Reactive oxygen in fruit flies acts as a cell signalling mechanism for immune response

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(PhysOrg.com) -- For years, health conscious people have been taking antioxidants to reduce the levels of reactive oxygen in their blood and prevent the DNA damage done by free radicals, which are the result of oxidative stress. But could excessive use of antioxidants deplete our immune systems?

Research at UCLA's Jonsson Comprehensive Cancer Center has raised that question.

It has been known for decades that reactive oxygen species (ROS) - ions or very small molecules that include free radicals - damage cells. But much to their surprise, Jonsson Cancer Center researchers found that in *Drosophila*, the common fruit fly, moderately elevated levels of ROS are a good thing.

These small molecules act as an internal communicator, signaling certain blood precursor cells, or blood stem cells, to differentiate into immune-bolstering cells in reaction to a threat. After the progenitor cells differentiate, the ROS levels return to normal, ensuring the safety and survival of the mature blood cells, said Utpal Banerjee, a Jonsson Cancer Center researcher and senior author of the study.

The study is published in the Sept. 24, 2009 issue of the peer-reviewed journal *Nature*.

The new finding was launched when Banerjee and his team set out to

discover why fruit flies had naturally occurring, slightly elevated levels of ROS in their blood cell precursors, which is atypical of most other precursor cells.

"Reducing levels of reactive oxygen is usually the goal, and what we found was surprising," said Banerjee, professor and chairman of the molecular, cell, and developmental biology department at UCLA. "Most stem cells don't want to be damaged, so they have very low ROS levels. We wanted to know why this was different in the cells that we were investigating."

Banerjee discovered that when ROS was taken away in the blood stem cells, they failed to differentiate into the immune-bolstering cells, called macrophages. On the other hand, when levels of ROS were further increased by genetic means, the blood stem cells "differentiated like gang busters," Banerjee said, making a large number of macrophages.

But how did this happen? The ROS, Banerjee said, acted as a signaling mechanism that kept the blood stem cells in a certain state - when levels rose, it was a message to the cell to differentiate.

The implications from the finding are several fold, Banerjee said. The blood stem cells are stress sensing cells, their function is to sense conditions that increase oxidative stress and react with an immune response. Keeping their ROS levels slightly elevated puts the cells on alert, sensitized and ready to respond to any threat quickly.

That sparked a question: If fruit fly blood stem cells and mammalian blood stem cells operate in the same way, is it a good thing for people to be taking antioxidants? Are antioxidants dulling the immune system and its ability to react to threats?

"On the one hand, it's good to have antioxidants to reduce the amount of

reactive oxygen in our body that causes DNA damage," Banerjee said. "But if we find that those blood stem cells aren't primed to respond because the ROS levels are reduced, that would not be a good thing. Our findings raise the possibility that wanton overdose of antioxidant products may in fact inhibit formation of cells participating in innate immune response."

It is known that certain types of mammalian blood stem cells, called common myeloid progenitors, do have elevated levels of ROS, but it isn't known whether those levels operate as messengers for differentiation. Studies of mammalian systems are needed to determine why ROS levels are elevated and what, if any, function that serves in the cell. It is interesting, however, that these types of blood progenitors in mammals also give rise to macrophages, Banerjee said.

"What we found is that the fruit fly keeps its own ROS levels in the blood stem cells slightly high for its own benefit," Banerjee said. "We do not have any direct evidence that this is true in humans, but our results suggest that further studies are needed to investigate a possible signaling role for ROS in the differentiation of precursor cells in mammalian myeloid cell development and oxidative stress response."

Source: University of California - Los Angeles