

Circadian clock may impact organ transplant success

4 October 2011

Health care providers assess blood and tissue type as well as organ size and health to enhance transplant success. New research indicates that checklist might also need to include the circadian clock. Rudic said.

While some human studies have shown the time of day transplant surgery is performed can influence the outcome, this study of mice with dysfunctional [internal clocks](#) is the first correlating circadian clocks with transplant success, said Dr. Daniel Rudic, vascular biologist at Georgia Health Sciences University and corresponding author of the study published in [Proceedings of the National Academy of Sciences](#).

The GHSU researchers found that arteries of mice with [circadian clock](#) dysfunction became thick and diseased within a few weeks of being transplanted to healthy mice. Arteries transplanted from healthy mice to the [mutant mice](#) remained healthy.

[Blood vessel disease](#), and resulting blood loss to donated organs, is a key pitfall for transplant patients, potentially leading to [organ failure](#) and rejection.

"You take an organ out of a human, you don't think about it having a bad clock," Rudic said. "But the fact is the time at which you do the organ transplant may influence overall success and, if you have a donor who has a sleep disorder or is a night shift worker, it may affect it as well."

Since even healthy clocks produce variability in tissue function across the span of a day, transplantation might be best performed during optimal organ function, he said.

In addition to enabling sleep/wake cycles, circadian clocks are found throughout the body and involved in a lot more than sleep. "The clock is expressed not only in the brain but everywhere in the body and can function autonomously in different areas,"

"Our research shows it's the clock within the blood vessel that is key to conferring the disease response in this case," said Dr. Bo Cheng, GHSU [postdoctoral fellow](#) and the study's first author.

While the researchers can determine whether clock gene expression is up, down or mutated, there is currently no way to do the tests in humans. Until screening tests are identified, donors could be screened for signs of dysfunction such as a sleep disorder or even aberrant behaviors that can impair healthy clocks, such as shift work, Rudic said. "Ideally this will open up some new research avenues," he said.

Interestingly, when blood vessels from the mutant mouse stay in that mouse, disease progression is much slower. "We believe that bad clock function worsens when it intersects with disease, so if you are eating a high-fat diet or if you undergoing a serious surgery like a transplant, and you have a bad clock, disease may occur and may occur quickly," Rudic said.

In 2009, he reported in the journal *Circulation* that mice with mutated or missing [clock genes](#) were prone to vascular disease similar to smokers and people with high blood pressure and cholesterol. That study showed the blood vessel clocks regulate key signaling that enables blood vessel dilation and remodeling.

Provided by Georgia Health Sciences University

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