Photosynthetic bacteria give biologists a cool new tool

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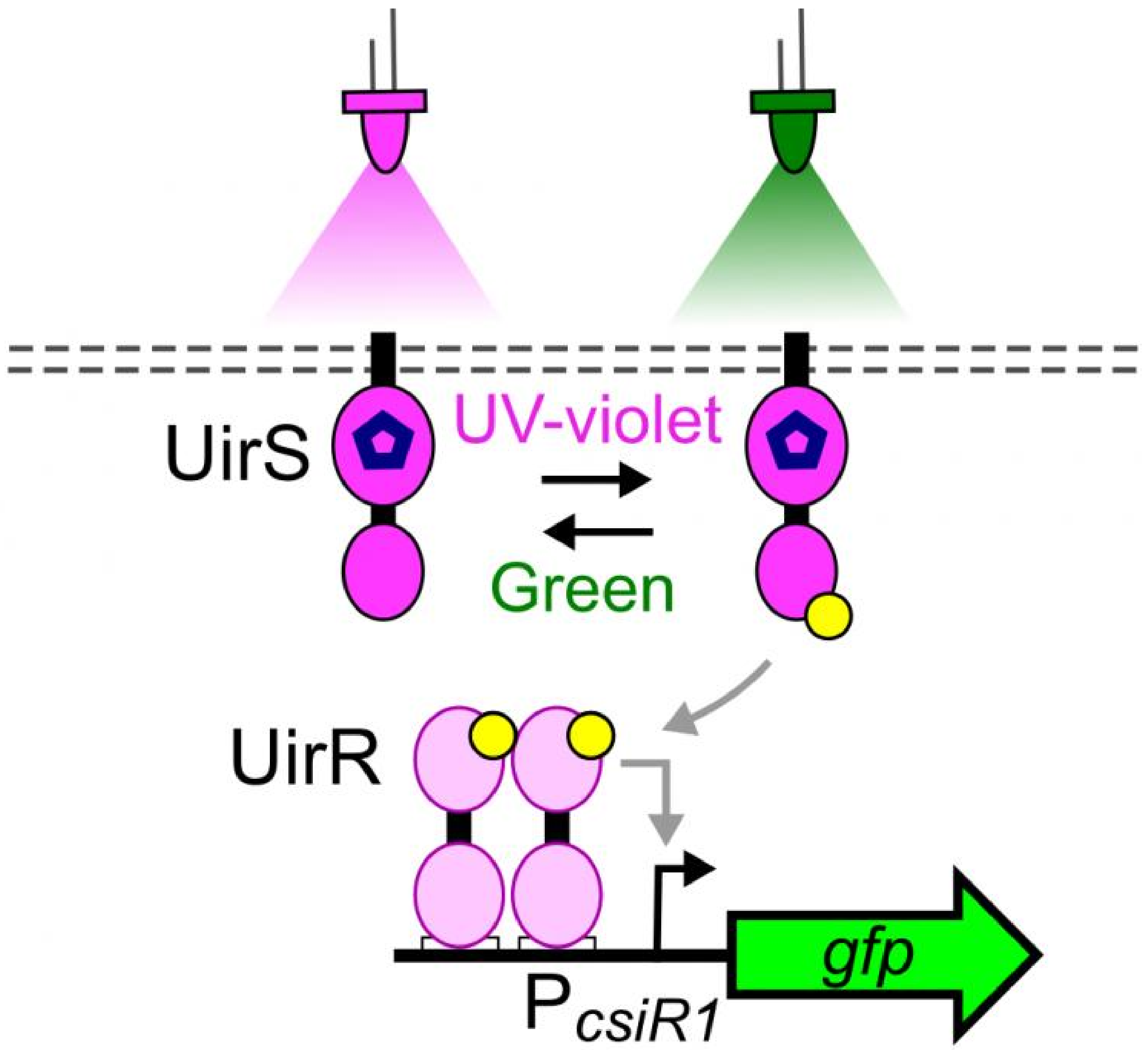

Rice University researchers have turned a protein pathway discovered in marine bacteria into a photoreversible regulatory tool that responds exclusively to UV-violet light. The UirS protein is anchored in the bacterial membrane where it “sees” the color illuminating the bacterium. If the illumination is UV-violet, UirS activates itself and relays this active state to a messenger protein, UirR. Active UirR is mobile, capable of binding a specific target DNA sequence called a promoter (PcsiR1), and turning on the expression of a desired gene, a fluorescent green protein (gfp). Switching to green light deactivates UirS, resulting in inactive UirR and turning off gene expression. Credit: Prabha Ramakrishnan/Rice University

Photosynthetic bacteria that have lived on Earth for 2.7 billion years are the source of a new and valuable biological regulatory tool being developed by Rice University bioengineers.

Synechocystis bacteria produce a protein pathway that senses the presence of UV-violet light and activates a motor protein that moves the single-cell organism into safer surroundings.

The pathway responds quickly to UV-violet light, a narrow band in the spectrum that includes long ultraviolet and short violet wavelengths, and is blind to all others. That makes it a perfect addition to the growing optogenetic suite of reversible photoreceptors being developed by researchers in the lab of Rice synthetic biologist Jeffrey Tabor. Tabor and graduate student Prabha Ramakrishnan co-authored a new paper about this research in the American Chemical Society journal *ACS Synthetic Biology*.

"The human eye can see colors that go all the way from violet to red," Ramakrishnan said. "It turns out that marine algae – especially the bacteria these sensors come from – have evolved to see these and other colors as well."

Optogenetics is a fairly new discipline in which light-activated, genetically encoded photoreceptors are used to sense or control molecular biological processes like the expression of desired proteins. Because light is easy to direct and control, photoreceptors are simpler to use than tools that respond to chemical prompts.

Rice University graduate student Prabha Ramakrishnan led the project to turn a protein found in freshwater photosynthetic bacteria into a photoreversible regulatory tool that can make the manufacture of substances by engineered cells more efficient. Credit: Jeff Fitlow/Rice University

The Rice researchers turned the photosynthetic bacterial proteins into photoreversible, transcriptional regulators and installed them in Escherichia coli bacterial for lab testing. They reported exploiting them to program gene-expression signals "with high predictability."

The protein pathway known as UirS-UirR is the only optogenetic tool that responds exclusively to UV-violet light and gives biologists the ability to program circuits with light-activated proteins that won't interfere with each other, Tabor said. "Biological systems are regulated by numerous interacting genes, and multiple optogenetic tools that don't optically cross-react are needed to study these networks," he said.

The photoreversible pathway can be turned on by exposure to ultraviolet light and turned off by exposure to green light, or vice versa, depending on how the circuit is designed. Tabor expects they will be useful tools for scientists who design metabolic pathways for drug manufacture and biological sensors.

Rice University synthetic biologist Jeffrey Tabor and graduate student Prabha Ramakrishnan turned a protein used by freshwater photosynthetic bacteria to avoid damaging ultraviolet light into a photoreversible regulatory tool for synthetic biologists. Credit: Jeff Fitlow/Rice University

The new sensors offer speed and versatility in circuit design. "We found that light sensors developed by others take more than two hours to switch on or off, and respond to a broad range of wavelengths," Tabor said. "These aspects are not ideal for studying and controlling bacterial processes."

By contrast, the UV-violet sensor can be switched on or off in 10 minutes, Ramakrishnan said. "That's good because producing proteins or controlling a biological process can be expensive for cells. Producing something that's neither necessary for the cell nor to the product you're trying to synthesize is wasteful."

Because the UV-violet sensor responds to such a narrow wavelength of light – from 380 to 420 nanometers – there's no crosstalk with the red and green photoreversible tools already developed by the lab. "When these are put together in a single system, the fact that they don't interact with each other at all and turn on and off rapidly is going to be very useful," Ramakrishnan said.

This could allow for "just-in-time" manufacturing on the cellular level. "There's been theoretical work that shows that you can model the dynamics and get higher yields of your product by using this approach," she said. "You turn a process on only when you need it and turn it off once you're done.

"That's where we see a lot of industrial potential for this type of technology," she said, "especially for drug design or for producing any sort of plastic intermediate, for example, that requires several different enzymes to make it."

Ramakrishnan said she looks forward to seeing how other labs use the discovery. "Jeff understands the power of developing reliable tools," she said. "We try to give biologists and scientists well-engineered, well-characterized tools. We want other people to use this."

More information: Prabha Ramakrishnan et al. Repurposing PCC6803 UirS-UirR as a UV-violet/green photoreversible transcriptional regulatory tool in , *ACS Synthetic Biology* (2016). DOI: 10.1021/acssynbio.6b00068

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