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DNA repair gene provides new ideas for disease treatment

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A gene known to repair DNA damage in healthy cells may also provide new insights about treating a genetic disorder of the bone marrow, Caltech researchers say.

This finding was published in the May 15 print edition of the journal *Cell Cycle*.

In the study led by Judith Campbell, professor of chemistry and biology at Caltech, the researchers investigated the relationship between two genes—FANCD2 and DNA2—both known to play roles in fixing broken or damaged strands of DNA within a cell, called DNA repair. A defective version of the FANCD2 gene can result in the genetic disease Fanconi anemia (FA), which is characterized by failure of the bone marrow (an inability to replenish the body's supply of blood cells) and a predisposition to certain developmental disorders and cancers. Although DNA2 has not been associated with an FA family as yet, genetic studies implicate DNA2 in the FA DNA repair pathway.

To determine the relationship between the genes, the researchers applied formaldehyde and other DNA-damaging substances to three types of cells: those lacking FANCD2, those lacking DNA2, and cells lacking both FANCD2 and DNA2. The groups of cells in which only one of the two genes had been deleted quickly succumbed to the formaldehyde-induced DNA damage; however, the cells lacking both FANCD2 and DNA2 were able to repair the DNA damage and survive.

"A key implication of this finding is the potential to manipulate DNA2 to improve the survival of FANCD2-deficient cells, and hopefully, by extension, the survival of FA patients," says Kenneth Karanja, a former postdoctoral scholar in Campbell's laboratory and first author on the study. Currently, the only treatment for FA is a bone marrow transplant, but even after the transplant the disease remains lethal.

"DNA2 is a well-studied gene, and this recent discovery could potentially become the basis for ameliorating the symptoms of this incurable disorder," Campbell says. Furthermore, she says, the protein DNA2 encodes is a nuclease—which is a specific type of enzyme that has become a promising drug target.

"Since much is known about the mechanism of action of DNA2, it is an attractive target for future drug treatments—like small-molecule inhibitors that could reduce an FA patient's cancer predisposition—as well as a possible gene therapy for aiding a patient's blood cell development," she says.

More information: "Preventing over-resection by DNA2 helicase/nuclease suppresses repair defects in Fanconi anemia cells," www.landesbioscience.com/journ … ls/cc/article/28476/

Provided by Landes Bioscience