Not just bleach: Hydrogen peroxide may tell time for living cells

November 3 2009

If a circadian rhythm is like an orchestra - the united expression of the rhythms of millions of cells - a common chemical may serve as the conductor, or at least as the baton.

The chemical is hydrogen peroxide (H_2O_2), the active ingredient in color safe bleach. Produced in all animal cells, hydrogen peroxide may act as a signal for the active and resting phases of living things, new research by USC biologists suggests.

A study published in the journal *PLoS ONE* shows that hydrogen peroxide given to fruit flies has dramatic effects on their daily rhythms and activity levels.

"H_2O_2 might be functioning as a systemic signal by which rhythms are regulated within cells and between cells," said lead author John Tower, associate professor in molecular and computational biology at the USC College of Letters, Arts and Sciences.

Most people are familiar with the concept of a circadian rhythm that governs sleeping and waking. But that is not the only circadian rhythm in the body.

Many organs and tissues within the body have their own independent circadian rhythms, and they also interact to coordinate their rhythms.

Tower's study suggests a link between metabolism - the production of

energy by mitochondria, often described as the energy factories inside cells - and an animal's daily rhythms.

Mitochondria produce hydrogen peroxide as a by-product of oxygen combustion, making the chemical a candidate signal molecule.

"This is a logical way to connect rhythms to metabolism," Tower said.

"We know a lot about how circadian rhythms are regulated within certain cells. However, we have very little information on what signals coordinate circadian rhythms and how these rhythms are linked between metabolism and behavior."

For the rhythms of even two cells to agree, some sort of signal has to pass between them.

Tower's research group set out to find the signal by probing the action of an enzyme in mitochondria that converts toxic by-products of the body's combustion process into hydrogen peroxide, itself a harmful but less toxic substance which other defenses later break down further.

Tower and his team had noticed that overexpression of the enzyme, known as superoxide dismutase (SOD), boosted the activity level of fruit flies and even increased the life span of certain genetically engineered strains.

Tower suspected that hydrogen peroxide was the key ingredient in SOD's action.

"Hydrogen peroxide is a great candidate for a signaling molecule that would be involved in rhythms and behaviors. It's the most stable and diffusible of the reactive oxygen species (by-products of combustion), but no one had demonstrated a role for it."

As a test, Tower's group administered hydrogen peroxide directly to fruit flies through feeding and injection.

The researchers observed similar effects from the direct administration of hydrogen peroxide and the over-expression of the SOD enzyme.

Both strategies increased the activity levels of adult flies. Long-term direct treatment with hydrogen peroxide suppressed daily rhythms, while SOD over-expression altered those rhythms.

Tower explained that he had not expected identical results from direct treatment versus genetic over-expression.

"I think it's just a little too crude of an intervention, to feed them or inject them with the drug," he said, because those effects will not be rhythmic, whereas production of hydrogen peroxide by the mitochondria and by SOD is expected to be rhythmic and to correspond to the rhythm of metabolism.

Still, the similarities in the flies' reactions to direct treatment and to SOD over-expression suggested to the researchers that hydrogen peroxide is the crucial chemical.

"It's a very exciting result for us that our data now start to point to hydrogen peroxide as perhaps being a relevant signaling molecule for coupling metabolism to behaviors and rhythms in the animal," Tower said.

Hydrogen peroxide would govern rhythms inside each cell as well as between cells, Tower added.

Every cell alternates between a metabolic phase - in which it burns oxygen to make energy - and a detoxification phase in which the cell

breaks down the harmful by-products of combustion.

Those rhythms must be coupled with the energy-producing activity of the mitochondria.

"Because hydrogen peroxide is produced by mitochondria as a product of metabolism, it's a great candidate for a relevant signal that might be modulating these cellular rhythms," Tower said.

Source: University of Southern California (news : web)