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Blood vessel receptor that responds to light may be new target for vascular disease treatments

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A team of researchers from Johns Hopkins Medicine has discovered a receptor on blood vessels that causes the vessel to relax in response to light, making it potentially useful in treating vascular diseases. In addition, researchers discovered a previously unknown mechanism by which blood vessel function is regulated through light wavelength.

The study is published in the Nov. 17 issue of *Proceedings of the National Academy of Sciences*.

"If we can develop novel ways of delivering light to blood vessels, this molecular switch for relaxation could be harnessed in all types of vascular disease treatment," says senior author Dan Berkowitz, M.D., of the Johns Hopkins University departments of Anesthesiology and Critical Care Medicine and of Biomedical Engineering.

The researchers had not originally intended to study the impact light would have on blood vessels. But, after Berkowitz's blood vessel analysis equipment was moved into a new space, the new room had motion detection lights, unlike the lab before. The team noticed the tension in the blood vessels would decrease when the motion detection lights came on. Noticing this, the team decided to look further into this phenomenon.

Berkowitz and his team found a similar discovery was made in the 1950s, but the mechanisms that had been proposed seemed unlikely to

him, and he wanted to do further research. "I had this slightly crazy idea," he says. "What if there were receptors for light on blood vessels? Perhaps blood vessels could 'see' the light or 'had eyes.'"

The researchers looked for expression of a light receptor in the blood vessels of mice and discovered a receptor called melanopisn, or opsin 4—one of a group of nonimage-forming light receptors. In mice without opsin 4, blood vessels did not relax in response to light.

Upon further study, Berkowitz and his team were able to determine the exact wavelength at which opsin 4 is activated and the blood vessel relaxation response is maximal. The scientists could use wavelength-specific light to increase blood flow in the tails of normal mice, but not in the tails of mice that lacked expression of opsin 4.

"This group's finding provides a perfect example of how following up on unexpected results can lead to important basic biomedical research discoveries," says Zorina Galis, Ph.D., chief of the vascular biology and hypertension branch of the National Heart, Lung and Blood Institute. "In addition, their basic discovery now opens the way to investigations of whether wavelength-specific light stimulation of blood vessels might be used to manage a variety of medical conditions."

It will be important to determine if this phenomenon is present across all species and in all vascular beds, and to uncover all of the signaling and regulatory mechanisms that are linked to the receptor. Also, investigators will want to know if problems associated with the receptor are present in patients with vascular disease.

Berkowitz sees a variety of applications for his research. For example, his group hopes to target the opsin 4 receptor with light as a therapeutic option for Raynaud's phenomenon, which is characterized by exaggerated vasoconstriction of the vessels of the fingers and toes. "We

plan to use high-intensity light-emitting diodes, or LEDs, incorporated into gloves as a potential mode of therapy for these patients. Additionally, socks with LEDs could be used in diabetic patients to potentially enhance blood flow and heal chronic ischemic ulcers."

More information: Melanopsin mediates light-dependent relaxation in blood vessels, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1420258111

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