Controlling gene expression with hydrogen peroxide 'switches'

1 August 2012

(Phys.org) -- Hydrogen peroxide doesn't just come in bottles from the drugstore - the human body makes it as well. Now researchers from North Carolina State University have found a way to use naturally occurring hydrogen peroxide inside cells to switch on gene expression. Their method also serves as a highly sensitive hydrogen peroxide detector, which may help scientists determine the molecule's role in cellular health and disease.

In a normally functioning cell, hydrogen peroxide serves as a messenger, carrying signals through a cell in order to allow the cell to respond to external stimuli or events. Once the message is transmitted, the hydrogen peroxide diffuses and disappears.

"It's an ideal messenger compound, because it's small, fast, and doesn't linger," says chemist Alex Deiters. "It works by oxidizing, or modifying, certain amino acids in proteins, which affects the protein's function."

Deiters and graduate students Jeane Govan, Andrew McIver and Chad Riggsbee wanted to see if they could harness hydrogen peroxide's oxidizing property as a way to control gene expression, using the gene that gives fireflies their "glow," or luminescence, as a test case. They designed a molecule that was sensitive to hydrogen peroxide and enabled expression of the firefly luciferase gene in live mammalian cells. When hydrogen peroxide was present, the luciferase gene was expressed, causing the cell to glow.

The researchers' results appear online in *Angewandte Chemie*.

"The exciting aspects of this synthetic gene switch are that you can use it not only as a way to detect the presence of hydrogen peroxide within cells, in this case, by making cells containing hydrogen peroxide glow, but also to express any gene of interest in response to the presence of hydrogen peroxide," Deiters says. "In terms of detecting hydrogen peroxide, the system is at least an order of magnitude more sensitive than anything used previously."

More information: "Hydrogen Peroxide Induced Activation of Gene Expression in Mammalian Cells using Boronate Estrone Derivatives" Jeane M. Govan, Andrew L. McIver, Chad Riggsbee and Alexander Deiters, North Carolina State University, *Angewandte Chemie*, 2012. onlinelibrary.wiley.com/doi/10 … e.201203222/abstract

Abstract
Keeping the boron out of the ER: A genetic switch was engineered that activates gene expression in the presence of H2O2. The use of a boronate group on an estrone molecule allows for activation of gene expression through binding of the estrogen receptor only when the boron group is oxidized by H2O2. This sensor is highly sensitive and specific for H2O2.

Provided by North Carolina State University