

Researchers use light to switch on gene expression

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Imagine being able to control genetic expression by flipping a light switch. Researchers at North Carolina State University are using light-activated molecules to turn gene expression on and off. Their method enables greater precision when studying gene function, and could lead to targeted therapies for diseases like cancer.

Triplex-forming oligonucleotides (TFOs) are commonly used molecules that can prevent gene transcription by binding to double-stranded DNA. NC State chemist Dr. Alex Deiters wanted to find a way to more precisely control TFOs, and by extension, the transcription of certain genes. So Deiters attached a light-activated "cage" to a TFO. When exposed to ultraviolet (UV) light, the cage is removed, and the TFO is free to bind with DNA, inhibiting transcription of the gene of interest.

"In the absence of light, transcription activity is 100 percent," says Deiters. "When we turn on the light, we can take it down to about 25 percent, which is a significant reduction in [gene expression](#)."

Additionally, Deiters fine-tuned the process by attaching a caged inhibitor strand to the TFO. In the absence of [UV light](#), the TFO behaves normally, binding to DNA and preventing gene expression. However, when exposed to UV light, the caged inhibitor activates and stops the TFO from binding with DNA, turning [gene transcription](#) on.

"We've created a tool that allows for the light-activation of genetic transcription," Deiters says. "By giving researchers greater temporal and spatial control over gene expression, we've expanded their ability to study the behavior of particular genes in whichever environment they choose."

More information: "Regulation of Transcription through Light-Activation and Light-Deactivation of Triplex-Forming Oligonucleotides in Mammalian

Cells" Authors: Alexander Deiters, Jeane M. Govan, Rajendra Uprety, James Hemphill, North Carolina State University; Mark O. Lively, Wake Forest University School of Medicine, Published in *ACS Chemical Biology*.

Abstract

Triplex-forming oligonucleotides (TFOs) are efficient tools to regulate gene expression through the inhibition of transcription. Here, nucleobase-caging technology was applied to the first temporal regulation of transcription through light-activated TFOs. Through site-specific incorporation of caged thymidine nucleotides, the TFO: DNA triplex formation is blocked, rendering the TFO inactive. However, after a brief UV irradiation, the caging groups are removed, activating the TFO and leading to the inhibition of gene transcription. Furthermore, the synthesis and site-specific incorporation of caged deoxycytidine nucleotides within TFO inhibitor sequences was developed and allows for the light-deactivation of TFO function and thus photochemical activation of gene expression. After UV-induced removal of the caging groups, the TFO forms a DNA dumbbell structure, rendering it inactive, releasing it from the DNA, and activating transcription. These are the first examples of light-regulated TFOs and their application in the photochemical activation and deactivation of gene expression. In addition, hairpin loop structures were found to significantly increase the efficacy of phosphodiester DNA-based TFOs in tissue culture.

Provided by North Carolina State University

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