Anti-aging pathway enhances cell stress response

February 19 2009

People everywhere are feeling the stress of a worldwide recession. Our cells, too, are under continual assault from stress.

Hidden from sight, our cells battle challenges such as their environment, bacteria, viruses, too much or too little oxygen, and physiological stressors. Molecular systems protect cells under assault, but those systems can break down, especially with age.

To better understand how cells are protected from stress and damage, a team led by Northwestern University researchers studied the effect of resveratrol, a beneficial chemical found in red wine, on human cells in tissue culture.

The findings may help explain what happens in neurodegenerative diseases, which are age-related, when cell protection fails, proteins misfold, lots of damage accumulates and the system falls apart.

The researchers discovered a new molecular relationship critical to keeping cells healthy across a long span of time: a protein called SIRT1, important for caloric restriction and lifespan and activated by resveratrol, regulates heat shock factor 1 (HSF1), keeping it active. HSF1 in turn senses the presence of damaged proteins in the cell and elevates the expression of molecular chaperones to keep a cell's proteins in a folded, functional state. Regulation of this pathway has a direct beneficial effect to cells, the research shows.

This role of SIRT1 -- a protein already of great interest to pharmaceutical companies -- was not previously known. The results will be published in the Feb. 20 issue of the journal *Science*.

"When SIRT1 levels are high, you are in a high-protection mode," said Richard I. Morimoto, Bill and Gayle Cook Professor of Biochemistry, Molecular Biology and Cell Biology in Northwestern's Weinberg College of Arts and Sciences. He led the research team.

"Ironically, triggering the stress response and perhaps maintaining the cell in a protective state over a long period of time can keep cells healthy," said Morimoto. "The cell is protected against an accumulation of damage when HSF1 is more active."

SIRT1 levels decrease as humans age, Morimoto explains. Cells can't respond to stress as well. This decrease in SIRT1 may help explain why protein misfolding diseases, such as Alzheimer's, Parkinson's, Huntington's and adult-onset diabetes, are diseases of aging.

"We now have a powerful way to think about addressing neurodegenerative diseases," said Morimoto. "We have identified a pathway that can be manipulated to alter lifespan. Discovering this new basis for therapeutics is very exciting."

Source: Northwestern University