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Understanding circadian transcriptional rhythms using next-generation sequencing

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Abstract

Eukaryotic circadian clocks include transcriptional/translational feedback loops that drive 24-hour rhythms of transcription. These transcriptional rhythms underlie oscillations of protein abundance, thereby mediating circadian rhythms of behavior, physiology, and metabolism. Numerous studies over the last decade have employed microarrays to profile circadian transcriptional rhythms in various organisms and tissues. Here we use RNA sequencing (RNA-seq) to profile the circadian transcriptome of *Drosophila melanogaster* brain from wild-type and *period*-null clock-defective animals. We identify several hundred transcripts whose abundance oscillates with 24-hour periods in either constant darkness or 12 hour light / dark diurnal cycles, including a number of non-coding RNAs (ncRNAs) that were not identified in previous microarray studies. Transcriptional profiling at the level of individual exons reveals alternative splice isoforms for many genes whose relative abundances are regulated by either *period* or circadian time, although the effect of circadian time is muted in comparison to that of *period*. Interestingly, *period* loss-of-function significantly alters the frequency of RNA editing at a number of editing sites, suggesting an unexpected link between a key circadian gene and RNA editing. We also identify tens of thousands of novel splicing events beyond those previously annotated by the modENCODE consortium, including several that affect key circadian genes. These studies demonstrate extensive circadian control of ncRNA expression, reveal the extent of clock control of alternative splicing and RNA editing, and provide a novel, genome-wide map of splicing in *Drosophila* brain.

Biography

Michael Hughes began his academic career at Stanford University, receiving co-terminal BS/MS degrees in Biology in 2002. From there, he began his doctoral studies at Harvard Medical School in the Division of Medical Sciences investigating how alternative splicing regulates dendrite morphogenesis. After receiving his PhD in 2007, heworked on circadian transcriptional rhythms as a postdoctoral fellow with Professor John Hogenesch at the University of Pennsylvania School of Medicine and Professor Michael Nitabach at Yale Medical School. He is currently an Assistant Professor of Biology at the University of Missouri – St. Louis.