Research explores role of hydrogen peroxide in cell health

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Hydrogen peroxide, the same mild acid that many people use to disinfectant their kitchens or treat cuts and abrasions, is also produced by the body to keep cells healthy. Now, researchers at Wake Forest University School of Medicine have solved how part of this complex process works.

Reporting in the January 3 issue of *Nature*, a team led by W. Todd Lowther, Ph.D., developed a three-dimensional snapshot of how two proteins produced by cells interact to regulate the levels of hydrogen peroxide.

For example, when the immune system is activated in response to bacteria, large amounts of hydrogen peroxide are produced by certain cells to fight the infection. Lowther and colleagues studied how a molecule known as peroxiredoxin (Prx) helps control levels of the agent. The role of Prx is important because if the levels of hydrogen peroxide become too high, the cell's DNA and other proteins can be damaged. Scientists suspect that this and similar processes are what leads to cancer, diabetes and other disease.

Prx actually has a dual role in the process. Its usual job is removing excess hydrogen peroxide from the cells by converting it to water. But if levels get dangerously high – and Prx needs help – it becomes inactive in its "converting" job and instead becomes a "signaler," telling the cell to produce or activate other proteins to help remove the excess.

“It basically acts as a sensor and warns the cell that levels are too high and that the cell needs to respond,” said Thomas J. Jönsson, Ph.D., lead author, and a post-doctoral fellow at Wake Forest. “Once that threat is gone, Prx needs to go back to its normal state.”

But how does Prx revert back to its usual job and become active again, so that it is available for a new wave of hydrogen peroxide? In 2003, scientists reported that a protein known as sulfiredoxin (Srx) was involved in the process. The goal of Lowther’s team was to use X-ray crystallography to learn exactly what happens.

“This technology gives us a three-dimensional snapshot of how the proteins interact,” said Lowther. “We wanted to know how Prx changes its structure to be repaired.”

The scientists knew that the repair of Prx would involve it binding with Srx. They also knew that the structure of Prx would need to change because the portion of the molecule that is repaired by Srx is initially hidden when it is in the inactive form.

“We found that the protein unfolded, flipped around and attached to the back side of Srx, known as an ‘embrace,’” said Lowther. “It basically put its arm around its buddy, which helps hold the repair protein in place.”

Jönsson said the binding of Srx causes a chemical reaction that repairs Prx. “The change in structure is dramatic and we found that it is critical for the repair to take place,” he said.

The scientists said that understanding this protective mechanism that keeps cells healthy may one day help reveal how the process goes awry in disease. They will continue the research by studying how the structural change may affect how Prx interacts with other proteins.

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Source: Wake Forest University