Stem-cell sentry sounds the alarm to maintain balance between cancer and aging

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(PhysOrg.com) -- Like a sentry guarding the castle walls, a molecular messenger inside adult stem cells sounds the alarm when it senses hazards that could allow the invasion of an insidious enemy: Cancer. The alarm bell halts the process of cell division in its tracks, preventing an error that could lead to runaway cell division and eventually, tumor formation.

"Our work suggests that to be able to prevent abnormal cell proliferation, which could lead to cancer, stem cells developed this self-checking system, what we're calling a checkpoint," said Yukiko Yamashita of the University of Michigan's Life Sciences Institute.

"And if it looks like the cell is going to divide in the wrong way, the checkpoint senses there's a problem and sends the signal: 'Don't divide! Don't divide!'" said Yamashita, a research assistant professor of life sciences and an assistant professor of cell and developmental biology at the U-M Medical School.

If everything looks OK, the checkpoint allows adult stem-cell division to proceed, providing new cells to replace damaged and worn-out tissues.

Yamashita and her colleagues have not yet identified the molecules that form the checkpoint mechanism. But they've seen it at work in adult stem cells of the fruit-fly testes, so-called germ-line stem cells.

"Aging is too few divisions and cancer is too many divisions, and people

have long speculated that some process controls the balance between them," Yamashita said. "We may have found the mechanism that maintains the delicate balance between over-proliferation---which can lead to cancer---and aging."

The team's findings will be published Oct. 15 in the online version of the journal *Nature*.

If humans possess a similar checkpoint system and if researchers could someday harness it, they could fine-tune the rate of cellular division to control tumor development as well as tissue aging. But Yamashita stressed that no mammal studies of the checkpoint have been undertaken, so talk of potential human applications is highly speculative.

In fruit flies, the checkpoint monitors germ-line stem cells as they're about to divide. It can sense problems that would derail the division process, which is called mitosis.

Under normal conditions, adult stem-cell division creates one new stem cell and one cell committed to develop into a specific tissue type – such as a skin cell, a blood cell or, in this case, a sperm cell. That form of mitosis is called asymmetric division, and it's exactly what stem cells need to maintain a healthy balance between uncommitted and committed cells.

Cell division is controlled in part by the location of a pair of cellular components called centrosomes. They provide the framework that helps direct how chromosomes are distributed between daughter cells during mitosis.

Normally, centrosomes in a dividing stem cell remain perpendicular to an adjoining messenger cell called the hub. Yamashita and her colleagues found that improper orientation of the centrosomes disrupts

the mitotic machinery, steering it on a course toward stem-cell over-proliferation and cancer.

The checkpoint mechanism senses when centrosomes are misaligned, then sounds the alarm that stops cell division.

By preventing faulty cell division, the checkpoint helps ward off cancer. But a balance must be struck: If the checkpoint mechanism slows cell division to a trickle, the resulting shortage of new cells will accelerate tissue aging.

"It's a double-edged sword, and both outcomes are bad," she said. "One path leads to cancer and the other leads to aging. And we haven't found a way to avoid aging without getting cancer."

Provided by University of Michigan

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