Study is decoding blue light's mysterious ability to alter body's natural clock

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Arabidopsis thaliana is a small flowering plant that is widely used as a model organism in plant biology.

A study funded by the National Institutes of Health is unraveling the mystery of how blue light from residential and commercial lighting, electronic devices and outdoor lights can throw off-kilter the natural body clock of humans, plants and animals, leading to disease.

Exposure to blue light is on the increase, says chemist Brian D. Zoltowski, Southern Methodist University, Dallas, who leads the study, "Protein : Protein interaction networks in the circadian clock."

At the right time of day, blue light is a good thing. It talks to our 24-hour circadian clock, telling our bodies, for example, when to wake up, eat and carry out specific metabolic functions.

In plants, blue light signals them to leaf out, grow, blossom and bloom. In animals, it aids migratory patterns, sleep and wake cycles, regulation of metabolism, as well as mood and the immune system.

But too much blue light—especially at the wrong time—throws biological signaling out of whack.

"As a society, we are using more technology, and there's increasing evidence that artificial light has had a negative consequence on our health," said Zoltowski, an assistant professor in SMU's Department of Chemistry.

"Our study uses physical techniques and chemical approaches to probe an inherently biological problem," he said. "We want to understand the chemical basis for how organisms use light as an environmental cue to regulate growth and development."

Zoltowski's lab was awarded $320,500 from the National Institute of General Medical Sciences of the National Institutes of Health to continue its research on the impact of blue light.

The lab studies a small flowering plant native to Europe and Asia, Arabidopsis thaliana. The flower is a popular model organism in plant biology and genetics, Zoltowski said.

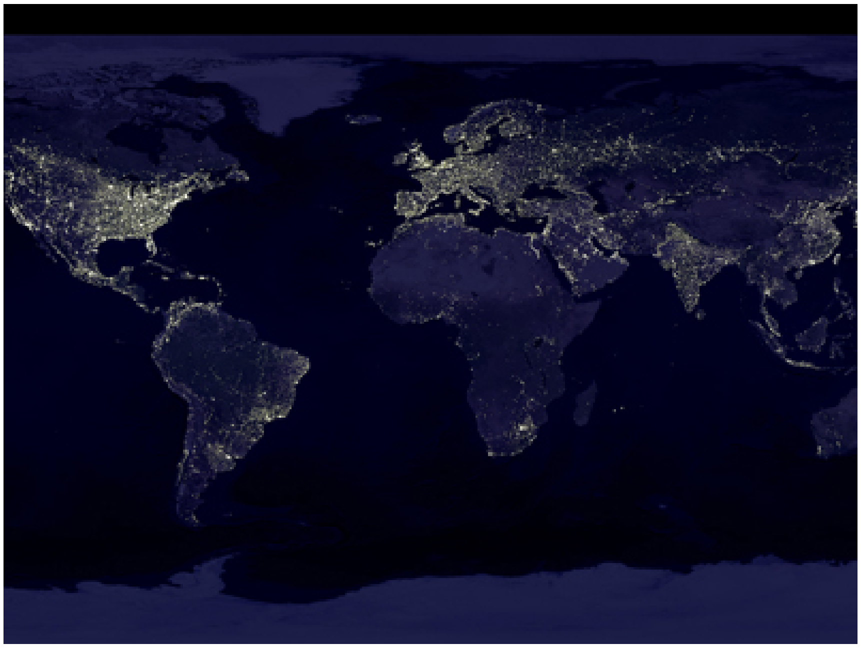
Although signaling pathways differ in organisms such as Arabidopsis when compared to animals, the flower still serves an important research purpose. How the signaling networks are interconnected is similar in both animals and Arabidopsis. That allows researchers to use simpler genetic models to provide insight into how similar networks are controlled in more complicated species like humans.

Understanding the mechanism can lead to targeted drug treatments

In humans, the protein melanopsin absorbs blue light and sends signals to photoreceptor cells in our eyes. In plants and animals, the protein cryptochrome performs similar signaling.

Much is known already about the way blue light and other light wavelengths, such as red and UV light, trigger biological functions through proteins that interact with our circadian clock. But the exact mechanism in that chemical signaling process remains a mystery.

"Light is energy, and that energy can be absorbed by melanopsin proteins that act as a switch that basically activates everything downstream," Zoltowski said.



An image of Earth’s city lights using data from the Defense Meteorological Satellite Program. Credit: NASA

Melanopsin is a little-understood photoreceptor protein with the singular job of measuring time of day.

When light enters the eye, melanopsin proteins within unique cells in the retina absorb the wavelength as a photon and convert it to energy. That activates cells found only in the eye—called intrinsically photosensitive retinal ganglian cells, of which there are only about 160 in our body. The cells signal the suprachiasmatic nucleus region of the brain.

"We keep a master clock in the suprachiasmatic nucleus—it controls our circadian rhythms," he said. "But we also have other time pieces in our body; think of them as watches, and they keep getting reset by the blue light that strikes the master clock, generating chemical signals."

The switch activates many biological functions, including metabolism, sleep, cancer development, drug addiction and mood disorders, to name a few.

"There's a very small molecule that absorbs the light, acting like a spring, pushing out the protein and changing its shape, sending the signal. We want to understand the energy absorption by the small molecule and what that does biologically."

The answer can lead to new ways to target diabetes, sleep disorders and cancer development, for example.

"If we understand how all these pathways work," he said, "we can design newer, better, more efficacious drugs to help people."

Chemical signal from retina's "atomic clock" synchronizes circadian rhythms

Besides increased reliance on artificial lighting indoors and outdoors, electronic devices also now contribute in a big way to blue light exposure. Endless evening hours on our smartphones and tablets with Candy Crush, Minecraft or Instagram don't really help us relax and go to sleep. Just the opposite, in fact.

The blue glow those devices emit signals our circadian clock that it's daytime, Zoltowski said. Red light, on the other hand, tells us to go to sleep.

Awareness of the problem has prompted lighting manufacturers to develop new lighting strategies and products that transition blue light to red light toward evening and at night, Zoltowski said.

Targeted solutions could neutralize destructive blight in staple

crops

In plants, the researchers study how the absence of "true dark" in nature due to artificial light can reduce yields of farm crops and promote crop disease.

For example, fungal systems rely on blue light to proliferate, forming pathogens known as blight in crops resulting in leaves that look chewed on and reducing yields.

"We study fusarium and verticillium," Zoltowski said. "They cause about $3 billion worth of crop damage a year to wheat, corn, soybeans—the staple food crops."

Understanding their ability to infect crops would allow scientists to potentially design small molecules that target and disrupt the fungal system's circadian clock and neutralize their proliferation.

Research to understand how light and clock regulation are coupled

In animals, Zoltowski's lab studies the blue light pathway that signals direction to birds and other animals that migrate. Blue light activates the protein that allows various species to measure the earth's magnetic field for directionality. For example, Monarch butterflies rely on the cryptochrome photoreceptor for their annual migration to Mexico.

"We're interested in how these pathways are regulated in a diverse range of organisms to understand how we can manipulate these pathways to our advantage," he said, "for health consequences and to improve agriculture yields."

The researchers will map the reaction trajectory beginning from the initial absorption of the photon to the point it alters an organism's physiology.

Zoltowski notes that light is just one of a handful of external cues from our environment that trigger biological processes regulating the circadian clock. Others include temperature changes, feeding and metabolites.

More information: "Mechanism-based tuning of a LOV domain photoreceptor." *Nature Chemical Biology* 5, 827 - 834 (2009) Published online: 30 August 2009 DOI: 10.1038/nchembio.210

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