

A novel disease-preventing antioxidant pathway

May 27 2014

Interested in antioxidants? They protect us against aging and cancer. It's one of the reasons we like our green tea and even our broccoli. But there is a new kid on the antioxidant block - uric acid. But wait, you're thinking, doesn't uric acid cause gout? A team in Singapore has recently showed that uric acid is a major intracellular antioxidant, possibly even more important than the antioxidants we try to eat. They also discovered how uric acid helps to prevent aging and disease and how it helps in the treatment of cancer.

Traditionally, <u>uric acid</u> has a bad reputation because high levels of the compound are associated with gout and other medical conditions. However, uric acid also has antioxidant properties. Since only humans and higher primates maintain high blood levels of uric acid near saturated levels, uric acid has been speculated to be one reason humans live so much longer than, for example, dogs and cats.

This recently released study, led by Assistant Professor Koji Itahana of Duke-NUS Graduate Medical School Singapore, has also discovered how uric acid gets into cells to protect them in the event of stress. It goes through a transporter GLUT9 and is regulated by the protein p53, one of the most important tumor suppressors that mutated in about a half of cancers worldwide.

The team from the Cancer and Stem Cell Biology Program at Duke-NUS showed first evidence of how the p53-GLUT9 pathway is a mechanism that prevents the accumulation of Reactive oxygen species



(ROS). ROS are molecules containing highly reactive oxygen and at times of environmental stress can increase dramatically, and result in cell damage known as <u>oxidative stress</u>. Oxidative stress has been proven to cause aging, cancer, cardiovascular and neurodegenerative diseases.

Understanding this antioxidant pathway will enable researchers and clinicians to better understand how to prevent aging and other such diseases. Interestingly, Dr. Itahana also showed that shutting down the GLUT9 antioxidant pathway in cancer may be an unorthodox way to target cancer once the patient already has the disease.

"While the p53-GLUT9 mechanism is a way that helps prevent disease in a healthy body, once the body already has cancer, disrupting that same mechanism may be a way to kill the cancer since cancer has already very high levels of ROS. For instance if a patient were to take probenecid, a gout drug that inhibits the function of GLUT9 and a chemo drug, ROS levels would become so high that <u>cancer</u> cells may not be able to survive in the body because there is simply no space," explained Dr. Itahana.

The study is published on May 26, 2014 in the journal Oncogene.

Provided by Duke University

Citation: A novel disease-preventing antioxidant pathway (2014, May 27) retrieved 19 November 2023 from https://medicalxpress.com/news/2014-05-disease-preventing-antioxidant-pathway.html

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