Circadian clock research may enable designer plants, and cancer and diabetes treatments

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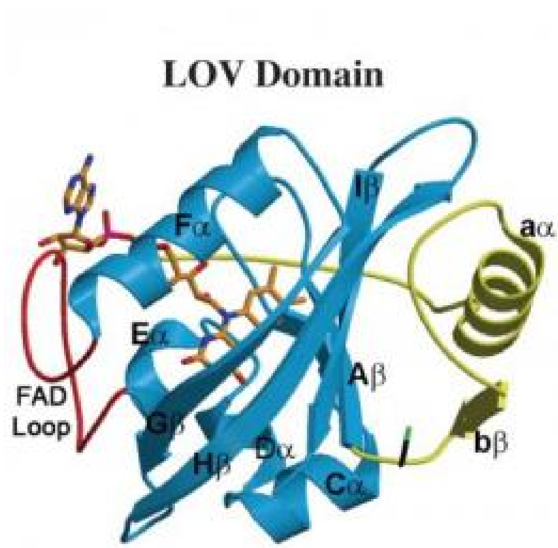

This image shows the domain architecture of a photoreceptor protein like the one responsible for regulation of circadian clocks in plants. Credit: Zoltowski

How does a plant know when to sprout a leaf, fold its petals or bloom? Why do humans experience jet lag after a trip abroad?

The answer is the internal circadian clocks that are present in nearly every organism and that respond to external cues such as light and temperature, says chemist Brian D. Zoltowski, Southern Methodist University.

Zoltowski's lab at SMU studies one of the many proteins involved in an organism's circadian clock. Called a photoreceptor, the protein responds to light to predict time of day and season by measuring day length.

The photoreceptor protein enables plants to know when spring and fall occur and to produce flowers or fruit at the appropriate time of year, says Zoltowski, an assistant professor in SMU's Department of Chemistry. The protein also allows plants to collect energy during the day in the scientific process called photosynthesis, and then refocus energy to grow at night.

Human photoreceptors also are intricately involved in regulation of the body's circadian clocks. They have been implicated in the development of cancer and diabetes, as well as neurological illnesses.

"If we can better understand how these proteins work, we can potentially re-engineer them or develop small molecules to regulate flowering times, plant growth and development," Zoltowski says. "By extension, we can potentially design therapeutics for the human circadian clocks."

The Herman Frasch Foundation for Chemical Research Grants in Agricultural Chemistry awarded Zoltowski a five-year $250,000 agricultural chemistry grant to fund the plant research. The foundation is administered by the American Chemical Society.

A natural 24-hour biological mechanism for regulating the body

The circadian clock is an internal biological mechanism that responds to light, darkness and temperature in a natural 24-hour biological cycle. The clock synchronizes body systems with the environment to regulate everything from sleep patterns and hunger in humans to growth patterns and flowering in plants.

"Our research focuses on understanding the chemical basis for how organisms perceive their surroundings and use light as an environmental cue to regulate growth and development," Zoltowski says.

Zoltowski's research focuses on a family of proteins related to Zeitlupe, a photoreceptor protein that is sensitive to blue light and historically considered responsible for regulating the circadian clock.

"We isolate the protein so we can study directly how it works independent of everything else," Zoltowski says. "So we look at the chemistry that is sensitive to blue light when the blue-light photon is absorbed by the protein. We figure out the chemistry and then how the chemistry changes the structure of the protein."

For example, he says, for a flower to open, light induces a chemical reaction in the protein that alters the way it's configured, which then starts a cascade of interactions that changes the plant's physiology completely.

The researchers use a combination of X-ray crystallography, nuclear magnetic resonance and solution biophysics to identify the fundamental chemical mechanisms of photo-activation, including local chemical events, alteration in protein structure and alteration in protein:protein interactions.

Goal is for discoveries that can regulate a plant's circadian clock

By understanding how the proteins work, scientists can ultimately create new strains of plants that are tolerant to more environments, says Zoltowski. In related research, the study of human proteins can reveal circadian clock irregularities that play a role in diseases such as diabetes by disrupting the release of glucose, for example. From that research, scientists can develop new drug therapeutics to treat the illness.

"We're having great success. We've worked with these families of proteins for a long time, so we have some strategies that improve the likelihood of making it work," Zoltowski says.

Provided by Southern Methodist University