THE UNIVERSITY OF MEMPHIS | Office of Technology Transfer

Novel Tool for Identifying Sleep-Disorder Drugs and Optimizing Timing of Administration of Drugs across Therapeutic Classes

Researchers at the University of Memphis and University of Pennsylvania report the development of robust new liver and fat cell models that report circadian clock function. These models are amenable to high throughput drug screening and could be used to find promising small molecules to resynchronize or help body clocks function normally. The consequences of modern life, eating and staying up later, shift work, cell phone addiction, and travel across time zones, all disturb internal clocks. These clocks are found in the brain where they regulate sleep, and also throughout the body, where they regulate much of our physiology and metabolism. Disrupting these clocks has been linked to metabolic problems even in healthy volunteers. These new cellular clock models could help scientists find new drugs that reset or help restore robust rhythms to metabolic clocks. A copy of that study, published in a recent issue of PLOS Genetics, is attached. IP rights to these tools are available for licensing.

Applications

- Discovery and development of new pharmaceutical compounds for treating insomnia and sleep problems related to shift work and jet lag.
- Identify currently approved drugs as modulators of biological clocks.
- Improve effectiveness of current drugs across therapeutic areas by understanding their impact on the body's internal clock.

Advantages

- Compatible with high throughput screening using inexpensive off-the-shelf recording devices
- First chronobiology cell line based on metabolically relevant cell types

The scientists started with metabolically relevant cells – hepatocytes and adipocytes – representing major functions of the liver and adipose tissues, and thus important aspects of the body's energy processing and storing system. Then they genetically engineered them to flash light with a daily rhythm much like an alarm clock. They validated the cell models and showed that changing clock gene function in these cells is similar to what happens in mice lacking clock genes.

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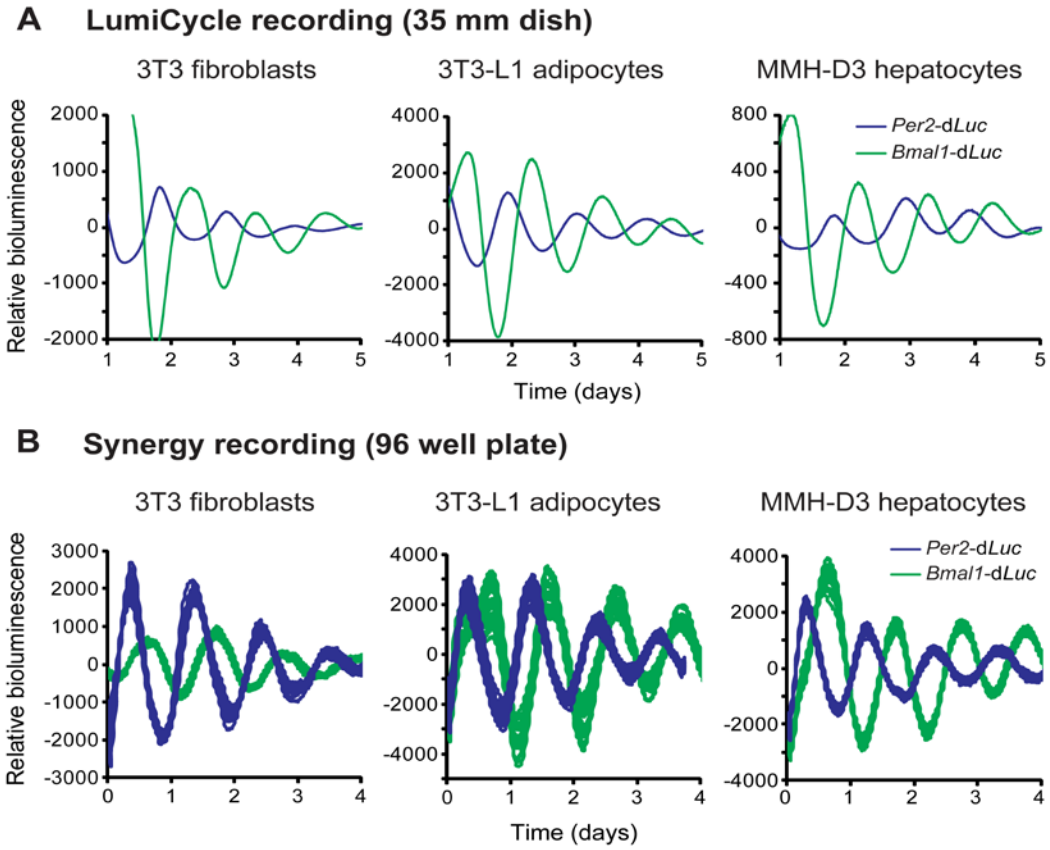
Data Graphic



Fibroblasts, adipocytes, and hepatocytes display robust bioluminescence rhythms.

(**A**) Representative bioluminescence rhythms of reporter cells recorded in a LumiCycle luminometer on 35 mm dishes. Baseline-subtracted bioluminescence data of both reporter lines are plotted together to show the expected, approximately anti-phasic reporter expression for each cell type.

(**B**) Representative bioluminescence rhythms of homogenous clonal cell lines recorded in a Synergy microplate reader on 96 well plates. Baseline-subtracted bioluminescence data of selected clonal lines representing two reporter types are plotted together to show anti-phasic reporter expression for each cell type. High reproducibility is illustrated by showing overlapping traces from 24 of the 96 wells for each reporter.

The Inventors

Andrew Liu, Assistant Professor of Biology at the University of Memphis
Dr. Liu received his Ph.D. from the University of Michigan and performed post-doctoral research at the Scripps Research Institute. The major focus of his lab is the biochemical and molecular basis of circadian rhythms in physiology and behavior. Dr. Liu uses mice and cultured mammalian cells as model systems and employ highly integrated approaches including biochemistry, genetics and genomics, as well as behavioral assays and real-time bioluminescence technology.

John Hogenesch, Professor of Pharmacology at the University of Pennsylvania Perelman School of Medicine
Dr. Hogenesch received his Ph.D. from Northwestern University and performed post-doctoral research at University of Wisconsin-Madison and the Genomics Institute of the Novartis Research Foundation. His basic research experiences have leveraged functional genomics, bioinformatics, and next generation sequencing to better understand physiology and behavior.

Chidambram Ramanathan, Research Assistant Professor, Department of Biological Sciences, University of Memphis
Dr. Ramanathan received his Ph.D. from Madurai Kamaraj University and has performed post-doctoral research at Michigan State University in neuroscience and University of Memphis in molecular biology. His research focuses on molecular and behavioral aspects of circadian rhythms in mammals.