secondary period was determined by fitting a regression line to the acrophases of cycles 3 to 6 in culture (blue line; period: 23.58h).



Supplementary Figure S2. TCDD treatment does not affect the secondary periods of PER2::LUC rhythms in liver explants. The period of the PER2::LUC rhythm in liver explants spontaneously changes after 2 to 4 days in culture. The mean (± SD) secondary periods of control (DMSO)- or TCDD-treated liver explants did not differ from each other.