News Release

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Scientists Find a Key to Cell Survival and Growth That May Help Explain Cancer

WINSTON-SALEM, N.C. – An enzyme that helps disease-causing bacteria withstand attacks by the body's natural defenses turns out to be a key to human cell survival and growth and may help explain why cancer cells can multiply unchecked.

Leslie B. Poole, Ph.D., of Wake Forest University Baptist Medical Center said the explanation begins with the way that bacteria -- such as one that causes food poisoning -- use the enzyme to combat hydrogen peroxide. Hydrogen peroxide, best known as hair bleach or as an antiseptic, is toxic to cells and is one weapon that the body's white blood cells release in an attempt to kill invaders.

Bacteria such as salmonella use the enzyme, called a peroxiredoxin, to inactivate the hydrogen peroxide coming from the white blood cells.

In the April 25th issue of *Science,* Poole, associate professor of biochemistry, and her colleagues at Oregon State University describe how the same group of peroxiredoxin enzymes work differently in people and other mammals. The enzyme becomes the biochemical switch that keeps the amount of hydrogen peroxide in the body low, but allows it to increase when it is used for signaling other cells to perform various functions or even to die.

The body's cells respond to their environment by generating signals to communicate between one another and between molecules inside the cells, Poole said.

"Hydrogen peroxide is an effective signaling molecule because it is rapidly produced, is reactive and is easily controlled by antioxidant enzymes," Poole said. The complex signaling pathways occur in mammals but not in bacteria.

What determines whether hydrogen peroxide acts as a dangerous oxidant or as a signal? The investigators propose that the peroxiredoxin enzyme controls the floodgates, keeping resting levels of hydrogen peroxide low, while permitting higher levels for signaling.

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After studying the enzyme using Oregon State's single crystal X-ray diffractometer, Poole and her colleagues found that related peroxiredoxins have unique structures that have different
shapes depending on whether they are used solely to prevent the flow of hydrogen peroxide or whether the hydrogen peroxide is also being used for signaling.

They propose that the enzyme ordinarily keeps the hydrogen peroxide in check, so that no signaling is produced. When the hydrogen peroxide is needed for signaling, an intracellular burst of hydrogen peroxide overwhelms the enzyme, switching it off and permitting the signal. When too much of the enzyme is present, the burst of hydrogen peroxide can't inactivate all of it, and the signal is blocked.

However, Poole said the bacterial peroxiredoxins -- like the ones in salmonella that she has studied -- "are resistant to this inactivation."

She explained, "Because the bacteria don't have the complex signaling pathways present in mammals, they don't need this ability to turn off the peroxiredoxin." So the enzyme is always available to eliminate hydrogen peroxide.

This discovery may shed light on human disease processes.

For example, Poole and her colleagues believe signaling may also be related to cancer. Ordinarily, abnormal cells in the body are programmed to die off, a process that scientists call apoptosis. In some cancer cells, apoptosis stops working, which means the cancer cells don't die off. The cancer cells may never get the signal to die because of the peroxiredoxin enzyme.

They found a correlation between this failure and too much peroxiredoxin, suggesting the two could be related.

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