Medical Xpress

New cell models for tracking body clock gene function

April 9 2014, by Karen Kreeger

The consequences of modern life—shift work, cell phone addiction, and travel across time zones—all disturb internal clocks. These are found in the brain where they regulate sleep and throughout the body where they regulate physiology and metabolism. Disrupting the clocks is called circadian misalignment, which has been linked to metabolic problems, even in healthy volunteers.

Researchers from the Perelman School of Medicine at the University of Pennsylvania and the University of Memphis describe in *PLOS Genetics* the development of new cell models that track and report clock gene function. These engineered cells can be used with inexpensive, off-the-shelf recording devices, making them suitable for small basic labs to large-scale pharmaceutical firms to screen candidate small molecules to help the body's clock function normally.

The team started with liver cells and fat cells because they govern the body's energy processing and storing system and 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.

"The previous cellular models were great," says co-senior author John Hogenesch, Ph.D., professor of Pharmacology at Penn. "But these older cell models needed high-end imaging equipment that is out of reach for most labs and early-stage startups." By expanding the number of labs that can do these studies, these models could catalyze better understanding of

peripheral clocks, as well as new genetic and chemical tools to improve their function.

"We are very excited about the prospect of using these more physiologically relevant cell-based models for gene and small molecule drug discoveries," says co-senior author Andrew Liu, from the University of Memphis.

More information: Ramanathan C, Xu H, Khan SK, Shen Y, Gitis PJ, et al. (2014) "Cell Type-Specific Functions of Period Genes Revealed by Novel Adipocyte and Hepatocyte Circadian Clock Models." *PLoS Genet* 10(4): e1004244. DOI: 10.1371/journal.pgen.1004244

Provided by University of Pennsylvania School of Medicine