

Scientists uncover new compounds that could affect circadian rhythm

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Scientists from the Florida campus of The Scripps Research Institute (TSRI) have discovered a surprising new role for a pair of compounds—which have the potential to alter circadian rhythm, the complex physiological process that responds to a 24-hour cycle of light and dark and is present in most living things.

At least one of these compounds could be developed as a [chemical probe](#) to uncover new therapeutic approaches to a range of disorders, including diabetes and obesity.

The study, which was published online ahead of print by the *Journal of Biological Chemistry*, focuses on a group of proteins known as REV-ERBs, a superfamily that plays an important role in the regulation of circadian physiology, metabolism and [immune function](#).

The new study shows that the two compounds, cobalt protoporphyrin IX (CoPP) and zinc protoporphyrin IX (ZnPP), bind directly to REV-ERBs.

REV-ERBs are normally regulated by heme, a molecule that binds to hemoglobin, helps transport oxygen from the bloodstream to cells and plays a role in producing cellular energy. While heme activates REV-ERB, CoPP and ZnPP inhibit it.

"These compounds are like heme, but when you swap out their metal centers their functions are different," said Doug Kojetin, a TSRI associate professor who led the study. "This makes us think that the key

is the chemistry of the metal ion itself. Altering the chemistry of this metal center may be an opportune way to target REV-ERB for diabetes and obesity."

Kojetin and his colleagues recently demonstrated that synthetic REV-ERB agonists, like the new [compounds](#), reduce body weight in mice that were obese due to diet.

More information: "Structure of REV-ERB_ Ligand-binding Domain Bound to a Porphyrin Antagonist," [www.jbc.org/content/early/2014...545111.full.pdf+html](http://www.jbc.org/content/early/2014/07/08/262.11.545111.full.pdf+html)

Provided by The Scripps Research Institute

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